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P0001 MEDICAL EVALUATION ON SUSPICION OF NON-ALCOHOLIC STEATO-HEPATITIS (NASH): REAL-WORLD OUTCOME FROM A COMMUNITY NASH CLINIC

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Introduction: Non-alcoholic steatohepatitis (NASH) with fibrosis is the phenotype of non-alcoholic fatty liver disease (NAFLD) that carries the highest risk of developing end-stage liver disease and the associated serious complications including cardiovascular disease. In line with recent international and national Danish guidelines for the management of NAFLD patients, we established a community NASH clinic including a multi-disciplinary-team. We here report our initial experience and real-world outcome for medical evaluation of referred patients on suspicion of NASH.
Aims and Methods: During 2017, patients from Bispebjerg Hospital clinics with a suspicion of NASH were referred to the NASH clinic. Suspicion of NASH was based on having at least 2 of the following risk factors: BMI≥25 kg/m^2, diabetes, or persistent ALT > 50 U/l. Based on a general work-up algorithm and an individualized approach, routine and NAFLD specific examinations were performed to exclude other causes of chronic liver disease (CLD). To diagnose and assess NAFLD disease grade and fibrosis stage, structured interview including thorough medical history, anthropometric measurements, NAFLD (hepatic, metabolic and fibrosis) blood tests (no genetics), ultrasound, US-elastography and US-guided liver biopsy was offered as appropriate. NASH diagnosis and fibrosis stage was based on histopathology. NAFLD activity, NAFLD fibrosis and FIB-4 index scores were calculated. Numbers of patients, percentages of total (%), medians (upper range-lower range) and means ± standard deviation are reported, as appropriate.
Results: 55 adult patients were referred to the NASH clinic on suspicion of NASH. 12 patients (22%) were found to have non-NAFLD CLD (including alcoholic hepatitis, hepatitis B, hepatitis C and autoimmune hepatitis). 30 of the remaining 43 patients accepted further specific medical work-up on suspicion of NASH: mean age was 56 ± 13 years, 16/30 (53%) were female and 24/30 (80%) were white Caucasians. Comorbidity included 8/30 (27%) with hypertension, 10/30 (33%) with diabetes, 23/27 (85%) with dyslipidemia and 23/27 (85%) with overweight (mean BMI = 32 ± 5 kg/m^2). 11/30 (37%) of patients refused undergoing liver biopsy. In the remaining 19/30 (63%) patients a liver biopsy was performed: histopathology revealed simple steatosis (NAFL) in 5/19 (26%), NASH with no or mild fibrosis stage (F0-F1) in 6/19 (32%), NASH with moderate to severe fibrosis (stage F2-3) in 7/19 (37%) and NASH with cirrhosis (stage F4) in the remaining 1/19 (5%). NAFLD median activity score was 5 (3–8) in F0-F1 vs. 6 (3–7) in F2-3 NASH patients; NAFLD mean fibrosis score was −2.2 ± 0.4 in F0-F1 vs. −0.9 ± 2 in F2-3 NASH patients; and FIB-4 mean index was 1 ± 0.6 in F0-F1 vs. 2.5 ± 3 in F2-3 NASH patients. No complications were reported following liver biopsy.
Conclusion: In our NASH clinic, about a quarter of the referred patients were diagnosed with NASH, about a quarter were diagnosed with non-NAFLD and about a quarter with un-resolved potential CLD. One-half of the diagnosed NASH patients had different stages of fibrosis and will as such require further close monitoring and management via our local community NASH outpatient clinic. Finally, the applied non-invasive fibrosis blood based score systems correlated well to histopathological findings and appear useful in clinical practice.
Disclosure: Nothing to disclose

P0002 A METHOD FOR DETERMINING LIVER FIBROSIS USING A ^{13}C-METHACETIN BREATH TEST

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Introduction: The aim of this study was to assess the clinical and diagnostic capabilities of the ^{13}C-methacetin breath test (^{13}C-MBT) in patients with chronic liver disease.
Aims and Methods: Using the ^{13}C-MBT, we examined 101 patients with various chronic liver disease (CLD). The study involved 55 men, 46 women aged 21 to 77 years, the median age was 47 years. In all patients, the degree of hepatic fibrosis was also determined by various clinical and laboratory methods such as puncture biopsy, fibrotests and elastometry. All patients were divided into groups according to the degree of fibrosis, and, subsequently, by the degree of functional reserve reduction: group F0 = 26 people, F1 = 23 people, F2 = 23 people, F3 = 12 people, F4 = 17 people.
Results: In our study, it was found that the differences in the ^{13}C-MBT data were in all the study groups. But statistically significant were differences in group 1 and 3, 1 and 4, 2 and 3, 2 and 4, 3 and 4 ($p < 0.05$ by chi-square, chi-square criteria with Yates correction for small groups).
Further, using the method of logical trees, threshold values of the cumulative dose were singled out in the first 30 minutes of the test. If CUM10 < 1%, the OR fibrosis 1-2 stage = 2.5, if CUM20 < 2.5, the OR severe fibrosis increases = 6.89, if CUM30 < 5.65, the OR of cirrhosis = 23.3, by based on these data, a formula was developed to evaluate liver fibrosis.
Conclusion: The results of the method of assessing fibrosis with ^{13}C-MBT in the determination of the degree of liver fibrosis, corresponded to the values of the liver biopsy, fibrotests, elastometry. N = 1a + 2b + 10c, where is the N- sum of scores, a is the coefficient calculated from the cumulative dose of ^{13}C for 10 min-1 in% (CUM10), b - the coefficient calculated from the cumulative dose of ^{13}C for 20 minutes in% (CUM20), c is the coefficient calculated from the cumulative dose of ^{13}C for 30 minutes in (CUM30), if CUM10 < 1%, then a = 1, if CUM10 > 1.00%, then a = 0 if CUM20 < 2.50%, then b = 1, and if CUM20 > 2.50%, then b = 0, if CUM30 < 5.65%, then c = 1, if CUM30 > 5.65%, then c = 0, and for N = 0, determine the degree of fibrosis of the liver as F0, that is, corresponding to the absence portal fibrosis, at a value of N = 1–3, the degree of liver fibrosis as F1-2, corresponding to the presence of portal fibrosis without septa and with a small number of septums, with a value of N = 10–13, determines the degree of fibrosis of the liver F3-4 corresponding to the presence of numerous septa without cirrhosis and cirrhosis. The invention is based on the first time we established constant relationship between the cumulative dose reduction indices ^{13}C at the 10th, 20th and 30th minute ^{13}C- metatsetinovogo performing the breath test and the risk of the presence of liver fibrosis in patients with CLD.
Disclosure: Nothing to disclose

P0003 INSULIN-LIKE GROWTH FACTOR1 AS A MARKER OF SEVERITY OF LIVER CIRRHOSIS

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Introduction: Liver cirrhosis is a leading cause of morbidity and mortality. Insulin-like growth factor 1 (IGF-1) is a soluble protein mainly produced by the liver secondary to the growth hormone stimulation on hepatocytes. IGF-1 plays an essential role in growth, development, and overall cellular regulation in the human body in health as well as in the pathophysiology of various diseases.
Aims and Methods: The aim of the work is to study the relationship between insulin like growth factor 1 and the severity of liver cirrhosis.
Methods: The study included 69 patients with liver cirrhosis of various etiologies from Menoufia University Hospitals (Egypt) and 18 healthy volunteers as a control group. They underwent physical examination and laboratory investigations (CBC, liver profile {ALT, AST, serum albumin, bilirubin, PT %}, urea, creatinine, fasting glucose, postprandial glucose and serum IGF-1). Abdominal ultrasonography was done for all patients. Child-Pugh Score, MELD score and AST/Platelet ratio index (APRI score) were calculated for all patients.
Results: IGF-1 of cirrhotic patients (73.1 ± 42.3 ng/ml) was significantly lower than controls (243.2 ± 78.1 ng/ml) ($p = 0.0001$). IGF-1 was significantly lower in Child class C (46.11 ± 6.66 ng/ml) than Child class B (64.8 ± 4.4 ng/ml) and A (149.1 ± 43.8 ng/ml) ($p = 0.002$ and 0.0001 respectively). Also IGF-1 was significantly lower in Child class B than class A ($p = 0.0001$). IGF-1 was significantly lower in patients with MELD score < 20 (45.62 ± 6.72 ng/ml) than MELD score 10–19 (61.28 ± 13.85 ng/ml) and MELD score >10 (152.1 ± 44.30 ng/ml) ($p = 0.0001$). IGF-1 was significantly lower in patients with APRI < 1.5

(46.62 ± 7.103 ng/ml) than APRI 1–1.5 (68.52 ± 13.99 ng/ml) and APRI >0.5 (155 ± 45.24 ng/ml) (p = 0.0001).
In cirrhotic patients group, there were an inverse correlation between IGF-1 and APRI score (r = −0.49), MELD score (r = −0.78), Child score (r = −0.77) and bilirubin (r = −0.54) (p = 0.0001 for all). There were a strong direct correlation between IGF-1 and albumin (r = 0.71), PT% (r = 0.79) and platelet count (r = 0.58 (p = 0.0001 for all).
Conclusion: IGF-1 can be used as an index for evaluating the severity of cirrhosis as it is correlated with variables of hepatic dysfunctions like serum bilirubin, albumin and PT% and indices of hepatic dysfunctions and fibrosis like Child-Pugh score, MELD score and APRI score. Therefore, serial measurements of IGF-1 in cirrhotic patient can predict patients with decline of liver synthetic capacity.
Disclosure: Nothing to disclose

P0004 METABOLOMICS IDENTIFIES ADVANCED FIBROSIS IN CHRONIC HCV INFECTION

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Introduction: Chronic HCV infection (cHCV) is a leading cause of liver disease and transplantation worldwide and a major burden on public health.
Thus, early diagnosis and classification of the degree of liver fibrosis is crucial in clinical practice to determine the urgency and need for anti-HCV antiviral therapy.
Aims and Methods: To assess the metabolites that are associated with fibrosis stages in chronic HCV infection, using metabolomic method.
A total of 40 patients were included in the study, 30 diagnosed with cHCV infection and 10 controls. Fibrosis were assessed using Fibromax elaborated by Biopredictive (R) (Paris, France). The metabolomic techniques (high performance liquid chromatography coupled with mass spectrometry (LC-MS) and principal component analysis (PCA) was performed from serum and urine samples of each patient, to identify final products of various metabolic pathways correlated with liver fibrosis.
Results: Of the 30 patients with cHCV included in the study, 20 patients (66.6 %) had advanced fibrosis (F3-4). The metabolomic profile identified 5 metabolites (3 of serum and 2 of urine) that are associated severe fibrosis (F3-4):hexacosanoyl carnitine > 26416 (AUC 0. 717; Se 61%, Sp 80%; p = 0.03); aspartylaspartic acid > 228956 (AUC 0. 700; Se 70.00%, Sp 70.00%; p = 0.05); prostaglandin E2 (PGE2) > 4265917 (AUC 0. 695; Se 65.00%, Sp 70.00%; p = 0.04) and hippuric acid (u) >70056 (AUC 0.766; Se 63.16%, Sp 100%; p = 0.003), taurine (u) < 50172(AUC 0.772; Se 78.95%, Sp 77.78%; p = 0.008).
The combined use of the metabolites determined an AUC of 0.863, with Se 82.35 and Sp 88.89, p < 0.001.
Conclusion: The study emphasizes the significance of metabolomics profiling as a promising technology for the non-invasive assesment of HCV-related liver fibrosis.
Disclosure: This work was supported by a grant of the Romanian Ministery of Research and Innovation, CCCDI-UEFISCDI, project number PN-III-P1-1.2-PCCDI-2017-0221/59PCCDI/2018 (IMPROVE), within PNCDI III.
Conflict of interest: none

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P0005 THE INFLUENCE OF HYPERGASTRINEMIA ON MOTILITY AND LIVER HISTOLOGICAL PECULIARITIES

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Introduction: The influence of hypergastrinemia on the motility and liver function is not well studied. The hypoacidity of gastric juice can occur in the case of prolonged use of proton pump inhibitors, atrophic gastritis, autoimmune processes etc. It leads to hypergastrinemia, decrease of pepsin activation, dysbiosis, motility violation.
Aims and Methods: The aim of our work was to study histological liver peculiarities due to the influence of hypergastrinemia, to estimate the severity of inflammation and to study the role of multiprobiotic in these conditions. We included 40 rats that were randomly divided into 4 groups with 10 rats in each. Group 1 (control) received intraperitoneanly 0.2 ml and per os 0.5 ml of water once per day during 28 days. Group 2 received 0.14 ml/kg multiprobiotic once per day during 28 days, Group 3 received 14 mg/kg omeprazole once per day during 28 days (model of prolonged hypochlorhydria). Group 4 received 0.14 ml/kg multiprobiotic + omeprazole in dose 14 mg/kg during 28 days. Of all of them the histological peculiarities of liver were studied, we measured the levels of IL-1, IL-4, IL-6, TNF-alpha. The expression of genes Nos2, Tgfb1, ChgA, Reg1a, Hgf was measured with semi-quantitative reverse transcription polymerase chain reaction with densitometry.
Results: A long-term suppression of gastric acid secretion leads to the violation of motility, hypergastrinemia, that increases dysbiosis. The inflammation was absent in the group that received multiprobiotic. In the group with marked hypochlorhydria IL-1 was increased in 4.7 times (p < 0.01), IL-6 was increased in 8.1 times (p < 0.01), during the histological examination leukocytes infiltration and edema were observed. The administration of multiprobiotic led to the increase of IL-4 and IL-10 in 2.1 and 2.7 times correspondingly. It was established the increase of relative gene nitric oxide synthase 2 (NOS2) expression in the liver and pancreas. In the liver was increased the expression of transforming growth factor beta 1 (TGFb1), chromogranin A (CHGA) and regenerating islet-derived protein 1 alpha (Reg1a). The expression of hepatocyte growth factor (Hgf) was absent that indicates on violations of molecular mechanisms of the regulation of antifibrotic processes.
Conclusion: The results of performed investigations clearly indicate the development of inflammation which is associated with the progression of oxidative stress in liver upon these experimental conditions. As the result of these disturbances, the damage of functional status and further possible formations of fibrosis in liver can occur. The leading role of pathogenic microbiota in violation of structural and functional state of liver upon long-term suppression of gastric acid secretion were established.
Disclosure: Nothing to disclose

P0006 AMNION-DERIVED MESENCHYMAL STEM CELLS AMELIORATES SCLEROSING CHOLANGITIS IN RATS

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Introduction: Cell therapy with mesenchymal stem cells (MSCs) is expected as a new therapeutic strategy, and large numbers of MSCs can be isolated from the amnion noninvasively. Sclerosing cholangitis is a chronic cholestatic disease, characterized by inflammation, obliterative fibrosis of bile ducts, stricture formation and progressive biliary destruction leading to cirrhosis. Many factors are involved in the development of sclerosing cholangitis; however, the effective medical therapy for sclerosing cholangitis has not been established. Therefore, a new strategy to delay or prevent disease progression of sclerosing cholangitis is urgently required.
Aims and Methods: We investigated the effects of human amnion-derived MSCs (hAMSCs) and conditioned medium (CM) obtained from hAMSC cultures in rats with sclerosing cholangitis. Sclerosing cholangitis was induced by the intragastric administration of 100 mg/kg alpha-naphthylisothiocyanate (ANIT) twice weekly for 4 weeks. ANIT is a toxin that targets intrahepatic bile ducts, and it is used to generate animal models of sclerosing cholangitis. hAMSCs were cultured in dishes until reaching a subconfluent state. After washing, cells were further cultured with serum-free medium for 48 hours and consequently, CM was collected. One million hAMSCs suspended in 200 μL of phosphate-buffered saline or 200 μL of CM were intravenously injected through the penile vein on days 15 and 22. All rats were sacrificed on day 29. In each animal, the left lobes of the liver were evaluated via histological, immunohistochemical, and mRNA expression analyses.
Results: Biliary hyperplasia, peribiliary fibrosis, and inflammation in Glisson's sheath were induced by ANIT. Histological scoring demonstrated that hAMSC transplantation and CM administration significantly suppressed biliary hyperplasia. The number of necrotic lesions was significantly decreased by hAMSC transplantation. In addition, immunohistochemical examination demonstrated that hAMSC transplantation and CM administration significantly improved

biliary hyperplasia, peribiliary fibrosis, and inflammation in Glisson's sheath. Accordingly, mRNA expression of CK19, MMP-9, TNF-α, and MCP-1 in the liver was also significantly decreased by hAMSC transplantation and CM administration.
Conclusion: hAMSC transplantation and CM administration ameliorated biliary hyperplasia, peribiliary fibrosis, and inflammation in Glisson's sheath in a rat model of sclerosing cholangitis. hAMSCs and CM may represent new modalities for treating sclerosing cholangitis.
Disclosure: Nothing to disclose

P0007 BODY MASS INDEX (BMI) AND ALCOHOL CONSUME ARE DIRECTLY RELATED WITH LIVER STEATOSIS. RESULTS FROM A PROSPECTIVE MULTICENTER STUDY OF PATIENTS REFERRED FOR HYPERFERRITINEMIA

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Introduction: Liver steatosis is often suspected in patients with hyperferritinemia.
Aims and Methods: To study the BMI and alcohol consumption of patients referred for HF to 6 hospitals in the Basque country, Spain. To study the prevalence of hepatic steatosis determined by MRI in these patients.
A prospective study of 312 consecutive with HF (>200μg/L women; 300 μg/L men) was conducted from December 2010 to April 2013. The presence of liver steatosis was determined by MRI 1.5 Tesla system. We systematically performed T1-weighted in-phase and opposed-phase imaging to determine the presence or not of liver steatosis. BMI and alcohol consumption were determined in all the patients in the study.
Results: 312 patients (272 men/ 40 women) were included. Mean age 55 (SD 13.5); Mean ferritin 729.6 (SD 449.6), mean TSI 40.8 (SD 15.8); In 286 patients a MR study for the presence of liver steatosis was performed: 196 no steatosis; 90 liver steatosis (31.47%). When we study if BMI and liver steatosis were directly related, liver steatosis was more frequent in the BMI > 30 group; BMI < 25-11/52(21.15); BMI25-30: 23/105(21.90%); BMI>30-45: 56/129(43.41%)/286; the results obtained were statistically significant ($p = 0.000$). Relationship with alcohol comsumption was also evaluated. Alcohol consumption was directly related with the presence of liver steatosis: 43/196 patients (21.94%) -no alcohol-mild consume-; 32/90 (35.56%) moderate/ heavy drinker. The results were statistically significant ($p = 0.015$).
Conclusion: BMI and alcohol consume are directly related with the presence of liver steatosis in patients referred for hyperferritinemia in our country.
Disclosure: Nothing to disclose

P0008 DYSMETABOLIC IRON OVERLOAD SYNDROME AND ITS RELATIONSHIP WITH HFE GENE MUTATIONS AND WITH LIVER STEATOSIS

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Introduction: The dysmetabolic syndrome with iron overload (DIOS) is characterized by producing hyperferritinemia (HF) with slight elevation of the hepatic iron concentration, together with one or more diagnostic factors of metabolic syndrome (MtS): obesity, hypertension, dyslipidemia, and/or abnormal metabolism of glucose or BMI> 25 kg/m^2. It is associated up to 50% with NAFLD/NASH. The diagnosis is made discarding the usual causes of hepatic iron overload.
Aims and Methods: To study the cases of DIOS in a cohort of patients with hyperferritinemia sent to 6 hospitals in the Basque Country and to determine its relationship with mutations of the HFE gene and with hepatic steatosis.
A prospective study of consecutive patients with HF (>200μg/L women; 300 μg/L men) and/or TSI>45%, confirmed in 2 determinations, was conducted from December 2010 to April 2013. Dysmetabolic iron overload syndrome (DIOS) was diagnosed (1) when LIC>36, one or more MtS criteria (2) or BMI >25. Exclusion criteria: C282Y/C282Y, LIC>80-phenotypic hemocromatosis-, alcohol >40 g/day men/>20 g/day women, viral infection (HCV, HBV), oral iron, blood transfusions. LIC was determined by MRI 1.5 Tesla system (SIR method) (3). We systematically performed T1-weighted in-phase and opposed-phase imaging to determine the presence or not of liver steatosis (4). We studied HFE gene mutations in all the patients.
Results: 312 patients (272 men/ 40 women) were included. Mean age 55 (SD 13.5); Mean ferritin 729.6 (SD 449.6), mean TSI 40.8 (SD 15.8); 82 patients were diagnosed with DIOS. H63D/H63D 19 (23.17%), C282Y/H63D 11 (13.41%), C282Y/wt 5 (6.10%), H63D/wt 21 (25.61%), wt/wt 25 (30.49%). When we compared the results with those of Basque general population (5), the differences were statistically significant for H63D/H63D ($p = 0.002$) and C282Y/H63D ($p = 0.009$) mutations.
In 286 patients a MR study for the presence of liver steatosis was performed: 196 no steatosis; 90 liver steatosis (31.47%). There were 71 DIOS patients (from 82) with MR for LS determination: 13 with LS (18.31%), 58 without LS (81.69%). From 215 patients without DIOS and with MR: 77 LS (35.81%), 138 without LS (64.19%). When we compared the patients from DIOS group with MR and the group without DIOS and MR, LS was more frequent in the group without DIOS ($p = 0.006$).
Conclusion: HFE gene mutations H63D/H63D and C282Y/H63D are more associated with DIOS patients than with general population in our country; liver steatosis is more frequent in patients without DIOS than in patients with DIOS.
Disclosure: Nothing to disclose

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P0009 NON-ALCOHOLIC FATTY LIVER DISEASE IS ASSOCIATED WITH CORONARY ARTERY CALCIFICATION IN ASYMPTOMATIC INDIVIDUALS

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is related closely to risk factors for coronary artery disease (CAD), but it is unclear whether NAFLD independently contributes to asymptomatic individuals. Coronary artery calcium (CAC) scanning is the predictor of coronary events. We investigated the association of coronary artery calcification with NAFLD in asymptomatic adults.
Aims and Methods: This is the cross-sectional study performed in Hansol Hospital Healthcare Center. NAFLD was defined as cases with the typical ultrasonographic findings without excessive alcohol consumption, medications causing hepatic steatosis or other chronic liver diseases. CAC was evaluated using the Agatston method.
Results: We enrolled 312 subjects (mean age, 46.8 ± 8.7 years; 60.7% males) without known liver disease or a history of ischemic heart disease. NAFLD was found in 27% of the enrolled 312 subjects and CAC > 100 with moderate-high risk of CAD was found in 10.3% of subjects. Male gender (odds ratios (OR), 2.857; 95% confidence intervals (CI), 1.169–6.147), diabetes mellitus (OR, 2.739; 95% CI, 1.092–5.638), increased age (OR, 1.208; 95% CI, 1.071–1.316), and NAFLD (OR, 1.862; 95% CI, 1.065–3.592) were the independent factors that increased the risk of CAC > 100 in binary logistic regression.
Conclusion: NAFLD is associated with increased coronary artery calcification independent of traditional risk factors. The assessment of CAC may be useful in identifying NAFLD patients at risk of future cardiovascular events even in asymptomatic individuals.
Disclosure: Nothing to disclose

P0010 A POTENTIAL LINK BETWEEN POLYCYSTIC OVARY SYNDROME AND NON-ALCOHOLIC FATTY LIVER DISEASE: AN UPDATE META-ANALYSIS

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Introduction: Polycystic ovary syndrome (PCOS) itself accounts for a high risk of developing non-alcoholic fatty liver disease (NAFLD). Alternatively, other specific factors in women with PCOS may contribute to this association, which presently remains unknown.
Aims and Methods: We aimed to shed some light into this issue, and thereby performed this meta-analysis. Relevant studies that were published before May 2017 were identified and retrieving from PubMed and Web of Science databases. Data were extracted, and the pooled odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated.
Results: A total of 17 studies were included into this analysis. Compared to the control group, the risk of NAFLD in the PCOS group was higher (OR = 2.25, 95% CI = 1.95–2.60). When stratified by BMI and geographic location, these results indicated that the frequency of NAFLD risk was significantly higher amongst obese subjects (OR = 3.01, 95% CI = 1.88–4.82), non-obese subjects (OR = 2.07, 95% CI = 1.12–3.85), subjects from Europe (OR = 2.00, 95% CI = 1.58–2.52), subjects from the Asia-Pacific Region, (OR = 2.32, 95% CI = 1.89–2.84) and subjects from America (OR = 2.96, 95% CI = 1.93–4.55), respectively. In addition, PCOS patients with hyperandrogenism (HA) had a significantly higher risk of NAFLD than controls (OR = 3.31; 95% CI = 2.58–4.24). However, there was no association between PCOS patients without HA and higher risk of NAFLD (OR = 1.46; 95% CI = 0.55–3.87).
Conclusion: In summary, women with PCOS are more likely to develop NAFLD. Furthermore, PCOS itself is not a major factor leading to the disease. An excess in androgen levels, which is the main feature of PCOS and is interrelated to IR, might be a contributing factor to the development of NAFLD in PCOS patients. These findings have clinical implications for NAFLD screening in hyperandrogenic women with PCOS.
Disclosure: Nothing to disclose

P0011 UDCA EFFICASY IN THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Dyslipidemia, insulin resistance, steatosis and fibrosis play a key role in the pathogenesis of NAFLD.
Aims and Methods: We aimed to evaluate the effect of UDCA in combination with of lifestyle modification on liver steatosis and fibrosis, insulin resistance (IR) and dyslipidemia in obese patients with NAFLD.
90 obese (BMI > 30, Mediana - 32) patients (men 49) with NAFLD were included in the study. The median (Me) age - 45.6 years. All patients had cytolysis (> 2 norms) and \ or Fibrosis (F) and Steatosis (S) > 1 stage by FibroScan 502 TOUCH with XL probe for obese patients and CAP technology. Blood lipid spectrum, IR, signs of inflammation were evaluated. Body metabolism (M) assessed by method of indirect calorimetry and impedancemetry (IM). It was done to prescribe the appropriate diet (minus 500 kkal/day with low level of carbohydrates ≤100g\day) in combination with exercises (plus 500 kkal/day). 63 patients were prescribed a diet in combination with daily aerobic exercise and UDCA 15 mg/kg/day (group 1), remaining 27 patients were recommended a daily aerobic exercise (group 2). Follow up period - 6 months.
Results: According to IM data in both groups there was a decrease in body weight (Me = 7% of baseline), basal metabolism (Me = 10%), fat mass in Me = 14%. At the same time muscle mass increased - with a parallel increase in muscle mass- metabolically active body mass-Me = 8. According to M evaluation there was an increase in respiratory exchange ratio by 12% with an increase in oxygen consumption (+ 15%) and a decrease in the o CO2 production (+13) in both groups, a decrease in the metabolic age by 5 years (Me). Metabolic parameters correlated (r > 0.3) with value of insulin, glucose, total cholesterol, LDL, S, F. There was a 25% decrease in Me of ALT, $p < 0.001$ (1st group), and 12% of the 2nd group ($p < 0.05$); reduction of AST by 36% and 8% respectively ($p < 0.001$), GGTP-36% and 27% respectively ($p < 0.001$), glycated Hb-20% and 11%, respectively ($p < 0.05$); insulin 16% and 14% respectively ($p < 0.02$), HOMA - 16% and 8% respectively ($p < 0.04$); total cholesterol 10% and 5% respectively ($p < 0.001$); triglycerides −27% and 10% respectively ($p < 0.05$); LDL 22% and 10% respectively ($p < 0.05$); S (dB/m^2) −19% and 13% respectively ($p < 0.05$); F -reduction in 1 stage (Metavir) in 40% of patients in group 1 only.
Conclusion: The UDCA administration in combination with of lifestyle modification in obese patients with NAFLD results in significant reduction of liver inflammation, insulin resistance and dyslipidemia compared with non-pharmacological therapy only.
Disclosure: Nothing to disclose

P0012 HIGHER NON-INVASIVE FATTY LIVER INDEXES PREDICT COLORECTAL NEOPLASM AMONG YOUNG POPULATION

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Introduction: Colorectal cancer (CRC) is one of the most common cancers and the leading causes of cancer-related death worldwide; however, the prevalence of colorectal neoplasm in young adults with obesity and the associated risk factors have not been clarified. We aimed to investigate the association of non-invasive fatty liver indexes with the colorectal neoplasm among young population.
Aims and Methods: From Jan, 2013 to Dec, 2016, 1,132 asymptomatic young people aged younger than 50-year-old receiving the health check-up colonoscopy in Health Management Center of Far-Eastern Memorial Hospital were enrolled. The ability of the fatty liver index (FLI), lipid accumulation product (LAP) and non-alcoholic fatty liver disease (NAFLD) fibrosis score to predict obesity and colorectal neoplasm was assessed.
Results: The mean age of the population was 39.2 ± 6.69 years old and 52.6% was male. Colorectal neoplasms were diagnosed in 15.5% of the population (tubular adenoma 87.5%, tubulovillous adenoma 8.52%, high-grade dysplasia 3.98%). Subjects with colorectal neoplasm tended to be older, male predominant, with higher body mass index, waist circumference, serum triglycerides, fasting blood glucose, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyltranspeptidace (γ-GT), and higher FLI, LAP and NAFLD fibrosis scores. Male sex, age and γ-GT were strongly associated with colorectal neoplasm than other variables (OR 1.536, 1.029 and 1.007, respectively; $p = 0.017$, 0.030 and 0.001, respectively). Using the multivariate analysis, the FLI (≥60, OR 1.830; $p = 0.004$) and LAP score (Men > 48.09, Women > 31.77, OR 1.489; $p = 0.045$), but not NAFLD fibrosis score ($p = 0.270$), can be representative indicators to predict colorectal neoplasm in young adults.
Conclusion: Among average-risk young adults, increasing risk for colorectal neoplasm was found to be associated with higher FLI and LAP scores, suggesting that the screening colonoscopy before 50 years of age with high fatty liver indexes might be beneficial.
Disclosure: Nothing to disclose

P0013 MOLECULAR INVERSION PROBE ASSAY TO IDENTIFY NOVEL GENES ASSOCIATED WITH POLYCYSTIC LIVER DISEASE

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Introduction: Polycystic liver disease (PLD) is an inherited disorder associated with the development of numerous liver cysts. The genetic spectrum of PLD currently consists of six genes related to autosomal dominant PLD (ADPLD) and two genes related to PLD in patients with autosomal dominant polycystic kidney disease (ADPKD). Contrary to ADPKD patients, the genetic background of the majority of ADPLD patients remains unknown. Identification of these genes is important for understanding of pathways leading to liver cysts as well as possible genotype-phenotype associations. The aim of our study was to identify novel genes associated with PLD.
Aims and Methods: We deployed molecular inversion probe (MIP) analysis for the discovery of genetic variants in 26 genes in a cohort of unrelated PLD patients. We developed probes for 5 known genes associated with PLD and 21 genes chosen for their association with liver or kidney cysts in literature. Variants identified using the MIP assay were filtered before validation using Sanger sequencing. The validated variants were then selected based on novelty or SNP frequency < 0.001, in silico prediction using bioinformatics prediction tools (PolyPhen-2; SIFT), and absence of pathogenic variants in known PLD-genes. If available, family members were screened to test for disease segregation.
Results: We included 625 unrelated patients with the primary phenotype of PLD. After the first filter steps of the MIP results we identified 280 variants in 15 genes not previously associated with PLD. For six remaining genes no variants were identified that complied to all filter steps. Sanger sequencing of these 280 variants lead to validation of 85 variants in 10 genes. Sixty-five of the non-validated variants occurred in the remaining 5 genes. Of the validated variants, 49 variants are either known SNPs with allele frequency < 0.001 (n = 36), have not been described before (n = 11), or frequency data is not available (n = 2). These 49 variants were all predicted to be likely pathogenic or pathogenic by in silico prediction and are found in 9 genes.
Conclusion: We identified 49 variants in 9 genes in a large international cohort of PLD patients. These are all novel or rare variants predicted to have deleterious effect on their corresponding protein. These genes are possibly associated with PLD and are excellent candidates for further functional studies to provide evidence for their relation with PLD.
Disclosure: Nothing to disclose

P0014 LOW BISPHENOL A CONCENTRATION INDUCES PROLIFERATION, OXIDATIVE STRESS AND EX-NOVO SYNTHESIS OF STEROID HORMONES IN HEPATOMA CELL LINE

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Introduction: Human liver is known as one of the target organs for estrogens, with mitogenic activity. Bisphenol A (BPA), is an artificial environmental endocrine disrupting chemicals (EDCs) that leaches from polycarbonate plastics that consequently leads to low-dose human exposure. The BPA environmental exposition was hepatic damage and worsening of non-alcoholic fatty liver disease (NAFLD). BPA is considered to be a xeno-estrogen and it can bind to estrogen receptors (ERs). Estrogens play important roles in the cell proliferation and invasion of estrogen dependent human neoplasms.
Aims and Methods: The aim of this study was to investigate the low dose of BPA effects on cell proliferation, oxidative stress and impaired synthesis of steroid hormones in human hepatocellular carcinoma cell line HepG2.
Cells were exposed to non-toxic BPA concentration (0.025 and 0.05 μM) for 48 and 72 h. Cell viability was assessed by adding 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. The level of Thiobarbituric Acid-Reactive Species (TBARS) was assessed as markers of lipoperoxidation. The effect of BPA on the expression of p-ERK, ERK, Caspase 3 and aryl hydrocarbon receptor (Ahr) was determined by Western blot analysis. The analysis of steroids extracted from cell culture medium were performed by mass spectrometer analysis.
Results: BPA was able to induce a significant increase of both cell proliferation ($p = 0.0013$) and TBARS concentration ($p = 0.0003$) after 48 hours of incubation. Moreover BPA increased the protein expression of key molecules involved in the regulation of proliferation and survival, as Erk, p-Erk and AKT, and reduced the expression of caspase 3. Low dose of BPA induced an increase estrogen/testosterone ratio compared to untreated cells. The major representative peaks present in the media of BPA-treated HepG2, obtained by mass spectrometry, were: 17β-estradiol 3-sulfate ($353.1 \pm 1 m/z$), methoxyestrone 3-sulfate ($381.3 \pm 1 m/z$), 17-hydroxyprogesterone ($331.3 \pm 0.2 m/z$), estrone ($269 \pm 1 m/z$),16α-oxoestrone ($283.3 \pm 1 m/z$), testosterone sulfate ($367.4 \pm 1 m/z$) and cholesterol ($393 \pm 1 m/z$).
Conclusion: In the present study we demonstrated that treatment of HepG2cells with low doses BPA elicited: 1) increase of proliferation rate; 2) regulation of ERK/MAPK and PI3K/AKT pathways probably binding to ERα 3) increase of oxidative stress 4) induction of oxidative metabolism of estrone.
Disclosure: Nothing to disclose

P0015 TRANSIENT ELASTOGRAPHY, APRI AND FIB-4 SCORES FOR STAGING OF FIBROSIS AND CIRRHOSIS IN WILSON DISEASE

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Introduction: Data on the predictive capability of cirrhosis through transient elastography (TE) in Wilson disease (WD) is scarce. Furthermore there is no data regarding its value to monitor therapy. Aim was therefore to assess whether TE is a suitable tool to identify cirrhosis in patients (i) newly diagnosed and (i) under treatment for WD.
Aims and Methods: Patient with WD underwent TE (results in kPa) either at the time of diagnosis or during a regular outpatient visit during treatment. Data are shown only for patients in whom a liver biopsy was available. Furthermore data on initial liver biopsy results and non-invasive fibrosis scores (APRI, FIB-4) were recorded.
Results: 55 patients were included in the study. Of those 6 were de novo patients [Male: 50%, Age: 34 ± 10, TE: 10,9 kPa (3.5–34.8), Cirrhosis at LBX: 50%] and 49 patients [Male: 49%, Age: 40 ± 14), TE: 7.4 kPa (3.5–15.4), Cirrhosis at LBX:36.7%] had received various length of treatment with chelators. Significantly more patients under treatment were found with TE values < 12kPa (93.6% vs. 62.5%; $p = 0.009$) irrespective of initial biopsy results. Moreover the APRI classification found no patients (0%) with cirrhosis in the treated group (vs. 33.3% in the no-treatment group, $p < 0.001$). No non-cirrhotic patient worsened under treatment according to the APRI classification (cirrhosis: 0%). In untreated patients, TE, APRI and FIB-4 values almost correctly classified patients with cirrhosis, whereas in treated patients with cirrhosis at LBX (n = 18) only 16.7%, 5.6% and 27.8% where classified with cirrhosis according to TE > 12kPa, APRI and FIB-4 scores respectively (see Table 1) suggesting a potential reversible effect of therapy on the course of the disease.
Conclusion: In conclusion, TE and non-invasive fibrosis scores are valid tools to discriminate cirrhosis in newly diagnosed WD patients. In cirrhotic patients on long-term treatment TE, APRI and FIB-4 were mostly below the threshold for advanced fibrosis, indicating that decoppering therapy prevents progression of liver disease.
[Table 1]
Disclosure: Nothing to disclose

P0016 US-FLI SCORE - IS IT POSSIBLE TO PREDICT THE STEATOSIS GRADE WITH AN ULTRASONOGRAPHIC SCORE?

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Introduction: A recently created ultrasonographic score (*Ultrasonographic fatty liver indicator* (US-FLI)) allows the grading steatosis severity using ultrasound (US) and correlates with its histological features when assessed with liver biopsy.
Aims and Methods: We aimed to assess the correlation of US-FLI with the controlled attenuation parameter (CAP) in patients with non-alcoholic fatty liver disease (NAFLD).
Initially, inter-observer agreement for the score was assessed between 3 physicians using a sample of 31 patients. Later, 96 patients with NAFLD were included and several anthropometric, clinical and analytical parameters were assessed and US and transient elastography was performed.
Results: Physicians showed an excellent absolute agreement regarding the total score, with an average Interclass Correlation Coefficient of 0.972 (95% CI 0.949–0.986).
Patients had a median US-FLI of 6 ± 3 points and a mean CAP of 311 ± 48 dB/m. Comparing US-FLI with CAP, and considering the previously defined cutoff for steatosis > S1 (268dB/m) and > S2 (280dB/m), we verified that US-FLI had a good discriminative capacity for both grades, with areas under the curve (AUC) of 0.88 ($p < 0.001$) and 0.90 ($p < 0.001$), respectively. We also verified that a US-FLI≤3 points had a negative predictive value of 100% for steatosis > S2 and that values of US-FLI ≥6 points had a positive predictive value (PPV) of 94.0% for steatosis > S2.
When comparing the clinical score *Fatty Liver Index* (FLI) for the same CAP cutoffs, it showed a weak discriminative capacity for both grades with AUC of 0.65 ($p = 0.030$) and 0.66 ($p = 0.017$). When comparing AUC for US-FLI and FLI scores, we verified that these were significantly diferente for both cutoffs ($p < 0.001$).
Conclusion: US-FLI has an excellent reproducibility and a good discriminative capacity for the different steatosis grades. Scores ≤3 points allow us to exclude significant steatosis and scores ≥6 points have a PPV of 94.0% for steatosis > S2. US-FLI was significantly superior to the clinical score FLI in the discrimination between steatosis grades.
Disclosure: Nothing to disclose

P0017 IDENTIFYING THE NEXT TREATMENT FOR POLYCYSTIC LIVER DISEASE USING A DRUG SCREENING LIBRARY

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Introduction: Autosomal dominant polycystic liver disease is caused by genetic defects in *PRKCSH* in the majority of patients. Pharmaceutical treatment of polycystic liver disease is aimed at curtailing cyst volume and limited to the use of somatostatin analogues. Disadvantages of somatostatin analogues are the moderate efficacy, common frequency of side effects, and high costs. There is an urgent need for a safe treatment that decreases cyst proliferation, and hence

Abstract No: P0015

	N	kPa	kPa >12	APRI median	APRI classification: cirrhosis	FIB-4 median	FIB-4 classification: F3/4
No-cirrhosis in untreated patients	3	5.3	0 (0%)	0.21	0 (0%)	0.39	0 (0%)
Cirrhosis in untreated patients	3	34.8	3 (100%)	2.15	2 (66.7%)	7.46	2 (66.7%)
Cirrhosis at time of Dg. in treated patients	18	7.9 (3.5–12.4)	3 (16.7%)	0.39 (0.23–1.27)	1 (5.6%)	1.25 (0.49–4.28)	5 (27.8%)
No cirrhosis at time of Dg. in treated patients	31	6.9 (3.5–15.3)	2 (6.5%)	0.25 (0.17–0.83)	0 (0%)	0.88 (0.28–4.23)	2 (6.5%)

cyst volume. The aim of our study is to design a diagnostic pipeline that is able to identify pharmaceutical compounds that target pathways related to hepatic cystogenesis: cell proliferation and fluid secretion caused by decreased calcium and subsequently increased cAMP levels.[1]

Aims and Methods: The Selleckchem FDA-approved drug screening library contains 1442 compounds with a wide spectrum of therapeutic targets. *PRKCSH* knockout H69 cholangiocytes were used as *in vitro* model for polycystic liver disease. Cells were incubated with compounds at 10 microM concentration for 24 hours in triplicate. Proliferation was measured as absorbance after addition of WST-1 proliferation reagent (Sigma-Aldrich) for 3 hours. Compounds changing proliferation >20% compared to DMSO controls were selected for incubation in wildtype H69 cholangiocytes. Compounds showing >50% of proliferation compared to control and >20% absolute difference between knockout and wildtype H69 cells were identified as most promising. Compounds were further tested for their effect on cyclic AMP levels after 24 hours incubation using ELISA (Cayman).

Results: 1278 compounds showed proliferation rates of 80–120% relative to control in *PRKCSH* knockout H69 cholangiocytes. 26 compounds increased proliferation >120% of control and 138 compounds decreased proliferation below 80% of control proliferation rate. These 164 compounds were further tested in wildtype H69 cholangiocytes, while octreotide was added as reference. 18 compounds showed proliferation >50% of control proliferation rate and >20% absolute difference between knockout and wildtype H69 cholangiocytes. These compounds were then screened for their effect on cyclic AMP levels. Of these, 3 compounds reduce proliferation more in *PRKCSH* knockout cells than wildtype cells and decreased cyclic AMP levels. These included 2 anti-cancer drugs and 1 antimicrobial agent. Octreotide showed no difference in proliferation between incubated cells and controls, nor between knockout and wildtype cells. As expected octreotide reduced cyclic AMP levels in both cell lines.

Conclusion: We identified 3 FDA approved drugs that reduce proliferation rates in *PRKCSH* knockout cholangiocytes without large effect on proliferation rates in wildtype H69 cells. These drugs show reduction of cyclic AMP as well. Target pathways of these compounds differ from somatostatin analogues, and may become future pharmaceutical options for patients unresponsive to current treatment.

Disclosure: Nothing to disclose

Reference

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P0018 LIVER FIBROSIS RISK IN ALPHA1-ANTITRYPSIN DEFICIENCY IS NOT LIMITED TO HOMOZYGOUS PATIENTS (PI*ZZ GENOTYPE)

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Introduction: Alpha-1 antitrypsin deficiency (A1AD) is an autosomal codominant disease associated with an increased risk of liver and lung disease in adults. The association between liver disease and homozygosity for the mutant Z allele (PiZZ) is well-established, however, contribution of other genotypes to the pathogenesis of adult liver disease is unclear. Moreover, the clinical course of liver disease in adults with A1AD remains poorly understood. Research is required to identify patients at risk of developing liver disease at an early stage.

Aims and Methods: Multicenter cross-sectional case-control study, including adult A1AD patients treated in Pulmonology departments of 10 hospitals (3/12 hospitals excluded with < 5 patients). Data pertaining pulmonary function, A1AT replacement therapy, A1AT phenotype/genotype, lung transplant and imaging were retrospectively collected. Clinical, demographic, laboratorial, family and personal history (including paediatric manifestations), and liver stiffness (LS), measured by transient elastography (TE, Fibroscan), data were prospectively collected at time of enrolment. Significant liver fibrosis was defined by LS≥7.1kPa. Controls were recruited within a prospective epidemiological study in the general adult population.

Results: We evaluated 218 A1AD patients and 199 controls. Our study comprised 59 PiZZ, 114 PiZ heterozygotes (55 MZ, 54 SZ, 4 MheerlenZ, 1 ZQ0s), 21 PiS (10 SS, 11 MS), 17 PiMmalton/PiMpalermo (PiMma/Mpa) carriers and 7 other rare genotypes. Cases and controls did not differ in terms of age, obesity (BMI > 30 kg/m^2), AUDIT score, serum lipids, glycaemia or CAP. Cases had significantly higher serum levels of ALT, AST and GGT ($p < 0.0001$). There was a significantly higher number of smokers in controls than patients ($p = 0.001$).

Median A1AT serum level in patients was 58 mg/dL (IQR 30) being lowest in PiZZ (27) and PiMma/Mpa patients (23). 16% of patients (34) underwent IV augmentation therapy, mainly Pi*ZZ patients, while 4 patients had undergone successful lung transplantation and 8% (18) needed regular oxygen therapy. 14% of patients were previously admitted in a Pulmonology department due to exacerbation of lung disease.

LS was defined 8.5% in controls and 17.4% in A1AD ($p = 0.007$) being highest in PiZZ (7.2 ± 4.8kPa) and PiZ heterozygotes (6.0 ± 7.2kPa). Liver fibrosis was detected in 17.4% (38/218) of patients. The genotype-specific prevalence was: PiZZ 36%(21/59), PiZ- 11,4%(13/114), PiMZ 17% (8/48), PiMma/Mpa 18%(3/17) and PiS carriers 5% (1/21), $p = 0.001$. Advanced liver fibrosis was verified in 1 control (0.5%) and 6% patients ($p = 0.002$), namely: 10% PiZZ, 5% PiZ- and 6% PiMma/Mpa. Liver fibrosis was significantly associated ($p < 0.05$) with male sex, BMI, ALT, AST, GGT, ALP, albumin, platelet, INR, CAP, glycaemia and diabetes. Laboratory liver scores (APRI and FIB-4) had a fair correlation with elastography.

Conclusion: Akin to PiZZ, PiZ heterozygoty, in particular PiMZ, is associated with liver fibrosis development. Moreover, our results suggest that rare A1AD variants, as PiMmalton also promote liver fibrogenesis. Routine laboratory tests are not predictive of significant liver fibrosis, highlighting the need for other non-invasive methods such as TE in A1AD patients follow-up.

Disclosure: Nothing to disclose

P0019 THE ROLE OF 5-HT$_{2A}$ RECEPTORS AND POST-RECEPTOR SIGNALING MECHANISMS IN VASCULAR HYPO-RESPONSIVENESS IN A RODENT MODEL OF CIRRHOSIS

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Introduction: Cirrhosis is characterized by a hyperdynamic circulatory state and altered vascular reactivity to circulatory and paracrine agents. Vascular hyporeactivity to vasoconstrictors has been suggested to play a role in human and animal models of portal hypertension. The studies of 5-HT$_{2A}$ receptor stimulation and post receptor signaling mechanisms have revealed conflicting results. Our study aims to investigate the role of 5-HT$_{2A}$ receptors and post-receptor signaling mechanisms in vascular hypo-responsiveness in a rodent model of cirrhosis.

Aims and Methods: Cirrhosis was induced in Sprague-Dawley rats by administering CCl_4 at a dose of 1.5 mg/kg (subcutaneously), twice weekly for 8 to 10 weeks. The control rats were administered olive oil. At week 10, rats were dissected to isolate aortae and liver tissues. Aortic preparations were mounted in tissue bath assembly for the assessment of vasoconstrictor effects of α-methyl 5-HT, a 5-HT$_{2A}$ receptor agonist 5-HT$_{2A}$ agonist. The mRNA levels of 5-HT$_{2A}$ receptors were carried out using real-time PCR, while the levels of ROCK$_2$ protein were measured using an enzyme-linked immunosorbent assay. Histology of Liver tissues was studied to confirm the presence of cirrhosis.

Results: In isolated aortae of control animals, α-methyl 5-HT, caused a concentration-dependent (0.1–10 μM) vasoconstriction with maximum effect of 99.94 ± 32.51% (mean ± s.e.m) relative to K (80 mM) contraction. In cirrhotic rat aortae, it also caused concentration-related vasoconstriction at similar range with attenuated maximum contractile effect of 44.52 ± 32.55% at 100 μM. Treated and untreated tissues challenged with graded concentrations of α-methyl 5-HT were tested to quantify the mRNA levels of 5-HT$_{2A}$ and ROCK$_2$ protein. Expression of 5-HT$_{2A}$ mRNA and ROCK$_2$ protein levels showed a decreasing trend in cirrhotic aortic tissues vs. control. Histological features of hepatic tissues confirmed the development of cirrhosis in diseased rats showing evidences of fibrosis and nodule development.

Conclusion: These data suggests that the resultant hypo-responsiveness in isolated aortic preparations of cirrhotic animals is due to attenuated activity/affinity of 5-HT$_{2A}$ receptors which was evident by suppressed vascular contractile response to 5-HT$_{2A}$ receptor agonist in cirrhotic animals vs. control. Though no significant difference was observed in the expression of mRNA levels of 5-HT$_{2A}$ and downstream ROCK$_2$ protein levels, a clear downward trend was noticed in both. Thus, this study provides an evidence to the contributing role of 5-HT$_{2A}$ receptors in vascular hypo-responsiveness in cirrhotic animals.

Disclosure: Nothing to disclose

P0020 *TM6SF2* AND *MBOAT7* GENE VARIANTS ARE NOT ASSOCIATED WITH THE RISK OF DEVELOPING LIVER FIBROSIS AND CIRRHOSIS IN AN EASTERN EUROPEAN POPULATION

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Introduction: Previous large-scale genetic studies identified single nucleotide polymorphisms (SNPs) of the *TM6SF2* and *MBOAT7* genes as risk factors for alcoholic liver cirrhosis and non-alcoholic fatty liver disease. In this study, we tried to evaluate whether *TM6SF2* (*rs58542926, rs10401969*) and *MBOAT7* (*rs641738, rs626283*) SNPs are associated with the risk of hepatic fibrosis or liver cirrhosis of different aetiology in an Eastern European population.
Aims and Methods: The study was conducted at the Department of Gastroenterology, Lithuanian University of Health Sciences Hospital, and included 334 patients with liver cirrhosis, 128 patients with liver fibrosis, and 550 controls. SNPs were genotyped by quantitative PCR, using TaqMan allelic discrimination assays.
Results: Genotype distributions of *TM6SF2* (*rs58542926, rs10401969*) and *MBOAT7* (*rs641738, rs626283*) SNPs were in Hardy-Weinberg equilibrium. The *TM6SF2 rs58542926* and *rs10401969* alleles and genotypes had similar frequencies in controls, liver fibrosis and cirrhosis groups ($p > 0.05$). The distribution of *MBOAT7 rs626283* and rs641738 genotypes did also not differ between the 3 groups ($p > 0.05$). Overall, none of the 4 analysed SNPs (*rs58542926, rs10401969, rs641738, rs626283*) was associated with the presence of hepatic fibrosis or liver cirrhosis in our population.
Conclusion: Our study showed no significant associations between *TM6SF2* (*rs58542926, rs10401969*) and *MBOAT7* (*rs641738, rs626283*) gene polymorphisms and liver fibrosis, alcohol or hepatitis C virus-induced liver cirrhosis in an Eastern European population. These findings point to a predominant role of exogenous risk factors for disease progression in these patients.
Disclosure: Nothing to disclose

P0021 ANTIOXIDANT PROPERTIES OF CELECOXIB REDUCE HEPATIC VASCULAR RESISTANCE AND PORTAL PRESSURE IN CIRRHOTIC RATS

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Introduction: Increased hepatic vascular resistance (HVR) due to architectural distortion and intrahepatic vasoconstriction is the primary factor for the development of portal hypertension in liver cirrhosis. Oxidative imbalance in cirrhotic livers, by decreasing nitric oxide (NO) bioavailability, contributes to increasing HVR and portal pressure (PP). Cyclooxygenase-2 (COX-2) is up-regulated in cirrhotic livers and correlated with fibrosis degree and PP.
Aims and Methods: To investigate the antioxidant capacity of celecoxib, a selective COX-2 inhibitor, and its effects on intrahepatic resistance during the development of portal hypertension in cirrhotic rats. *In vivo* study, peritoneal injection of thioacetamide (TAA) was employed to induce liver cirrhosis for 16 weeks. 36 male *Sprague-Dawley* rats were randomly assigned to the control, TAA, and TAA+celecoxib groups. TAA-cirrhotic rats received celecoxib or its vehicle by gastric gavage for last 8 weeks. PP, portal blood flow (PBF) and HVR were measured before sacrificed. Oxidative stress levels were evaluated by *in situ* superoxide (O_2^-) fluorescent staining and activity of superoxide dismutase (SOD). cGMP and arachidonic acid metabolomics in liver homogenate were quantitated. Hepatic expressions of pivotal molecules in NO bioavailability (eNOS, AMPK, nitrotyrosine), oxidation/antioxidation (NOX4, SOD) and COX pathway (COX2, EP2, TXA2R) were analyzed by RT-qPCR or Western blot. *In vitro* study, the recombinant plasmid with COX-2 or empty vector were transfected into LSECs (SK-Hep1) and hepatocytes (L02). After treatment with PGE2, AH6809 (EP2 antagonist), U46619 (TXA2R agonist), Terutroban (TXA2R antagonist), Dorsomorphin (AMPK inhibitor) and GKT137831 (NOX4 inhibitor), *in situ* O_2^- levels and protein expressions were evaluated.
Results: Celecoxib administration significantly decreased PP by 22.8% (12.51 ± 0.69 vs. 16.20 ± 0.84 cmH_2O, $p < 0.05$) and HVR by 31.6% (0.91 ± 0.05 vs. 1.33 ± 0.10 $cmH_2O \cdot mL^{-1} \cdot min$, $p < 0.05$), with a significant increase in PBF (13.83 ± 0.83 vs. 12.25 ± 0.75 mL/min, $p < 0.05$). Compared with the TAA group, celecoxib ameliorated oxidative stress by enhancing SOD activity ($p < 0.05$) and suppressing NOX4 expression ($p < 0.05$). Consistently, the up-regulation of hepatic O_2^- level and nitrotyrosine protein induced by TAA was significantly inhibited after celecoxib administration ($p < 0.05$). Furthermore, treatment with celecoxib increased hepatic cGMP level (0.59 ± 0.14 vs. 0.44 ± 0.09 pmol/mgprot, $p < 0.05$) by accelerating the phosphorylation levels of eNOS and AMPK. COX-derived metabolites showed that PGE2 and TXA2 were significantly increased in TAA-cirrhotic rats ($p < 0.05$), and remarkably decreased after celecoxib treatment ($p < 0.05$). The mRNA and protein levels of COX-2, EP2 and TXA2R were significantly down-regulated by celecoxib administration ($p < 0.05$). In cultured SK-Hep1 and L02 cells, COX-2 plasmid, PGE2, U46619 and Dorsomorphin significantly decreased phosphorylation level of AMPK ($p < 0.05$) and increased NOX4 expression ($p < 0.05$). The effects caused by PGE2 or U46619 could be inhibited after the blockage of EP2 or TXA2R ($p < 0.05$). GKT137831 down-regulated NOX4 expression ($p < 0.05$) without affecting AMPK phosphorylation.
Conclusion: Therapeutic administration of celecoxib efficiently decreased HVR and PP in TAA-cirrhotic rats. These effects may due to the acceleration of NO generation and the suppression of NO scavenging by superoxide radical. Inhibition of COX-2 by celecoxib significantly reduced ROS generation in LSECs and hepatocytes by suppressing PGE2/TXA2-EP2/TXA2R-AMPK-NOX4 pathway.
Disclosure: Nothing to disclose

P0022 THE ROLE OF VON WILLEBRAND FACTOR AS A MORTALITY PREDICTOR IN DECOMPENSATED LIVER CIRRHOSIS

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Introduction: The von Willebrand factor (vWF) is a marker of endothelial dysfunction that is closely associated with the degree of hepatic dysfunction in the cirrhotic patient. Thus, it is assumed that there is a correlation between vWF level and the prognosis of the cirrhotic patient.
Aims and Methods: We aimed to evaluate the role of vWF as a predictor of short and medium-term mortality in patients with decompensated liver cirrhosis; to determine its prognostic accuracy and to compare it with the Child-Pugh (CP), MELD and CLIF-AD prognostic scores.
Prospective study including patients admitted for acute decompensation of cirrhosis between July 2016 and October 2017. The value of vWF-antigen, CP, MELD, CLIF-AD was determined. In-hospital, as well as 30, 90, 180 and 365-day mortality was calculated. The accuracy of vWF and each of the scores in the prediction of mortality was evaluated and compared.
Results: 41 patients included, 90.2% male, mean age 61 ± 9.6 years. MELD 15.74 ± 6.62, CP 9.98 ± 1.54 and CLIF-AD 53.34 ± 9.98. The mean value of vWF was 594.69 ± 344.52 (reference value 42–176.3%), presenting significantly higher values in patients who died at admission as well as at 30, 90, 180 and 365 days (829.5 ± 164.32 vs. 557.39 ± 347.78, $p < 0.05$; 797.36 ± 191.66 vs. 539.48 ± 352.51 $p < 0.05$; 752.64 ± 217.91 vs. 542.6 ± 357.69, $p < 0.05$; $702\text{-}26 \pm 192.09$ vs. 548.39 ± 395.36, $p < 0.05$; 729.32 ± 214.43 vs. 455.58 ± 236.27, $p < 0.05$). The area under the curve (AUC) of vWF as predictor of in-hospital and 30-day mortality was 0.831 and 0.815, respectively, $p < 0.01$, not presenting values significantly higher than CP, MELD and CLIF-AD scores. The best cut-off value of vWF to predict in-hospital and 30-day mortality was 636.
Conclusion: The vWF constitutes a mortality predictor independent of the CP, MELD and CLIF-AD scores, identifying decompensated cirrhotic patients with poor short term prognosis. Thus, it is a promising biological marker, requiring more studies in order to be integrated into a new prognostic score.
Disclosure: Nothing to disclose

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P0023 GRAM-NEGATIVE BACTERIA INDUCE CELL-CYCLE ARREST AND INTESTINAL EPITHELIAL BARRIER DESTABILIZATION - AN *IN VITRO* MODEL FOR THE STUDY OF BACTERIAL TRANSLOCATION IN LIVER CIRRHOSIS

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Introduction: Patients suffering from liver cirrhosis display impaired intestinal characteristics compared to healthy individuals, indicated by a suppressed immune system with bacterial overgrowth and a reduced microbial diversity. Of special importance an increased permeability of the intestinal epithelial barrier due to liver cirrhosis is observed. Together, these changes promote bacterial translocation, driving spontaneous bacterial peritonitis (SBP) - one of the most harmful complications of liver cirrhosis. Up to now, a molecular mechanism explaining bacterial translocation in this setting has not been elucidated. To uncover under lying pathomechanisms, an *in vitro* model using Caco-2 intestinal epithelial cells was established. Effects of bacterial stimulation were evaluated

regarding changes in cell-cycle regulation and *tight junction* composition of Caco-2 cells.
Aims and Methods: Caco-2 - human intestinal epithelial cells were cocultured at day 6 post confluence with *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*) at MOI 0 - 10 for up to 4 hours. To clarify whether observed effects were due to living bacteria, bacterial components like *lipopolysaccharide* (LPS) and bacterial metabolites in form of supernatant of an *E.coli* overnight culture were also used for stimulation. Heat-inactivated bacteria served as reference. Changes in cell-cell-contact proteins (oocludin and E-cadherin) were analyzed by Western blot and fluorescence microscopy. Moreover, effect on cell-cycle regulation was examined by flow cytometry.
Results: Bacterial stimulation of Caco-2 cells with *E.coli* or *K. pneumoniae* resulted in a G1 arrest with up to 11% more cells in Go/G1 phase compared to the unstimulated control. Coincubation with *K. pneumoniae* at MOI 5 resulted in a decreased production of occludin, while *E.coli* reduced both protein levels of occludin and E-cadherin. Bacterial metabolites in the supernatant of the overnight culture reduced protein levels around 30%, but less strong compared to vivid bacteria with a downregulation of 50% compared to unstimulated cells. In contrast, heat-inactivated bacteria and LPS however failed to induce changes on the level of cell-cell-contact proteins.
Conclusion: Gram-negative bacteria such as *E.coli* and *K.pneumoniae* are capable of regulating cell-cell-contact-forming proteins of intestinal epithelial cells and therefore impair integrity of the epithelial barrier. Furthermore, presence of both bacteria resulted in a G1 cell-cycle arrest. Both effects might be part of a bacterial mechanism to escape intestinal immune responses and promote bacterial translocation followed by the development of SBP.
Disclosure: Nothing to disclose

P0024 INFLAMMATORY ACTIVITY IN ASCITIC FLUID OF LIVER CIRRHOSIS PATIENTS - ON THE WAY TO NOVEL POTENTIAL BIOMARKERS FOR DIAGNOSIS OF SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: Spontaneous bacterial peritonitis (SBP) is defined as bacterial infection of ascitic fluid without any intra-abdominal, surgically treatable focus. It is a well-known and severe complication in decompensated liver cirrhosis with a 1-year-mortality of 93%. Although SBP pathogenesis is still not yet fully understood, bacterial translocation of intestinal bacteria from the gut to mesenteric lymph nodes into the ascitic fluid is regarded to be the underlying mechanism. Intestinal bacteria translocating into ascitic fluid are mostly gram-negative bacteria, most common is *Escherichia coli*. According to the German S3-Guideline "Ascites, spontaneous bacterial peritonitis, hepatorenal syndrome", diagnosis of SBP is assured with detection of more than 250 polymorphonuclear (PMN) cells per µl. Since patients need an immediate antibiotic treatment, molecular markers indicating a beginning SBP need to be identified to be able to improve early diagnosis of SBP.
Aims and Methods: To identify novel potential biomarkers for SBP, ascitic fluid was collected from patients suffering liver cirrhosis at the University Hospital of Regensburg. Protein levels of the potential biomarkers lactoferrin, C3a, IP-10, IL-6, IL-8 and IL-10 withinascitic fluids were analyzed by ELISA. Total protein content of ascitic fluid was measured by BCA protein assays.
Results: In total, 69 ascitic fluid samples from 41 different patients were analyzed. The range of age in our cohort was between 36 and 77 years at date of paracentesis. 78% (32 patients) of the cohort were male and 22% (9 patients) were female. The development of liver cirrhosis in our population was alcohol-toxic (58.5%), cryptogenic (19.5%), nutritive-toxic (7.3%), viral (4.9%), autoimmune (2.4%), PBC (2.4%), non-alcoholic steatohepatitis (2.4%) and Budd Chiari Syndrome (2.4%). In 11.6 % (8) of the samples diagnosis of SBP was confirmed with the definition of $>$ 250 PMN/µl. The use of aPMN cell count of more than 100 PMN/µl ascitic fluid detected SBP in 13 samples (18.8%). Lactoferrinlevels in ascitic fluid with SBP (1006 ng/ml) were higher than in ascitic fluid without SBP (75ng/ml). Follow-up samples indicated that lactoferrin concentrations were elevated in early stages of SBP and coincided with the course of the disease and therapeutic response. In contrast C3a levels in infected ascitic fluids (511 ng/ml) was reduced compared to healthy controls (974 ng/ml) and correlated with the course of disease. IP-10 was detected in all samples, but did not display any correlation with disease activity. Also relevant amounts of cytokines such as IL-6, IL-8 and IL-10 were detected in ascitic fluid of liver cirrhosis patients. However, these parameters did not display any relation with the early onset of SBP.
Conclusion: Lactoferrin and C3a are molecular components of ascitic fluid which levels are in relation with the course of SBP. Moreover, a variety of other inflammatory molecules and cytokines is present in ascitic samples. These results highlight the tremendous inflammatory activity in ascitic fluids of liver cirrhosis patients and provide a potential platform for a new perspective of SBP and an earlier diagnosis and treatment of SBP in hospital or ambulant patient care leading to a reduced mortality.
Disclosure: Nothing to disclose

P0025 OUTCOMES OF LARGE-VOLUME PARACENTESIS IN CIRRHOTIC PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: Pakistan ranks second among highest prevalent countries for chronic hepatitis C with a prevalence of 5.2%. Here we have an exponential increase in chronic liver disease patients, so burden of morbidity and mortality is high due to lack of transplant centres. Spontaneous bacterial peritonitis (SBP) occurs in 10–30% of cirrhotic patients and is associated with high mortality rate among hospitalized patients and its associated incidence of acute kidney injury (AKI) and hepatorenal syndrome (HRS). Large-volume paracentesis (LVP) decreases the burden of infective fluid. Outcomes of LVP in SBP patients has not been clearly addressed in previous studies. Furthermore, in the abcense of more viable therapeutic options for preventing kidney impairment in SBP, the managment really looms around time and need for renal replacment therapy (RRT). This study will assess the outcome of LVP in patients with SBP, both in terms of mortality, length of stay and effect on renal function.
Aims and Methods: This cross-sectional study was conducted in the Medicine Unit of Aga Khan University Hospital. A total of 113 patients with diagnosed SBP were assessed. Among these patients 61 underwent LVP while 51 were managed conservatively. LVP was done as per routine practice of safety and monitoring. All the patients received intravenous albumin and hydration as per protocol. Baseline and 48 hours clinical outcomes (including creatinine and ascitic fluid total leucocytes (TLC) count) were compared including a number of other parameters. The development of AKI and post-paracentesis induced circulatory dysfunction (PPCD) were also assessed and model for end-stage liver disease (MELD) and Child-Turcotte-Pugh (CTP) scores were also calculated.
Results: There was statistically significant improvement in post 48 hours creatinine among patients undergoing LVP ($p < 0.001$) whereas no significant improvement was seen in patients without LVP (p 0.32). Similar improvements were seen for special care unit stay and total length of stay in patients with LVP, need for RRT and incidences of AKI and HRS amnong both groups.
Conclusion: LVP in patients with SBP translates into significantly positive outcomes in terms of length of hospital stay, spceial care unit stay, need for RRT and development of AKI and HRS. Hence LVP is recommended as a favoured therapeutic option.
[Outcome of LVP in SBP]
Disclosure: Nothing to disclose

Abstract No: P0025

Outcome measures	All patients n = 113	No LVP group n = 52 Mean (SD)*	LVP group n = 61 Mean (SD)	P-value
Special care unit stay (days)	2.08 (2.81)	3.23 (3.45)	1.10 (1.56)	<0.001***
Total stay (days)	4.93 (3.60)	6.44 (4.58)	3.64 (1.63)	<0.001***
Baseline ascitic fluid TLC	5559.77 (10735.36)	7221.37 (12523.50)	4143.34 (8796.86)	0.14
48hrs asictic fluid TLC	1450.34 (2666.50)	2005.08 (2683.28)	986.54 (2583.5)	0.04*
Baseline creatinie mg/dl	1.69 (1.36)	1.96 (1.73)	1.47 (0.88)	0.68
48 hours creatinine mg/dl	1.32 (1.31)	1.71 (1.77)	0.99 (0.58)	0.004*
Post 48 hours TLC in peripheral blood	12.51 (7.72)	14.28 (9.58)	11.01 (5.32)	0.03*
Acute kidney injury/hepatorenal syndrome development	7 (5.8%)	5 (7.7%)	2 (3.3%)	0.26
Post paracentesis induced circulatory dysfunction	25 (23.4%)	16 (64.0%)	9 (36.0%)	0.01%

P0027 ROLE OF APRI AND FIB4 AS A NON INVASIVE TESTS FOR ASSESSMENT OF LIVER FIBROSIS IN CHRONIC HCV INFECTION

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Introduction: Liver biopsy is the gold standard for assessing hepatic fibrosis in patients with chronic hepatitis C virus infection, but it is invasive and has many sequelae.
Aims and Methods: This study was performed to verify the role of the aspartate aminotransferase-to-platelet ratio index (APRI) and fibrosis 4 (FIB-4) tests as non-invasive alternatives to liver biopsy.
Our study included 757 patients with a median age of 42.6 ± 10.3 years. All patients underwent liver biopsy for fibrosis stage estimation, and the APRI and FIB-4 tests were performed. The liver biopsies were scored using the METAVIR system: 13 patients were F0 (1.7%), 356 (47%) were F1, 227 (30%) were F2, 160 (21%) were F3, and 1 (0.1%) was F4.
Results: For predicting fibrosis stages $F \geq 3$, APRI and FIB-4 had a specificity of 90% at cut-off values of 1.1 and 2.7, respectively, and a specificity of 95% at cut-off values of 1.67 and 3.3, respectively. The area under the receiver operating characteristic curve (AUC) was 0.663 (95% confidence interval [CI], 0.617–0.709) for APRI and 0.673 (95% CI, 0.627–0.719) for FIB-4. For predicting $F \geq 2$, APRI and FIB-4 had a specificity of 90% at cut-off values of 0.94 and 2.4, respectively, a specificity of 95% at cut-off values of 1.14 and 2.7, respectively. The AUC was 0.642 (95% CI, 0.603–0.681) for APRI and 0.676 (95% CI, 0.638–0.714) for FIB-4.
Conclusion: For the non-invasive prediction of liver fibrosis stage, using higher cut-off values for APRI and FIB-4 is advised to improve the specificity
Disclosure: Nothing to disclose

P0028 HEALTH-RELATED QUALITY OF LIFE IN PRIMARY BILIARY CIRRHOSIS

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Introduction: Primary biliary cirrhosis (PBC) is a chronic autoimmune disease, characterized by progressive inflammation, destruction of intrahepatic bile ducts and cholestasis. Symptoms of PBC, especially itching and fatigue, lead to a reduction in Health-Related Quality of Life (HRQoL). HRQoL can be determined using general or disease-specific questionnaire. Further studies investigating the HRQOL of patients with PBC, demonstrated an urgent need for a disease specific instrument, separate from other chronic liver disease and general quality of life questionnaires including the chronic liver disease questionnaire (CLDQ) and the short form health survey-36. Therefore, the first disease specific quality of life questionnaire for PBC, the PBC-40, was created.
Aims and Methods: A cross-sectional study was conducted for period of 9 months in 3 tertiary institutions. The study included consecutive patients with PBC. The diagnosis of PBC was based on a significant elevation of antimitochondrial antibody titre, biochemical cholestasis and/or pathohistological finding. The data on the anamnestic and clinical characteristics of the patients were collected. HRQoL was assessed using of a validated PBC-40 questionnaire. Descriptive and analytical statistics are used. The t-test and One-way ANOVA were used to estimate the significance of the difference, while Pearson's correlation was used for correlation estimation. The determination of predictor variables of the total PBC-40 score was performed using multiple regression analysis.
Results: The study included 94 patients, with an average age of 59.26 ± 10.04 years. Of the total number of patients, 97.9% ($n = 92$) were women.
The score for the "Itch" domain is significantly higher (worse) in patients of the age ≤ 56 years than in older patients (5.36 ± 4.16 vs. 3.65 ± 3.66) ($p = 0.043$). Patients with edema have lower HRQoL for the domains "Emotional" (11.80 ± 3.11 vs. 7.09 ± 3.14) ($p = 0.002$) and "Social" (29.60 ± 9.99 vs. 19.83 ± 8.78) ($p = 0.018$). The score for the "Social" domain is significantly lower in patients on diuretics therapy (27.93 ± 9.33 vs. 19.00 ± 8.38) ($p = 0.018$). The score for the "Itch" domain positively correlates with the values of alkaline phosphatase (ALP) ($r = 0.335$; $p = 0.020$), gamma glutamyl transferase (GGT) ($r = 0.303$; $p = 0.040$) and alanine aminotransferase (ALT) ($r = 0.231$; $p = 0.028$). The "Fatigue" domain positively correlates with the value of ALP ($r = 0.274$; $p = 0.010$), while the domain "Social" correlates with prothrombin time ($r = 0.264$; $p = 0.024$). The value of the score for the "Emotional" domain significantly negatively correlates with serum albumin value ($r = -0.242$; $p = 0.033$).
A significant regression equation was obtained to determine the prediction of the total PBC-40 score ($F(1, 61) = 8.258$, $p = 0.006$) for $R^2 = 0.119$. Significant predictor of the total PBC-40 score is value of GGT ($\beta = 0.315$, $p = 0.006$).
Conclusion: HRQoL in patients with PBC are affected by: age, edema, diuretics, and some laboratory parameters. Significant predictor of total PBC-40 is GGT.
Disclosure: The study was conducted on the same sample as the validation of the Serbian version of the PBC-40 questionnaire (1).

Reference

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P0029 EFFECT OF THE PROPRANOLOL THERAPY ON THE INCIDENCE OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CIRRHOSIS: A RETROSPECTIVE OBSERVATIONAL STUDY IN A TERTIARY CENTER

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Introduction: Hepatocellular carsinoma (HCC) is the most frequent type of the primary malign tumors of the liver and at the same time it is the third most common cause of mortalities among all kind of cancers. Despite the recent advances in this field, new strategies are need for prevention of HCC.
Aims and Methods: The objective of this study is to determine the effect of propranolol on the incidence of HCC regarding patients with cirrhosis caused by various etiologies in our center.
Data from patients with cirrhosis caused by different etiologies (who were registered in a HCC surveillance program in our center between June 2011 and December 2017) were retrospectively studied and comparatively (patients taking propranolol therapy and those without propranolol therapy) analyzed.
Results: Total 231 patients (135 male (58.4%) and 96 female (41.6%)) were included in this study. The median age was 58.1 +/- 14 years and average cirrhosis period was 7.7 +/- 4 years. 153 (66.2%) patients had used propranolol and other 78 (33.3%) had not used. HCC progression was observed in 36 patients (15.6%). HCC evolution in patients undergoing propranolol treatment was 7.8% (12 patients) in response to 30.8% (24 patients) in those who were not taken propranolol ($p < 0.001$). According to this result, the incidence of HCC was 5.22 times greater in patients not taking propranolol with respect to those undergoing propranolol therapy.
Conclusion: Although the cirrhosis etiologies and onset phase of the illness were similar in both groups, HCC incidence was importantly lower in propranolol group with respect to the non-propranolol group. This result shows that propranolol theraphy has a protective effect on HCC in patients with cirrhosis.
Disclosure: Nothing to disclose

P0030 LIVER CIRRHOSIS AND LEFT VENTRICLE DIASTOLIC DYSFUNCTION: RETROSPECTIVE STUDY

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Introduction: Patients with liver cirrhosis are reported to have a hyperdynamic circulation, which manifests as a high cardiac output, decreased systemic vascular resistance, and widespread arterial vasodilatation. Based on studies, cirrhosis is associated with cardiovascular abnormalities. A definition "cirrhotic cardiomiopathy" had been proposed in 2005. It states that "cirrhotic cardiomyopathy is a form of chronic cardiac dysfunction in patients with cirrhosis, characterized by blunted contractile responsiveness to stress, and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of other known cardiac disease."
Aims and Methods: The aim of a research was to evaluate the association between diastolic dysfunction of letf ventricle and the severity of cirrhosis. 150 patients with diagnosed liver cirrhosis, waiting for the liver transplantation, were retrospectively analyzed between 2006 and 2015 at Vilnius University Santaros Clinics. Etiology of cirrhosis, Child-Pugh classification, Model for End-Stage liver disease score, echocardiographic indicators of diastolic dysfunction, concentrations of bilirubin, creatinine and albumin, international normalization ratio were recorded. Diastolic dysfunction was divided into 3 grades by increasing severity by American Society of Echocardiography 2016. Data were analyzed by SPPS v.19. A $p < 0.05$ was considered as statistically significant.
Results: Final statistical analysis included 47 patients. The majority of patients were men (66%), patients' mean age was 48.5 ± 1.175 years. All patients in our study had liver cirrhosis. Hepatitis C virus infection was the most common etiology of cirrhosis (38.3%). Normal diastolic function was presented in 20 (42.6%), first grade dysfunction in 7 (14.9%), second grade in 18 (38.3%) and third grade in 2 (4.3%) cirrhotic patients. There was a significant relation between diastolic function and age ($p = 0.039$; $r = 0.3$), Model for End-Stage liver disease ($p = 0.007$, $r = 0.4$).
Conclusion: According to the relation between diastolic dysfunction and Model for End-Stage liver disease score, we recommend cardiac assessment in patients with higher Model for End-Stage liver disease scores.
Disclosure: Nothing to disclose

P0031 NON-INVASIVE PARAMETERS FOR ASSESSMENT OF ESOPHAGEAL VARICES

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Introduction: Bleeding from ruptured esophageal varices (EV) is the most severe complications of patients with liver cirrhosis and portal hypertension. Upper endoscopy is the golden standard for diagnosis of esophageal varices. Non-invasive diagnosis of esophageal varices in cirrhotic patients is beneficial because it help us to select the patients likely to have esophageal varices to do endoscopy for them.
Aims and Methods: The aim of this study was to assess esophageal varices by noninvasive parameters in patient with liver cirrhosis using some clinical, laboratory and ultra-sonographic parameters.
Methods: The study included 120 patients with liver cirrhosis of various etiologies from Menoufia University Hospitals (Egypt) and 20 healthy volunteers as controls. They underwent physical examination and laboratory investigations (CBC, liver profile {ALT, AST, serum albumin, bilirubin, PT %} and creatinine). Abdominal ultrasound and upper endoscopy were done for all patients. Child-Pugh score, MELD score, AST/Platelet ratio index (APRI score), Platelet count/spleen diameter ratio (PC/SD) and NIEC Index were calculated for all patients.
Results: Serum albumin at cutoff less than 3.65gm/dl is significant in prediction of EV with sensitivity 70% and specificity 86.2%. Platelet count at cutoff less than 99000/mm^3 is significant in prediction of EV with sensitivity 87.5% and specificity 55%. PC/SD ratio at cutoff less than 919.6 is significant in prediction of EV with sensitivity 57.5% and specificity 95%. APRI score at cutoff cut off greater than 1.14 is significant in prediction of EV with sensitivity 68.8% and specificity 65%. Spleen longitudinal diameter at cutoff more than 140.5 mm is significant in prediction of EV with sensitivity 73.8% and specificity 70%. Portal vein diameter (PVD) at cutoff more than 15.2 mm is significant in prediction of EV with sensitivity 62.5% and specificity 90%. Prothrombin time at cutoff more than 15.1 second is significant in prediction of EV with sensitivity 63.8% and specificity 82.5%. NIEC Index at cutoff more than 25.4 is significant in prediction of variceal bleeding risk with sensitivity 90% and specificity 50%. Platelet count at cutoff less than 74000/mm^3 is significant in prediction of variceal bleeding risk with sensitivity 82.5% and specificity 55%. PC/SD ratio at cutoff 851.6 is significant in prediction of variceal bleeding risk with sensitivity 45% and specificity 90%. Multiple logistic regression analysis of risk factors of development of esophageal varices revealed that serum albumin, prothrombin time, PC/SD ratio and PVD are significant predictors for development of esophageal varices. Multiple logistic regression analysis of risk factors of variceal bleeding revealed that NIEC index is the most significant predictor for variceal bleeding.
Conclusion: Non-invasive predictors for presence of esophageal varices in patients with liver cirrhosis provide a method for selecting patients for endoscopic screening based on laboratory, clinical and ultrasonographic variables such as serum albumin, platelet count, PC/SD ratio, APRI score, SLD, PVD, prothrombin time and Child-Pugh score. Therefore, the number of unnecessary endoscopies will be reduced. NIEC Index, platelet count and PC/SD ratio can provide information help in prediction of variceal bleeding risk in patients with liver cirrhosis.
Disclosure: Nothing to disclose

P0032 LONG-TERM PREVENTION OF OVERT HEPATIC ENCEPHALOPATHY IS POSSIBLE WITH LACTULOSE ALONE BUT MORE EFFECTIVE IF COMBINED WITH RIFAXIMIN: A SYSTEMATIC REVIEW WITH NUMBER NEEDED TO TREAT ANALYSES OF RANDOMISED CONTROLLED TRIALS

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Introduction: Overt hepatic encephalopathy (OHE) is a serious complication of liver cirrhosis and it occurs in 30–40% of these patients. Frequent hospitalisations and a high mortality rate make prevention essential. Thus, patients should be offered the most effective treatment available. Previous systematic reviews have aggregated both treatment and prevention plus different time scales. This more focused systematic review analysed the long term OHE-preventive efficacy of lactulose versus its combination with rifaximin. An NNT analysis was also performed to understand the clinical relevance of the efficacy outcomes.
Aims and Methods: PubMed was searched for titles and abstracts published by 16 November 2017. Search terms were: 'hepatic encephalopathy + rifaximin' and 'hepatic encephalopathy + lactulose'. Randomised controlled trials with long-term (≥6 months) effectiveness and/or safety/tolerability endpoints for lactulose and/or rifaximin were selected for NNT analysis if statistically significant between-group differences were reported in the rate of OHE recurrence. Studies of primary prophylaxis and different dosing regimens of rifaximin were excluded.
Results: A total of 570 articles including 201 with primary clinical data were identified. Long-term treatment was reported in 8 articles for lactulose alone and in 19 articles for rifaximin, alone or in combination with lactulose. NNTs were calculated from 5 studies (Table 1). Lactulose prevented OHE episodes versus placebo or nothing, NNT [95% CI]: 3.28 [2.15, 6.90] and 3.68 [2.33, 8.75]. Combining lactulose with rifaximin prevented OHE episodes more than lactulose alone, NNT [95% CI]: 3.28 [2.27, 5.90] and 4.21 [2.93, 7.46]. Rifaximin alone offered additional prevention for some patients versus its combination with lactulose, NNT [95% CI]: 6.88 [3.50, 203.90].
Conclusion: In the systematic literature review of the long-term prevention of OHE, further clinical benefit is shown by adding rifaximin to lactulose than with lactulose alone. The number needed to treat to prevent a further recurrence of OHE improves the clinical relevance of this outcome.
[Table 1. Long term prevention of overt hepatic encephalopathy]

Study	Duration (months)	Treatment A	Treatment B	Number needed to treat, mean [95% CI]
Sharma 2009	12	Lactulose	Placebo	3.68 [2.33–8.75]
Agrawal 2012	14	Lactulose	Placebo	3.28 [2.15–6.90]
Bass 2010	6	Lactulose+rifaximin	Lactulose	4.21 [2.93–7.46]
Bajaj 2015	6	Lactulose+rifaximin	Lactulose	3.28 [2.27–5.90]
Neff 2012	12	Rifaximin	Lactulose+rifaximin	6.88 [3.50–203.90]

Disclosure: Marcus Schuchmann, advisory Boards and Speaker: Norgine, Abbvie, Gilead, Falk; Nadya Mason, employee of Norgine; Mark Hudson, speaker, consultant and an advisory board member for Norgine.

P0033 DERIVATION AND VALIDATION OF A STATISTICAL MODEL TO FORECAST THREE-MONTH, ALL CAUSE MORTALITY IN SUBJECTS ADMITTED WITH INCIDENT DIAGNOSIS OF CIRRHOSIS

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Introduction: For many patients the first presentation with cirrhosis is a non-elective admission with decompensation. In the UK, approximately only one-third survive. Prognostic scores including markers of liver synthetic function and complications of liver disease already exist (MELD, MELD sodium and Child Pugh score). The aim of this study was to develop a statistical model to identify those most at risk of death within 3 months of their first diagnosis, using both liver and more general metrics, that are recorded routinely in primary care in the UK population.
Aims and Methods: The data source used for this study was the Clinical Practice Research Datalink (CPRD) with corresponding Hospital Episode Statistics (HES). Data included demographics, diagnoses, symptoms, investigations, referrals and prescriptions, and routine hospital inpatient data. Incident cases of patients with cirrhosis were identified between 1998 and 2014. Cases were ≥18 years at diagnosis. Explanatory co-variates were included in a logistic regression model: age, gender, BMI, blood pressure, sodium, albumin, alcohol status and various measures of prior clinical morbidity to predict mortality within 3 months of diagnosis. Markers of coagulation were not included as they are not routinely measured in general practice. The model was validated using a confusion matrix and a receiver operator characteristic (ROC) curve.
Results: Of 17,012 subjects, 32% of patients died within 3 months of first diagnosis of ESLD. The most influential variable was ascites (aHR = 2.56 (2.34–2.81)) followed by a history of end stage renal disease (aHR = 1.81(1.65–1.98)). Patients with sodium < 125mmol/L had an aHR of 1.49 (1.02–2.18), albumin < 34 g/l had an increased aHR of 1.46 (1.32–1.62) and those with variceal bleeds had an increased aHR of 1.42 (1.11–1.81). The model had 64% accuracy and the ROC curve indicated that the model was correctly predicting mortality.
Conclusion: It was possible to create and validate a reliable model to characterise those people who are most likely to die within the first 3-months following incident diagnosis of cirrhosis, using parameters commonly recorded in routine clinical practice.
Disclosure: Craig J. Currie, Director of Pharmatelligence; Ellen Berni, employee of Pharmatelligence; James Orr, nothing to disclose; James Whitehouse, employee of Norgine, Daniel Murphy, employee of Norgine, Pete Conway, contractor of Pharmatelligence; Bharat Amlani, employee of Norgine; Mark Hudson, Speaker, Consultant and an Advisory board member for Norgine. Pharmatelligence, a research consultancy receiving funding from Norgine.

P0034 DERIVATION AND VALIDATION OF A STATISTICAL MODEL TO FORECAST LONG-TERM ALL-CAUSE MORTALITY IN PEOPLE WITH CIRRHOSIS

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Introduction: The objective of this study was to develop a time-dependent, statistical model to identify key factors that relate to mortality as cirrhosis progresses. MELD and MELD sodium are reliable measures of mortality risk derived from patients in the US. This study set out to see if the same key factors predict outcome in a population of patients with cirrhosis in the UK. The model considered a number of directly and indirectly recorded test results, and morbid effects whilst adjusting for damage to various organs.

Aims and Methods: The data source used for this study was the Clinical Practice Research Datalink (CPRD) with corresponding Hospital Episode Statistics (HES). Data included demographics, diagnoses, symptoms, investigations, prescriptions and routine hospital inpatient data. Incident cases of patients with cirrhosis were identified between 1998 and 2014. Cases were ≥18 years at diagnosis. Explanatory co-variates were included in a time-dependent Cox regression model including; age, gender, body mass index, systolic blood pressure, estimated glomerular filtration rate, sodium, albumin, bilirubin, units of alcohol consumed per week, cumulative number of liver admissions, cumulative number of infection admissions and presence of renal complications. All variables were included in the model as categorical variables in order to include all patients.

Results: The Cox regression model gave adjusted hazard ratios (aHR) for all variables included. The variable that had the greatest value in predicting death was sodium values less than 125mmol/L with aHR of 3.2 (95% CI; 2.5–4.2). Patients that were admitted for a renal complication had an increased aHR of 2.6 (95% CI; 2.1–3.3) and those with albumin >34 g/L had an increased aHR of 2.4 (2.18–2.67). Those with bilirubin >50 umol/L had an increased aHR to 1.74 (1.51–2.01) and those with an eGFR of 15–30 ml/min had an increased aHR of 1.64 (1.32–2.05). The model was validated using receiver operator curves (ROC) at 2, 3, 5 and 10 years following diagnosis of cirrhosis.

Conclusion: It was possible to build a reliable statistical model to forecast the likelihood of all-cause mortality in cirrhotic patients confirming the significance of hyponatraemia and renal dysfunction in the prognosis of patients with cirrhosis.

Disclosure: Craig J. Currie, Director of Pharmatelligence; Ellen Berni, employee of Pharmatelligence; James Orr, nothing to disclose; James Whitehouse, employee of Norgine, Daniel Murphy, employee of Norgine, Pete Conway, contractor of Pharmatelligence; Bharat Amlani, employee of Norgine; Mark Hudson, Speaker, Consultant and an Advisory board member for Norgine. Pharmatelligence, a research consultancy receiving funding from Norgine.

P0035 SAFETY AND EFFICACY OF RIFAXIMIN IN PROPHYLAXIS OF SPONTANEOUS BACTERIAL PERITONITIS: IS THIS TIME TO ABANDON FLUOROQUINOLONES FOR PREVENTION OF SPONTANEOUS BACTERIAL PERITONITIS?: A SYSTEMATIC REVIEW

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Introduction: The role of rifaximin in the prevention of spontaneous bacterial peritonitis (SBP) is not well studied.

Aims and Methods: The aim of this meta-analysis was to evaluate the role of rifaximin in the prevention of SBP.

A computerized literature search for relevant clinical trials was conducted during August 2017. Data on Frequency of SBP, the success rate of prevention of SBP, mortality rate, hepatorenal syndrome, septic shock, hepatic encephalopathy, and GIT bleeding were extracted and pooled as risk ratio (RR) with their 95% confidence interval (CI) in a meta-analysis model. Heterogeneity was assessed by Chi-square test.

Results: 6 studies involving 973 patients were included in the final analysis. The pooled effect estimate showed that the rifaximin plus norfloxacin group had less incidence of SBP (RR 0.58, 95% CI [0.37, 0.92], p = 0.02) and hepatic encephalopathy (RR 0.38, 95% CI [0.17, 0.84], p = 0.02) than the norfloxacin-based regimen group. No significant difference between rifaximin and norfloxacin in terms of frequency of SBP and success rate of primary prevention of SBP (RR 0.49, 95% CI [0.24, 1.01], p = 0.05; RR1.21, 95% CI [0.95, 1.55], p = 0.13, respectively).

Conclusion: Based on our analysis, Rifaximin is a promising drug and appears to be a good alternative to norfloxacin in prevention of SBP.

Disclosure: Nothing to disclose

P0036 EFFECTS OF FOOD AND CALCIUM CARBONATE ON PHARMACOKINETICS OF LUSUTROMBOPAG, A NOVEL THROMBOPOIETIN RECEPTOR AGONIST

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Introduction: Thrombocytopenia (TCP) is a common complication in chronic liver disease (CLD) patients, and hence TCP patients with CLD may benefit from access to approved pharmacotherapeutic options that will help raise platelet counts prior to undergoing planned invasive procedures. Lusutrombopag (LUSU) is a small-molecule orally active thrombopoietin receptor agonist discovered by Shionogi & Co., Ltd., and currently approved for use in Japan in this patient population. The aim of these studies was to assess the effects of food and calcium carbonate on the pharmacokinetics (PK) of LUSU in healthy subjects because a potential of drug-food interactions will affect the PK profiles and may inadvertently reduce or increase the drug effect. Not having a consistent treatment effect in raising platelet counts, CLD TCP patients may experience a delay or avoidance of a necessary invasive procedure.

Aims and Methods: 3 single-dose, open-label, and crossover studies were conducted. In Study 1, 18 healthy subjects were administered LUSU 2 mg as a 2-mg tablet in the fasted or fed state or the solution in the fasted state. In Study 2, 15 healthy subjects were administered LUSU 0.75 mg as 3 0.25-mg tablets in the fasted or fed state, or the fasted state with co-administration of calcium carbonate 4000 mg. In Study 3, 15 healthy subjects were administered LUSU 4 mg as a 4-mg tablet in the fasted or fed state. The PK parameters were estimated from plasma concentrations of LUSU in each treatment and compared between the treatments.

Results: Mean (90% confidence intervals) ratios of maximum plasma concentration and area under the plasma concentration-time curve were: for fed versus fasted, 0.90 (0.86–0.95) and 0.92 (0.89–0.96) in Study 1, 0.97 (0.86–1.09) and 1.02 (0.94–1.11) in Study 2, and 0.92 (0.84–1.00) and 0.91 (0.86–0.96) in Study 3, respectively; for calcium versus fasted, 1.08 (0.96–1.21) and 0.99 (0.91–1.07) in Study 2, respectively. No clinically significant effect of food or calcium carbonate on the bioavailability of LUSU was demonstrated. Each treatment was well tolerated.

Conclusion: No specific restrictions are required for LUSU administration with regard to meals (including those with dairy products), mineral supplements, or co-administration of antacids.

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P0037 INFECTIONS IN THE CIRRHOTIC PATIENTS AND THE IMPACT OF PROTON PUMP INHIBITORS

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Introduction: Liver cirrhosis (LC) is associated with a state of immunosuppression resulting in elevated risk of infection. Infections in the cirrhotic patient are one of the main causes of decompensation of the disease associating with high morbidity and mortality. Recent studies suggest that the use of proton pump inhibitors (PPI) increases this risk.

Aims and Methods: To characterize infections and agents isolated in patients with LC, to evaluate the impact of PPI therapy on the risk of infection and the impact of infection in the mortality rate.

Retrospective study of cirrhotic patients admitted for more than 48h in a tertiary center between 2014–2015. Group 1- with infection; group 2- without infection. Patients with hepatocellular carcinoma were excluded. We compared both groups for the outcomes: impact of Infection in transplant-free survival and impact of PPI on the risk of infection.

Results: 202 patients were included and 290 hospitalizations were analyzed. 77.7% were male with mean age of 60.3 ± 11.8 years. Infection was present in 187/290 hospitalizations (64.5%) (group 1). In both groups the most frequent etiologies of LC were: alcoholic (group 1- 51.6%, group 2- 61.8%) and HCV infection (group 1- 16.7%, group 2- 13.2%). At admission, group 1 presented higher severity of disease decompensation (group 1- Child-Pugh score B-48.4% and C-42.1% vs. group 2- Child-Pugh score B-53.4% and C- 24.3%[U1]). The most prevalent infections were: urinary tract (n = 90/187, 48.1%), pneumonia (n = 58/187, 31.0%) and spontaneous bacterial peritonitis (SBP) (n = 48/187, 25.7%). Sepsis was present in 32.1% (n = 60/187). Gram-negative agents were the most prevalent microorganisms in urinary infection (50%) and SBP (18.8%). PPI therapy was associated with higher prevalence of infection (75% vs. 65.6%, p = 0.016). We found no significant correlation between PPI and mortality rate (56.8% vs. 43.2%, p = 0.362). We found a trend for higher infection rate in patients under SBP prophylaxis (77.8%, n = 49/63 vs. 69%, n = 138/200, p = 0.205), including multiresistant strains (26.5% vs. 22.1%, p = 0.558).

Group 1 showed a trend to higher mortality rate (59.1% vs. 40%, p = 0.130). Mortality was also correlated with sepsis, bilirubin value, MELD-Na^{+} score and ECOG score (p = 0.05).
[U1]
Conclusion: Cirrhotic patients present a high rate of infections and this group present higher mortality rate. Our results suggest that PPI therapy is in fact, associated with higher risk of infection, which should lead us to be more strict in the indications of PPI's in these patients.
Disclosure: Nothing to disclose

P0038 ABCPS: A NEW SCORE PREDICTING IN-HOSPITAL MORTALITY IN CIRRHOTIC PATIENTS

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Introduction: Cirrhotic patients have high rates of hospital readmissions and mortality. Recently, a new score - ABCPS - has emerged and allows predicting in-hospital mortality in cirrhotic patients. To date, there are no cut-off values defined for this score.
Aims and Methods: The aim of the study was to evaluate the power of ABCPS in predicting in-hospital mortality and to define cut-off values for this score.
Retrospective study, including patients hospitalized for decompensated cirrhosis within 9 years. The ABCPS Score was calculated using the formula: 0.04 + 0.03 x albumin + 0.05 + 0.02 x Creatinin + 0.04 + 0.04 x Bilirubin + 0.05 + 0.28 x Potassium + 0.04 x 0.07 x Sodium.
Results: 362 patients included, 271 (74.9%) males with mean age of 57.4 ± 11.7 years. The majority of patients (85.9%) had alcoholic cirrhosis.
Ascites was present in 80.4% patients, hepatic encephalopathy in 39.8%, acute kidney injury in 31.8%, variceal bleeding in 12.4%, spontaneous bacterial peritonitis in 28.7%, other infections in 3% and hepato-renal syndrome in 3.6%.
The mean hospitalization time was 11.7 ± 10.5 days. In-hospital mortality was found in 85 patients (23.5%). The mean value of ABCPS was 2.17 ± 1.88.
The area under ROC curve (AUC) that predicts mortality for ABCPS score was 0.645 and the cut-off predictor for mortality was > 2.16 with sensitivity of 53% and specificity of 77%.
Patients with ABCPS > 2.16 presented higher mortality (39.1% vs. 16.2%, p < 0.001).
Conclusion: The ABCPS score is a tool to be used in the evaluation of cirrhotic hospitalized patients for its ability to predict in-hospital mortality. This study also allowed to determine cut-off values for this score.
Disclosure: Nothing to disclose

P0039 VALIDATION OF EXPANDED BAVENO VI CRITERIA FOR PREDICTING ESOPHAGEAL VARICES

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Introduction: According to Baveno VI, patients with chronic liver disease with platelets > 150,000 uL and liver stiffness measured by elastography < 20kPa can avoid upper endoscopy. These criteria were widely validated presenting high specificity but low sensitivity. Recently, Augustin S et al proposed expanded Baveno criteria (platelets > 110,000 uL and liver stiffness < 25).
Aims and Methods: Retrospective study of patients with chronic liver disease submitted to elastography between January 2013 and December 2015. Small varices with red wale marks or large varices were considered as high risk varices. The aim this study was to validate Baveno's expanded criteria in our center.
Results: A total of 104 patients were included; mean age 57 years, 69% male. The etiology of chronic liver disease was hepatitis C in 80%, alcohol in 12%, hepatitis B in 4% and other causes in 5%. The prevalence of varices was 25%.
Baveno's expanded criteria had a sensitivity of 92% and a specificity of 74% for the prediction of esophageal varices (100% and 62% Baveno's classical criteria). If we considered only high-risk varices the sensitivity of expanded criteria was 100% and sensitivity was 65% (100% and 50% classic criteria).
Conclusion: The expanded Baveno's criteria present similar sensibility as classic criteria but with higher specificity. In clinical practice, it continues to correctly identify patients with varices but decreases the number of potential screening endoscopies.
Disclosure: Nothing to disclose

P0040 RESISTANCE PATTERNS IN HOSPITAL-ACQUIRED URINARY TRACT INFECTIONS IN PATIENTS WITH LIVER CIRRHOSIS: SINGLE-CENTER EXPERIENCE

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Introduction: Decompensated cirrhosis patients are inherently immunocompromised and highly susceptible to bacterial infections due to translocation of gut flora and altered defense mechanisms. Healthcare-associated infections with multi-drug resistant (MDR) bacterial uropathogens in patients with cirrhosis have increased significantly over the last decades.
Aims and Methods: The aim of our study was to investigate rates of antimicrobial resistance among cirrhotic patients with hospital-acquired (HA) urinary tract infection (UTI) and to determine factors that significantly impact outcome associated with MDR infection.
Retrospective single-center surveillance analysis of microbiological isolates obtained from decompensated cirrhosis patients with HA UTI, defined as event on-set > 48 hours after admission, with pyuria and monomicrobial growth ≥ 105 CFU/ml on urine culture. Microbial susceptibility testing was performed using the Kirby-Bauer disk diffusion method. Isolated pathogens were classified as MDR if resistant to ≥ 1 drug from ≥ 3 groups of antibiotics. *In vitro* resistance to empiric therapy defined therapy failure. Independent predictors for MDR UTIs were identified with multivariate logistic regression.
Results: A total of 65 patients were included in the analysis. The mean age was 60.8 ± 11.3 years (range 39–84 years), 48 (73.8%) were males. All patients had decompensated liver disease, 21 (32.3%) CP class B, and 44 (67.7%) CP class C, with a mean MELD score of 21.88 ± 6.07, and a mean CLIF-C AD score of 88.34 ± 10.26. Ascites was seen in 55 (84.6%) patients, and 32 (49.9%) had hepatic encephalopathy either at admission or during hospitalization. 15 patients (23%) had a diagnosis of DM. 33 patients (50.8%) were catheterized. *Enterococcus* spp was the most common pathogen (52.3%), followed by *Klebsiella* spp (14.4%) and *Escherichia coli* (9.2%). 35 (53.8%) isolates were MDR. *Enterococcus* spp were more commonly non-MDR (n = 22, 64.7%, p = 0.003); Enterobacteriacae were mainly MDR strains (n = 18, 81.1%, p = 0.001). VRE was isolated on 7 occasions (20.6%), and 16 of the Enterobacteriacae isolates (72.7%) were ESBL-E. The overall resistance rates to ceftriaxone, ciprofloxacin, imipenem and meropenem were 93.1%, 80.0%, 47.2%, and 45.4%, respectively. Resistance to amikacin and gentamcin were 33.3% and 48.6%. Resistance to vancomycin and nitrofurantoin were 23.2% and 60.0%. Therapy failure was more frequent in patients with MDR UTIs (p = 0.039). In regression analysis, age > 65 years (OR 6.328, 95% CI 1.662–24.097, p = 0.007), cephalosporin prophylaxis (3.611, 1.815–17.239, p = 0.042) and hepatic encephalopathy (4.986, 1.437–17.304, p = 0.011), were independent predictors for MDR UTI.
Conclusion: Increase in antimicrobial resistance to commonly used antibiotics for treatment of bacterial infections in patients with cirrhosis contributes to high mortality and morbidity associated with these infections. It emphasizes the significance of early recognition and proper management of these infections by choosing appropriate antibiotic in order to reduce morbidity and mortality.
Disclosure: Nothing to disclose

P0041 ASSOCIATION OF GENETIC POLYMORPHISMS IN CHEMOKINES (CCL2 AND CCL5) AND CHEMOKINE RECEPTOR(CCR2) WITH THE OUTCOME OF HCV INFECTION IN EGYPTIAN FAMILIES: A MULTICENTER STUDY

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Introduction: Chemokines are major mediators of leukocyte trafficking into the sites of the immune response. Chemokine-induced signaling is mediated by a group of G protein-coupled receptors, They participate in defense against

microbial infection. Several functional polymorphisms of chemokine and chemokine receptor genes have been described that are able to deregulate chemokine system and, therefore, in HCV infection it was assumed that these polymorphisms may be associated with persistence or clearance of the virus.
Aims and Methods: This study was performed to investigate the association of single nucleotide polymorphisms (SNPs) of chemokines and chemokine receptor with the susceptibility to HCV infection in Egyptian families.
Methods: A total of 3014 subjects comprising 845 Egyptian families were recruited from The Upper and Lower Egypt governorates and were classified into 3 groups: 1460 patients with chronic HCV (CHC), 108 subjects with spontaneous virus clearance (SC), and 1446 subjects taken as a healthy control group. All subjects were genotyped for rs13900 C/T SNP of CCL2 gene, rs3817655 T/A SNP of CCL5 gene, and (rs743660 G/A, rs1799864 G/A) SNPs of CCR2gene using allelic discrimination real time PCR (RT-PCR) technique.
Results: The carriage of the allele A of CCR2 rs743660 and the allele A of CCR2 rs1799864 were significantly higher in the CHC (OR = 4.03 and OR = 1.97, respectively, $p < 0.0001$) when compared with both SC (OR = 4.03 and OR = 1.97, respectively, $p < 0.0001$) and control groups (OR = 1.42 and OR = 2.13, respectively, $p < 0.0001$) while the carriage of allele C of CCL2 rs13900 and the allele T of CCL5 rs3817655 were significantly higher in SC group when compared with both CHC (OR = 0.19 and OR = 0.24, respectively, $p < 0.0001$) and control group (OR = 0.65 and OR = 0.45 $p < 0.0001$ respectively)
Conclusion: Susceptibility to HCV infection is associated with A alleles of both(rs743660 and rs1799864 G/A) of CCR2 gene while SC of HCV is associated with C allele of rs13900 of CCL2 gene, and T allele of rs3817655 of CCL5 gene in the Egyptian families.
Disclosure: Nothing to disclose

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P0042 DENGUE HEPATITIS: A DIFFERENTIAL DIAGNOSIS TO REMEMBER IN EUROPE

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Introduction: Globally, there are 50 million infections per year from the dengue virus (DV) spread over 100 countries. With the documented dispersion of dengue fever, physicians from temperate climates such as Europe are finding more often travellers with this infectious disease that frequently affects the liver, sometimes with major impact. Indeed, DV has been implicated as an important cause of acute liver failure (ALF) in endemic countries. In addition, the secondary dengue mosquito, *Aedes albopictus*, has established in the Mediterranean region and the primary, *Aedes aegypti*, is on the verge of invading the southernmost parts of Europe.
Aims and Methods: We aimed to characterize the DV-induced hepatic alterations and the associated eventual mimickers of chronic liver disease.
Retrospective study in a southern-European hospital to identify all patients with a positive IgM antibody for DV in the last 6 years, using the laboratory data at the time of admission or first evaluation. In addition, diagnosis was further confirmed through positive DNA and/or a highly suggestive clinical picture and epidemiological context.
Results: Out of 2138 anti-DV IgM requests, we identified 1282 individuals with a positive result, including 279 under an age of 18 years old. Of the 1003 adults, 61.6% were female and the mean age was 45.2 years ± 16.7. Laboratory results revealed median adult haemoglobin levels of 13.9 g/dL ± 1.37, haematocrit 41.4% ± 4.05, leukocytes 4400/μL ± 2160, lymphocytes 31.5% ± 12.54, AST 112 U/L (13–1033), ALT 107 U/L (8–1220), total bilirubin 0.63 mg/dL (0.14–5.68), GGT 112 U/L (9–957), ALP 78 U/L (23–469), albumin 39 g/dL (20–51), urea mg/dL 26.9 ± 12.02, creatinine mg/dL 0.95 ± 0.22 and prothrombin time (PT) 14.9 seconds ± 4.02 (for an upper limit of normal (ULN) of 12.5 s). 62% of adult patients had AST > ALT while 68.7% had thrombocytopenia and only 4.1% of the tested patients had hyperbilirubinemia. A higher PT on admission was associated with a lower platelet count (mean = $133x10^3$/μL; $p = 0.003$) while a low albumin was significantly associated with higher age ($p = 0.019$), lower haemoglobin (0.001), ALP ($p = 0.023$) and sodium ($p = 0.027$).
Conclusion: Dengue virus hepatitis should be considered in any patient with fever within 14 days after any trip to tropics or subtropics, taking into account that the virus frequently induces thrombocytopenia in addition to elevation of transaminases that may be very significant, prolongation of PT/INR and rarely hyperbilirubinemia.
Dengue should also be considered in the differential diagnosis of acute liver failure and as an acute component of chronic liver disease, in the appropriate setting.
Disclosure: Nothing to disclose

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P0043 THE RELATION OF QUANTITATIVE INDICATORS OF PLASMACYTOID DENDRITIC CELLS IN THE BACKGROUND OF APPLICATION OF VARIOUS TREATMENT REGIMENS IN PATIENTS WITH CHC

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Introduction: The special role of plasmocytoid dendritic cells (pDCs) in the immunopathogenesis of CHC puts them in the first place, not only as the main producers of IFN, but also as direct participants in the interaction between innate and acquired immune responses. Therapeutic regimens using direct-acting antiviral agents (DAAs) have revolutionized the treatment of CHC patients, but long-term interaction of the immune system with the hepatitis C virus forms a close immunological relationship in the adaptation process, which leads to a change in the functioning both at the cellular and systemic levels. Changing the cellular response against the background of the therapy can dramatically affect the work of the immune system as a whole.
Aims and Methods: We examined 45 patients taking different regimens of CHC therapy. 27 of them received standard therapy and 18 people received DAAs. The amount of pDCs was determined by flow cytometry using monoclonal antibodies CD123 and CD 303.
Results: Quantitative indicators of pDCs have been reduced in all patients with CHC and vary depending on the type of CHC therapy. In patients treated with IFN, the absolute number of pDCs is 2 times lower (abs.−3.5) in comparison with the group receiving DAAs (abs.−6.2; $p = 0.007$). In the application of DAAs reduction of the absolute number of pDCs noted only on 4th week, whereas at the end of therapy (12 weeks - DAAs and 48 weeks - IFN) quantitative indicators pDCs did not differ (IFN: %−0.18, abs.−5.1; ADF: %−0.17, abs.−8.3; $p > 0.05$). According to catamnesis (patients examined after 12 months after the end of treatment CHC) pool pDCs after the use of drugs IFN was restored and did not differ from the indicators in healthy individuals (IFN: %−0.18, abs.−8.4; healthy: %−0.27, abs.−10.25; $p > 0.05$). The number of pDCs in DAAs as at the end of therapy, and in the history (%−0.18, abs.−9.5; $p > 0.05$) did not differ from those of healthy people.
Conclusion: pDCs values vary and depend on the type of therapy being performed. The use of DAAs leads to rapid eradication of the HC virus antigen from the body, which affects the dynamics of the pDCs pool and can lead to delayed changes in the immune system. Further observation and detailed study of this issue are needed.
Disclosure: Nothing to disclose

P0044 THE EFFECTIVENESS OF SOFOSBUVIR AND DACLATASVIR IN THE TREATMENT OF HEPATITIS C IN THALASSEMIA MAJOR PATIENTS AND THEIR EFFECT ON HEMATOLOGICAL FACTORS

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Introduction: Patients with thalassemia are at risk for infections such as Hepatitis C Virus (HCV) due to their repeated blood transfusions; meanwhile, the treatment of thalassemia patients who develop HCV infection is a controversial issue.
Aims and Methods: Although the effectiveness of Direct-Acting Antivirals (DAAs) on HCV infection has been confirmed, their side-effects as well as effects on hematological factors due to the resultant need for blood transfusion remain to be further understood.
This study examined 61 patients with major beta thalassemia and HCV infection who had a history of interferon treatment failure. The patients underwent a 24-week treatment with Sofosbuvir (SOF) and Daclatasvir (DAC). To assess the response to treatment, SVR12 was used. At the end of the study, the need for blood transfusion and serum ferritin were evaluated
Results: A total of 98.4% of the subjects responded to the treatment, and only one patient with genotype 1b did not respond positively. No significant complications necessitating treatment cessation were observed, and all the subjects tolerated the treatment well. The level of liver enzymes showed a significant reduction 12 weeks after the treatment. The need for blood transfusions in

patients before treatment was averagely 1.595 ± 0.65 bag per month, which received 1.593 ± 0.64 bags after treatment (p = 0.9). This regimen did not affect the amount of anemia in patients and did not differentiate the need for blood transfusions. The rate of hemoglobin before treatment was 9.5 ± 1.42 g/dl, which reached 9.6 ± 1.6 g/dl after treatment (p = 0.54). Ferritin levels decreased significantly in patients after treatment, and from 1948.08 ± 1539.54ng/ml to 1315.73 ± 1207.67ng/ml (p = 0.001).

Conclusion: The combination of Sofosbuvir and Daclatasvir is an effective and tolerable treatment regimen without affect the amount of anemia in patients and did not differentiate the need for blood transfusions.

Disclosure: Nothing to disclose

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P0045 REAL-WORLD DATA OF DIRECT-ACTING ANTIVIRALS FOR 2,063 JAPANESE CHRONIC HEPATITIS C PATIENTS: THE KYUSHU UNIVERSITY LIVER DISEASE STUDY GROUP (KULDS)

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Introduction: Little real-world data has been reported for Asians who have received interferon-free regimen with direct-acting antivirals for chronic hepatitis C.

Aims and Methods: Our large, multicenter, real-world cohort study of Japanese chronic hepatitis C patients was done to assess the effectiveness of Japan-approved direct-acting antiviral (DAA) treatment for patients who were both treatment-naïve and -experienced with or without compensated cirrhosis. This multicenter cohort consisted of 2,063 (GT1: 1,312, GT2: 751) consecutive Japanese patients who initiated a 12-week course of the following DAA treatment. Patients with under aged 20 years, decompensated cirrhosis, or co-infection with HBV/HIV were excluded: GT1: Sofosbuvir (SOF)/Ledipasvir (LDV) (n = 1,101), Ombitasvir (OBV)/Paritaprevir (PTV)/Ritonavir (r) (n = 106), Elbasvir (EBR)+Grazoprevir (GZR) (n = 223), GT2: Sofosbuvir (SOF)+Ribavirin (RBV) (n = 751). For GT1 patients, NS5A gene amino acid positions 31(L31I/F/M/V) and 93 (Y93C/F/H/N/S) were measured by direct-sequencing. These resistance associated variants (RAVs) were examined at baseline and at the time of relapse.

Results: The sustained virological response (SVR) rate of the GT1 patients who underwent SOF/LDV was 98.7%, only 14 relapsers (1.3%) were found, by intention-to-treat analysis. SVR rate of those with cirrhosis plus RAVs was 87.5%; ratio among all was just 6% (n = 53). The 14 relapsers included 5 with failure of Daclatasvir+Asunaprevir. The SVR rates of the GT1 patients who underwent OBT/PTV/r and EBZ+GZR were 98.1% and 99.1%, respectively, by intention-to-treat analysis. The SVR rate of the GT2 patients who underwent SOF+RBV was 96.4%, 27 non-SVR patients (3.6%) were found, by intention-to-treat analysis. SVR rate of those with cirrhosis plus treatment-experience was 86.0%; ratio among all was just 6.7% (n = 50).

Conclusion: Japan-approved DAA treatment for both HCV GT 1 and GT2 was exceptionally effective. However, NS5A RAVs undermined the virological effect for cirrhosis GT1 patients, and RBV-experience did the effect for cirrhosis GT2 patients.

Disclosure: Nothing to disclose

P0046 RISK OF RECURRENT HEPATOCELLULAR CARCINOMA AFTER HEPATITIS C VIRUS ELIMINATION FOLLOWING DIRECT-ACTING ANTI-VIRAL TREATMENT

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Introduction: Direct-acting antiviral agents (DAAs) have improved the treatment response for chronic hepatitis C virus (HCV) infection. Several predictive factors of de novo hepatocellular carcinoma (HCC) after sustained virological response (SVR) have been reported, including liver cirrhosis and serum alpha-fetoprotein (AFP) level.

Aims and Methods: The aim of this study was to evaluate the risk of recurrent HCC among patients with prior HCC who achieved SVR by DAAs. This retrospective multicenter study consisted of 759 consecutive patients who achieved SVR by treatment with interferon-free DAA regimens (Daclatasvir/Asunaprevir, Ombitasvir/Paritaprevir/ritonavir, Sofosbuvir/Ledipasvir, Elbasvir/Grazoprevir, Sofosbuvir/Ribavirin). Of these, 75 patients had prior HCC. The Kaplan-Meier method and Cox proportional hazard analysis were used to estimate the cumulative HCC incidence and predictive factors of developing HCC.

Results: The 1-, 2-, 3-year cumulative rates of HCC were 9.8%, 30.6%, 70.8% for the patients with prior HCC, while 1.1%, 2.9%, 7.4% for those without prior HCC (log-rank test: p < 0.001). Among the 75 patients with prior HCC who achieved SVR by DAAs, the median age was 73 years and 36 (48%) had cirrhosis. Median duration from the first HCC diagnosis to the initiation of antiviral therapy was 28.4 months and 29 (38.7%) had received HCC treatments two or more times. During the follow-up period (median: 23 months), 30 of 75 (40%) patients with prior HCC developed recurrent HCC. Univariate analysis showed that higher serum AFP level at the end of treatment (EOT-AFP), lower platelet count, longer duration from the first HCC and HCC treatments 2 or more times were associated with recurrent HCC. Multivariate analysis extracted only EOT-AFP as independent predictor of recurrent HCC (hazard ratio 1.02, 95% confidence interval 1.01–1.04, p < 0.001). In contrast, liver cirrhosis, sex, age and metabolic features were not associated with recurrent HCC. The 1, 2, 3-year cumulative rates of recurrent HCC were 23.7%, 50.8%, 75.4% for the patients with EOT-AFP 5.9ng/mL or more and 6.7%, 15.2%, 50.1% for those with EOT-AFP less than 5.9ng/mL, respectively (log-rank test: p = 0.012). The 1, 2, 3-year cumulative rates of recurrent HCC were 18.0%, 37.2%, 77.1% for cirrhosis patients and 5.3%, 24.6%, 62.9% for non-cirrhosis patients, respectively (log-rank test: p = 0.20).

Conclusion: For the patients with prior HCC, the risk of recurrent HCC after HCV elimination was very high. Serum EOT-AFP was significant predictor of HCC recurrence. However, even in the patients with low EOT-AFP or those without cirrhosis, the rate of recurrent HCC was still high. Duration and number of treatment from the first HCC may influence the rate of recurrent HCC. The patients with prior HCC should be considered for careful ongoing HCC surveillance.

Disclosure: Nothing to disclose

P0047 TREATMENT OUTCOME OF CHRONIC HEPATITIS C VIRUS (HCV) INFECTION WITH DIRECTLY ACTING ANTIVIRALS (DAA) IN PATIENTS WITH EXTRAHEPATIC MALIGNANCIES

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Introduction: Chronic HCV infection in patients with extrahepatic cancer results in mutual ill effects with respect to natural history and successful treatment of both the diseases. Availability of DAA make it possible to treat patient concomitantly for both HCV infection and cancer.

Aims and Methods: To assess the outcome of HCV treatment with DAA in patients with extrahepatic cancers either on treatment or completed treatment. A retrospective audit of Chronic HCV patients referred to Hepatology clinic in a leading cancer centre in India for the period of April 2015-December 2017 was done. Data were collected regarding demography, cancer site, cancer treatment, prior anti HCV treatment, current anti HCV treatment, adverse events, possible events of drug-drug interaction, status of underlying liver function and treatment response for anti HCV therapy. Treatment of HCV was prescribed in accordance with current AASLD/EASL guidelines and that of cancer as per NCCN/ESMO guidelines. Patient with Haemoglobin less than 10 gm/dl, Ribavirin (RBV) was avoided.

Results: Out of total 48 patients assessed 7 patients could not be followed up, 2 died during treatment and in 1 patient anti HCV treatment stopped before completion due to cancer progression. 38 patients were included in the analysis. 6 (16 %) patients were cirrhotic (Child Pugh A, n = 5; Child Pugh B-8, n = 1). 1 patient

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Parameters	**n = 38**
Age in years (Mean ± SD)	45.53(± 14.23)
Male/ Female	17(45%)/21(55%)
Genotype 1/3/4	10(26%)/27(72%)/1(2%)
Mean Baseline RNA (IU/ml)	> 500000 IU/ml
Concurrent cancer	Hematolymphoid, n = 10 (ALL, n = 4; Chronic myeloproliferative disease, n = 1; Plasma cell leukemia, n = 1; Plasmacytoma, n = 1; Non-Hodgkin's lymphoma, n = 2; Multiple myeloma, n = 1). Breast, n = 5. Genitourinary, n = 9 (Cervix cancer, n = 5; Ovarian cancer, n = 2; Uterine cancer, n = 1; Urinary bladder, n = 1). Gastrointestinal, n = 7 (Stomach adenocarcinoma, n = 4; Stomach GIST, n = 1; Colon cancer, n = 2). Head and neck region, n = 3 (Buccal mucosa squamous cell cancer, n = 2; Thyroid cancer, n = 1). Musculo-skeletal, n = 4 (Osteosarcoma, n = 1; Fibromatosis, n = 1; Rhabdomyosarcoma, n = 1; Paediatric neuro-ectodermal tumour, n = 1)
Comorbid conditions	Diabetes, n = 2; Hypertension, n = 2; Ischemic heart disease, n = 1
Anti HCV therapy	Sofosbuvir+Daclatasvir, n = 15 (39%); Sofosbuvir+Ledipasvir, n = 10 (26%); Sofosbuvir+Daclatasvir+Ribavirin, n = 3 (8%); Sofosbuvir+Velpatasvir, n = 4 (10%); Sofosbuvir+Ribavirin, n = 6 (15%)
Concurrent chemotherapy (n = 14)	CAPOX, n = 1; Paclitaxel-Carboplatin, n = 1; Paclitaxel, n = 2; Imatinib, n = 3; R-CHOP, n = 2; FOLFIRI, n = 1; Cyclophosphamide-Adriyamycin, n = 1; Gemcitabine-Carboplatin, n = 1; VCD,n = 2
Adverse events requiring drug modification of HCV therapy	Anaemia, n = 4 (44% among those receiving RBV, Overall 10%)
Adverse events not requiring drug modification of HCV therapy or cancer therapy	Dyspepsia, nausea or vomiting, n = 6 (15%); Constitutional, n = 2 (5%); Skin rash, n = 1 (2%)

was treatment experienced with PEG-IFN and RBV. Most common associated extrahepatic malignancies are hematolymphoid, gynaecological and gastrointestinal. 7 patients had HBV coinfection and all of them received concomitant anti HBV therapy and none had HBV flare. 1/3rd of patients received cancer therapy concomitantly with anti HCV therapy. The rest were under surveillance post cancer treatment. All 38 patients had achieved ETR and SVR 12. Overall adverse event rate was 34%. Most common being anaemia requiring modification of ribavirin therapy (n = 5). Other adverse events noted were skin rash, dyspepsia, nausea, occasional vomiting or constitutional symptoms, none of which required modification for either anti HCV therapy or cancer therapy. No drug -drug interaction was noted.
[Table 1]
Conclusion: Real-life data of concomitant cancer chemotherapy and DAA is scarce. This study demonstrates that SVR rate is excellent (100%) in this cohort of patients with chronic HCV infection. Concomitant cancer therapy and DAA are safe. Adverse events are not serious among most of the patients and usually does not mandates cessation of either cancer or HCV therapy. 90% of patients could tolerate full dose of RBV.
Disclosure: Nothing to disclose

P0048 COMPARISON OF THE LEVELS OF CIRCULATING MICRORNA-122 IN HCV-RELATED CIRRHOSIS PATIENTS WITH AND WITHOUT HEPATOCELLULAR CARCINOMA

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Introduction: miR-122 has the advantage of being hepato-specific. It plays a key role in HCV replication and its knockout in animal model proved to promote de novo hepatic carcinogenesis. To date miR-122 role in HCV-related HCC remains a matter of debate
Aims and Methods: The aim was to investigate the difference in expression levels of circulating miR-122 in cirrhotic HCV patients with and without hepatocellular carcinoma (HCC). We included 41 HCV-related cirrhotic patients recruited from Ain Shams University hospitals' clinics and in-patient department. Patients were divided into 2 groups: I) non-HCC group of 14 patients with different Child-Turcotte-Pugh (CTP) classes, II) HCV-related HCC group of 27 patients having different patterns of tumor aggression - classified using CT/MRI imaging features into low and high aggressive HCC patterns, defined as: a) Low aggression/ small sized focal HCC = single lesion < 2 cm or ≤ 3 nodules < 3 cm each, b) High aggression patterns either multicentric HCC (> coexisting 3 nodules) or infiltrative HCC (ill-defined large sized HCC with no focal mass formation).

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			Plasma miR-122 level (Ct value)		p value
			Mean	**SD**	
Age:	56.68 ± 7.35				0.317
Gender	Males (n = 31)	- Females (n = 10)	31.80–29.74	5.8–5.5	0.325
Study groups	Non-HCC (n = 14)		27.99	3.9	**0.002 (t = −3.26)**
	HCC (n = 27)		33.02	5.8	
CTP class	All patients				0.074
	Non-HCC group	Class A (n = 7)	27.05	2.8	0.691
		Class B (n = 6)	29.05	5.3	
		Class C (n = 1)	28.27	–	
	HCC group	Class A (n = 10)	30.79	6.1	0.321
		Class B (n = 5)	33.83	6.7	
		Class C (n = 12)	34.53	5.06	
Imaging criteria of tumor	Small sized focal HCC (n = 7)		27.49	5.69	**0.005 (F = 6.68)**
	Multicentric HCC (n = 9)		33.63	4.5	
	Infiltrative HCC (n = 11)		36.03	4.5	
ALT					0.060
AST					0.084
AFP					0.139

RNAs were extracted from plasma using (mirVana PARIS kit). Reverse-transcription (TaqMan microRNA RT Kit) and miRNA-specific stem-loop primers (has-miR-122) done according to instructions of the manufacturer. For real-time PCR, TaqMan MicroRNA Assay probe was used. The cycle threshold (Ct value) defined as the number of cycles required for the fluorescent signal to cross the threshold in qPCR and inversely correlates with the miRNA level
Results: There were significantly lower levels of circulating miR-122 in patients with HCC compared to non-HCC patients ($p = 0.002$). However, no significant differences were found regarding different CTP classes among all patients ($p = 0.074$), or within each group: HCC ($p = 0.69$) and non-HCC groups ($p = 0.32$). Regarding tumor aggression there were significantly lower levels of miR-122 for multicentric or Infiltrative HCC as compared to small sized focal HCC ($p = 0.02$, 0.001 respectively). No significant differences were found in respect to patients' gender, and no correlation was found with age, ALT, AST, or alpha-fetoprotein (AFP).
[Table 1: summary of miR-122 levels in our study.]
Conclusion: There were significantly lower miR-122 levels in patient with HCC on top of HCV related cirrhosis than patients with no HCC regardless of liver cirrhosis status, moreover, the levels were significantly lower in high aggressive patterns of HCC as compared to low aggressive patterns.
Disclosure: Nothing to disclose

P0049 PREVALENCE OF OCCULT HEPATITIS C INFECTION AMONG EGYPTIAN PATIENTS WITH SUSTAINED VIROLOGIC RESPONSE TREATED WITH SOFOSBUVIR/DACLATASVIR

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Introduction: The optimal goal of HCV treatment is to achieve SVR 12 weeks after treatment (SVR12). However, this term was appraised with the emergence of occult C infection (OCI) by detecting HCV-RNA in peripheral blood mononuclear cells (PBMCs), and/or other compartment.
Aims and Methods: To determine the prevalence of OCI in PBMCs in patients achieved SVR after sofosbuvir/daclatasvir therapy and to determine the different predictors of OCI persistence.
A cross-sectional study enrolled all consecutive patients with SVR12 between January 2017 to August 2017 post Sofosbuvir 400mg/ Daclatasvir 60mg for 12 weeks. Patients were either treatment naive or experienced to previous Interferon/ribavirin regimen. All patients were HCV genotype 4, compensated cirrhosis.
Basic laboratory and liver stiffness score measurements were done. PBMCs were obtained using Ficoll-Hypaque density gradient of EDTA anticoagulated blood according to the manufacturer's instructions (Lymphoflot, Biotest,Dreleich, Germany). HCV-RNA was tested for isolation from PBMCs in all patients.
Results: HCV RNA was detected in PBMC in 5 (3.9%) patients out of 128, all of them are experienced to Sofosbuvir/ Daclatasvir regimen, with advanced fibrosis score F3/F4 3/2 and have raised ALT at pre-treatment tests. Logistic regression analysis comparing OCI with Non OCI revealed Pre-treatment prolonged prothrombin time, low albumin level and advanced fibrosis are the most significant predictor of presence of OCI.
Conclusion: Occult hepatitis C infection post DAAs therapy is not uncommon finding and should be raised in patients with high fibrosis score and/or with non-normalized ALT post-treatment.
Disclosure: Nothing to disclose

P0050 DIRECTLY ACTING ANTIVIRALS ARE SAFE, EFFECTIVE AND NOT ASSOCIATED WITH TUMOR RECURRENCE IN HCV PATIENTS WITH NON-HEPATIC CANCER

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Introduction: Patients with chronic HCV infection can be cured of their disease with 8–12 weeks of DAA therapy. However, in patients with a history of hepatocellular carcinoma (HCC) there are concerns regarding an increased risk of HCC recurrence after sustained virological response (SVR) to DAA therapy. Although the reasons are still unclear, an altered immune control of pre-existing neoplasia deriving from the rapid clearance of the virus has been hypothesized. Little is known about the recurrence rate of non-hepatic tumors in HCV patients who received DAA.
Aims and Methods: Our aim was to evaluate the recurrence rate of non-hepatic neoplasia in consecutive HCV patients treated with DAA.
We included all consecutive HCV patients treated with DAA from February 2015 to January 2017 with solid non-hepatic tumor diagnosed in the 5 years before the start of antiviral therapy. For breast cancers no time limit was fixed. Patients with hematological malignancies were excluded. All tumors had achieved complete control before starting DAA treatment.
Results: 313 HCV patients were treated with DAA and 20 (6.4%) had a positive anamnesis for solid non-hepatic tumor. 6 patients had a history of breast cancer, 4 gastrointestinal tumors, 2 non-melanoma skin cancer, 5 uro-genital cancers, 1 spinocellular carcinoma of the oral cavity, 1 pituitary and 1 lung tumor. Median time from cancer diagnosis to DAA was 3.7 years and patients were followed-up for a median of 22.38 months after DAA therapy. No patient underwent DAA treatment concomitantly with chemotherapy. Median age at DAA therapy was 67.66 years and 45% were men. 65% were genotype 1, 15% genotype 2, 10% genotype 3 and 10% genotype 4. 70% had evidence of cirrhosis, well compensated in everyone (CPT score A). An SVR was achieved in 19 patients (95%), and no serious adverse events were reported. During a median of 22.38 months after DAA therapy no patient included in the study had cancer recurrence.
Conclusion: HCV treatment in patients with solid non-hepatic tumors is safe and effective. Although findings are preliminary, an SVR to DAA therapy was not associated with any case of tumor recurrence.
Disclosure: Nothing to disclose

P0051 DO WE SCREEN HEPATITIS C BEFORE SURGERY FOR THE BENEFIT OF THE SURGEON OR FOR THE PATIENT?

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Introduction: The success rate of anti-viral treatments of hepatitis C infection now approaches 100%. Therefore, it is important to conduct community screenings and raise awareness. Pre-operative hepatitis serology is routinely considered in most countries of the World.
Aims and Methods: We aimed to detect the prevelance of anti-HCV and HCV-RNA positivity rate in patients undergoing pre-operative HCV screening and also the awareness rate of having chronic hepatitis C infection in these patients. Patients who had pre-operative anti-HCV testing in surgical clinics of our hospital were screened from 2013 to 2017. All patients who were positive were questioned for HCV-RNA positivity and whether they were treated for hepatitis C. Hospital records were screened for HCV-RNA results. Treatments reports were reached through the integred database system of social security with our hospital. HCV-RNA untested patients were called by phone and asked whether they were aware of being anti-HCV positive.
Results: During 5 years, 21897 patients were screened for hepatitis C. A total of 125 patients (0.57 %) were found to be positive (58M, 67F, mean age 59.1 ± 15.7) HCV-RNA was tested in 76 of these patients, 22 were HCV- RNA negative(29%), 24 were positive and treatment-naive, 19 were positive and treatment experienced. From 125 patients with Anti-HCV positivity, 49 patients had no HCV-RNA assay (39%), we called them by phone and noticed that just 5 (10 %) patients knew that he/she was anti-HCV positive.
Conclusion: Anti-HCV positivity was detected in approximately 0.6% of 21897 patients who were operated in surgical departments of a tertiary medical center. Approximately 40% were not tested for HCV - RNA and most of these patients were not aware of being Anti-HCV positivity. Testing hepatitis C serology before surgery seems that do not contribute to catch new patients. Surgeons need to be more aware towards chronic hepatitis C infection.
Disclosure: Nothing to disclose

P0052 PREVALENCE OF HEPATO-BILIARY MANIFESTATION IN IBD

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Introduction: The IBD are frequently associated to the extra intestinal manifestation: dermatologic, ophthalmic, hepato-biliary. We observed a high prevalence of hepato-biliary manifestation in IBD (up to 50%) and one of the most serious complication is PSC. We also noted various pathogenesis of these hepato-biliary abnormality; the common pathogenesis of IBD, direct or indirect complication of IBD.
Aims and Methods: The aim of our study is, first of all, to assess the frequency of hepato-biliary manifestation on the IBD, and secondly to study clinical, advancement characteristics of IBD and liver disease occurrency. In our study, we have removed the abnormal transient liver test and the drug which caused hepatitis. This retrospective study concerned the population with IBD of the occurrence's liver disease during period: 2000 - 2013. Initially, all the patients get a clinical, biological and morphological investigation, and also a clinical, biological and endoscopic during active colitis. All the patients with permanent abnormal liver test got a complementary and etiologic investigation.

Results: We observed 686 patients with IBD; 459 Crohn's disease and 227 ulcerative colitis with a mean age of 42,5 years (24 years - 61 years). During the follow up, we noted 3.2% liver disease, among them: 13 cases of Crohn's disease (8 male - 5 female), 9 cases of ulcerative colitis (6 male- 3 female). 18 cases of liver disease was reveal by abnormal liver test, 3 cases by portal hypertension, and one by jaundnice. All the investigation were determinated :14 PSC, 3 steatosis, 1 peliosis, 1 overlap syndrome (HAI + PSC). Clinical and morphological characteristic study revealed that hepato-biliary manifestation are more common for male patient and also in ileo-colonic, pan-colitis forms. The IBD is the most of the time chronically active with growing period for more than 5 years.
Conclusion: The hepato-biliary manifestation are rare, they are generally revealed by abnormal liver test which occurred the most often on long lasting and extensive IBD and PSC represented the most frequent etiology.
Disclosure: Nothing to disclose

P0053 CHANGE IN BILIRUBIN WITH OBETICHOLIC ACID TREATMENT IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH HIGH BASELINE BILIRUBIN: A RETROSPECTIVE ANALYSIS OF POISE, 201, AND 202

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Introduction: In patients with primary biliary cholangitis (PBC), bilirubin (BILI) is a recognized marker of disease progression and a strong predictor of survival. Recently, the Global PBC Study Group reported the risk with elevated BILI extends into the normal range with a cutoff of 0.67x ULN identifying patients at risk. Obeticholic acid (OCA) is indicated for treatment of PBC in patients with an inadequate response or intolerability to ursodeoxycholic acid.
Aims and Methods: The aim of this retrospective analysis was to evaluate the effect of OCA on BILI in this patient subpopulation. OCA has been evaluated in patients with PBC in 1 12-month Phase 3 double-blind (DB) placebo (PBO)-controlled trial (POISE) and 2 3-month Phase 2 PBO-controlled trials (201 and 202). Patients were eligible to continue treatment in open-label extensions (OLE) with all patients receiving OCA. Patients from the Phase 2 and 3 studies with baseline (BL) total BILI (TBILI) ≥0.67x ULN were evaluated for change in TBILI over 12 months in the following manner: 1) DB comparison of OCA vs. PBO at 12 months in POISE and 2) DB+OLE OCA use totaling 1 year of treatment (POISE randomized to PBO, evaluated at 12 months OLE; Phase 2 randomized to OCA for 3 months, evaluated at 9 months OLE; and Phase 2 randomized to PBO, evaluated at 12 months OLE).
Results: The analysis included patients with TBILI ≥0.67x ULN at their OCA BL: POISE, n = 51; 201, n = 7; and 202, n = 7. In patients with BL TBILI ≥0.67x ULN, TBILI increased after 12 months of PBO treatment, and decreased after 12 months of OCA (Table 1). In the DB phase of POISE, of the 7 PBO-treated and 9 OCA-treated patients with abnormal TBILI at BL, 14% of PBO-treated and 78% of OCA-treated patients attained normal TBILI levels after 12 months. Further, of 10 PBO-treated and 20 OCA-treated patients with normal TBILI at BL, 60% of PBO-treated and 15% of OCA-treated patients worsened to abnormal TBILI after 12 months.
Conclusion: Patients treated with OCA had a trend toward reduction of TBILI compared with those treated with PBO. These data suggest that OCA may reduce progression of patients with more advanced liver disease.
[Table 1. Mean (SD) Change From BL in TBILI (μmol/L) in Patients with BL TBILI ≥0.67x ULN]

12 Month Treatment	PBO	OCA				
Phase	DB			OLE		
Study	POISE			201	202	POISE
Dose (mg)	–	5 to 10	10	10 or 50	10, 25, or 50	5 to 10
n	17	15	14	7	7	17
Mean (SD) change from BL to TBILI	2.6 (6.5)	−3.3 (3.6)	−4.0 (7.8)	−8.1 (6.4)	−10.1 (8.1)	−1.6 (7.9)

OCA BL is defined as: - OCA-randomized patients: if time from last visit in DB to first visit in OLE ≤30 days, mean of evaluations prior to first DB dose is used; if ≥30 days, last assessment prior to first dose in OLE is used; the initial OLE visit is included as a BL evaluation. -PBO-randomized patients: last assessment prior to first dose in OLE is used; initial OLE visit is included as baseline evaluation.

Disclosure: This study was funded by Intercept Pharmaceuticals, Inc.

P0054 DEVIATIONS IN PERIPHERAL BLOOD SUBPOPULATIONS ARE CONNECTED WITH THE PRESENCE OF PRURITUS IN PRIMARY BILIARY CHOLANGITIS PATIENTS

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Introduction: Primary biliary cholangitis (PBC) constitutes an autoimmune liver disease characterized by progressive destruction of small- and medium-sized intrahepatic bile ducts. The role of particular peripheral blood (PB) subpopulations in the course of PBC remains still uncertain. Bile acids, endogenous opioids, autotaxin and lysophosphatidic acid (a potent itch neuron activator) seem to have a key role in the pathogenesis of cholestatic pruritus in PBC patients. However, there is a growing body of evidence that PB subsets are of great importance in pathological appearance of this liver disease.
Aims and Methods: The aim of our study was to assess the relationships between analyzed peripheral blood cell subsets and the presence of pruritus in patients with newly diagnosed PBC. The frequencies of PB subpopulations were measured by flow cytometry in 34 previously untreated female patients with PBC. 19 participants from research group presented pruritus. The control group consisted of 20 healthy age- and sex-matched volunteers. The diagnosis of PBC was based on the commonly known criteria. The severity of pruritus was assessed according to Visual Analogue Scale (VAS) questionnaire and the mean result was 4.1/10 points. The degree of severity of PBC was evaluated by histologic stages of PBC. This parameter was described in all patients and they were divided into 4 groups, according to histologic stages of PBC (I - portal stage - 7 patients, II - periportal stage - 16 patients, III - septal stage - 9 patients and IV - cirrhotic stage - 2 patients). Before the initiation of treatment of PBC, lymphocyte subsets, values of PB cell count parameters, and immunoglobulin serum levels were measured.
Results: PBC patients complaining of pruritus had significantly lower percentages of CD3+/CD16+CD56+ NKT-like cells ($p = 0.04$) and CD3+ T lymphocytes ($p = 0.03$) than PBC patients without pruritus. Additionally, PBC patients with itch presented significantly lower absolute counts of CD4+/CD3+ cells ($p = 0.01$) and CD3+CD25+ cells ($p = 0.03$) in comparison to PBC patients without itch. Percentages of CD3+/CD16+CD56+ NKT-like cells and absolute counts of CD3+CD25+ cells were significantly higher in PBC patients compared to controls ($p < 0.01$). There were no significant differences in percentages of CD3+ T lymphocytes and absolute counts of CD4+/CD3+ cells between research and control group.
Conclusion: The results obtained in our survey suggest that deviations in PB subsets might be involved in the pathogenesis of cholestatic pruritus in PBC patients and this issue should be undoubtedly clarified in further studies.
Disclosure: Nothing to disclose

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P0055 A NOVEL UK REGIONAL REAL-WORLD REGISTRY FOR PRIMARY BILIARY CHOLANGITIS (PBC) ALLOWING DATA LINKAGE FROM PRIMARY AND SECONDARY CARE

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Introduction: PBC is a model autoimmune liver disease affecting approximately 35/100,000 population. Data for PBC and rare diseases appears scarce, fragmented. Coordinated efforts are required to bring various datasets together to provide integrated care for patients. A real-world registry linking primary and secondary care for PBC does not exist.
Aims and Methods: Following ethical approval, a regional observational feasibility study was set up collecting data from 3 regional hospitals and 10 primary care providers (General Practice surgeries) in the region of Surrey South East England, UK which has a population 1.1 million. From primary care, data was collected using READ codes and 725 data points were collected for each patient. In secondary care, data was collected from multiple sources including histology, fibroscan, immunology, biochemistry, virology, endoscopy, patient workflow systems, patient notes/letters, radiology and hospital coding departments. A total of 286 data points were collected for each patient. The datasets from primary and secondary care were linked for each patient using a unique patient identifier (NHS number) which was hashed using a pseudonymisation algorithm.
Results: A total of 375 patients with confirmed PBC were identified in primary and secondary care giving a regional PBC prevalence of 34.1/100,000 population. All patients from primary care were successfully linked to secondary care providing a holistic overview of the patients' journey and the disease's natural history.

Conclusion: Our novel method of establishing a rare disease registry for PBC is able to link datasets from various sources which are otherwise found in disjointed silos. Our registry is collecting more data points than existing PBC registries and does not rely on manual data entry from time-stretched clinicians and nurses which can affect data quality and lead to errors. This robust methodology has enabled us to generate real-world data on a large number of PBC patients and better understand the natural history and regional impact of this rare condition. Moreover, it will inform the development of regional frameworks for integrated care which are currently lacking for PBC and for rare liver diseases. This work will complement the efforts of larger consortia including UK-PBC and GlobalPBC.
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P0056 THE EFFECTIVENESS OF STANDARD TREATMENT ON CHRONIC AND ACUTE PRESENTATION-AUTOIMMUNE HEPATITIS MAY BE SIMILAR

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Introduction: At present, many studies are still controversial for the response of acute presentation-AIH (A-AIH) after immunosuppressive treatment. Some studies reported that acute presentation-AIH had a worse response than chronic AIH (C-AIH) due to its more severe liver injury
Aims and Methods: Our study analyzed the effectiveness of standard treatment (corticosteroids alone or combined with azathioprine) between A-AIH and C-AIH. First, we collected patients prospectively according to the International Autoimmune Hepatitis Group (IAIHG) revised score and the experience of hepatologists. Patients who had a probable diagnosis (IAIHG score $\geq$10) of AIH were included in our study. And all of these patients were treated with standard treatment. Patients who were concurrent with other liver diseases or used other immunosuppressive agents were excluded. Then, all the patients were divided into the A-AIH group and the C-AIH group. Patients in A-AIH group needed to meet at least 1 of the following conditions: (1) total bilirubin $\geq$ 5mg/dL; (2) alanine aminotransferase $\geq$ x 10 upper limits of normal (ULN), or (3) aspartate transaminase $\geq$ x 10 ULN. Finally, the complete biochemical remission rate, time of reaching complete biochemical remission and mortality of the 2 groups were retrospectively analyzed.
Results: 88 patients were included in our study, of which 48 patients were in the A-AIH group and 40 patients in the C-AIH group. The follow-up period was 0.3–33.1 months. There was no statistical difference in the rates of complete biochemical remission between A-AIH group and C-AIH group (50%, 55%, $p = 0.640$). The median time of reaching complete biochemical remission was 3.2 (1.3, 9.2) months in A-AIH group, while that in the C-AIH group was 2.4 (1.3, 4.6) months, and there was still no significant difference ($p = 0.474$). During the follow-up, 9 patients were dead owe to hepatic decompensation, of which 5 (10.4%) patients were A-AIH and 4 (10%) patients were C-AIH ($p = 1.000$).
Conclusion: Although the serum bilirubin and aminotransferase were obviously increased in A-AIH patients, the response after standard treatment of A-AIH may not be significantly different from that of C-AIH. Moreover, the different level of serum biochemical indicators may not be the most important factor influenced prognosis for neither A-AIH or C-AIH.
Disclosure: Nothing to disclose

P0057 URSODEOXYCHOLIC ACID FOR THE TREATMENT OF PRIMARY BILIARY CIRRHOSIS/CHOLANGITIS AND PRIMARY SCLEROSING CHOLANGITIS: ARE OUR PATIENTS UNDERDOSED?

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Introduction: Ursodeoxycholic Acid (UDCA) is used to treat the cholestatic liver diseases primary biliary cirrhosis/cholangitis (PBC) and primary sclerosing cholangitis (PSC). Current guidance states an optimum dose of UDCA is 13–15mg/kg in PBC, with the same dose used but not specifically recommended in PSC. A survey undertaken by the PBC Foundation in 2013 implied a third of patients were underdosed. Optimal dosing of UDCA leads to improved biochemical reposes in both PBC and PSC patients, and delayed disease progression and reduced transplant rates in PBC.
Aims and Methods: The objective of this study was to assess whether locally, our patients are optimally dosed on UDCA (using the upper end 15mg/kg) and whether this has had any impact on their biochemical response to treatment.
A database of outpatient correspondence was searched for the terms "primary biliary cirrhosis", "primary biliary cholangitis" and "primary sclerosing cholangitis". 85 patients were identified with a confirmed diagnosis of PBC or PSC (antibody positive or biopsy proven). 7 patients were excluded from the study as they had not yet been commenced on UDCA, leaving 78 treated patients (59 PBC, 19 PSC). Using the most recently documented weight around time of diagnosis/commencement of treatment, optimum doses of 15mg/kg were calculated for each patient and compared to the actual dose prescribed. Biochemical response was assessed using the Barcelona Criteria - either greater than 40% reduction in alkaline phosphatase (ALP) or normal after 1 year of UDCA treatment.
Results: Of the 78 patients, 33 (42%) were found to be at least optimally dosed at 15mg/kg, with 45 patients (58%) underdosed on UDCA. In the optimally dosed group, 19 patients (58%) showed biochemical response, and 9 patients (27%) had a worsening of their ALP (1 identified as non-compliant). The remaining 5 patients (15%) had a normal ALP at the time of commencing, which remained normal to date.
In the suboptimally dosed group, 20 patients (44%) showed biochemical response, with 16 patients (36%) having a worsening in their ALP and 9 patients (20%) having had a normal ALP at diagnosis which again remained normal to date. 71% of patients with PBC responded to UDCA compared to 53% of those with PSC.
Conclusion: This study shows that a higher proportion of our local patient group diagnosed with PBC or PSC are underdosed with UDCA than optimally dosed. We have demonstrated in this group that UDCA appears effective in improving biochemical response to treatment or at least maintaining a normal ALP, when used at the optimum dose, supporting a drive towards ensuring patients are prescribed 15mg/kg of UDCA. Interestingly there was still a partial response to treatment despite underdosage, and all patients who had normal baseline ALP maintained this regardless of UDCA dose. This may generally imply efficacy of UDCA in the treatment of PBC and PSC. Looking at potential reasons for underdosing, it was identified in some cases that patients' weight had changed (mainly increased) but not led to a subsequent adjustment of UDCA dose, raising the importance of regularly reviewing the dose (especially if there has been no adequate biochemical response), as well as reviewing compliance. Lastly the results suggested a better response to UDCA overall in PBC compared to PSC, correlating with current literature. It would be useful to perform this analysis again following dose adjustment for the suboptimal group, and reviewing the dose for our optimally dosed but non-responsive group, in the hope that a positive effect is seen leading to an improvement in their overall outcome.
Disclosure: Nothing to disclose

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P0058 DIAGNOSIS OF TYPICAL FOCAL NODULAR HYPERPLASIA IN THE LIVER - USE OF A NOVEL ULTRASONIC VASCULAR DOPPLER TECHNIQUE

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Introduction: Examination of vascular structures and flow dynamics is important in order to differentiate benign from malignant focal liver lesions (FLL). Diagnostic ultrasound in combination with contrast-enhanced ultrasound (CEUS) has a high accuracy and diagnostic value for FLL (1,2). CEUS ideally allows the visualization of the very specific spoke wheel pattern in the arterial phase and is standard of reference (SOR) in the diagnosis of FNH smaller 3 cm (3). Conventional colour Doppler has limitations in visualizing microvasculature and low velocity blood flow. Superb Micro-Vascular Imaging (SMI) is a novel ultrasound Doppler technique with high resolution imaging, minimal motion artefacts and high frame rates. SMI has not been studied in FNH lesions, which have a unique vascular supply that is diagnostic in most cases. Diagnosis of this benign FLL is important to avoid unnecessary biopsies and surgical procedures. In contrast to hepatocellular adenoma, the management of FNH is conservative because there is no risk of malignant transformation, no risk of bleeding and no need to stop contraception (4,5).
Aims and Methods: The diagnostic value of the novel SMI technique for diagnosing FNH lesions in comparison to CEUS was studied. SMI offers a unique algorithm allowing visualization of microvasculature with low velocity flow without the need of a contrast agent. SMI analyzes clutter motion and uses a new adaptive algorithm to identify and remove tissue motion and reveal true blood flow. CEUS was performed as standard of reference by using 1.5 ml intravenously injected contrast agent (sulphur hexafluoride microbubbles) and was performed according to international guidelines (1). Representative still images and video clips were recorded.
Results: We present a case series of 5 female patients between 25 and 55 years with FNH. CEUS revealed in almost all cases FNH with typical early centrifugal arterial spoke-wheel enhancement without washout up to 5 minutes after injection of the contrast agent. We could demonstrate the excellent visualization of

the spoke wheel-like vessels by SMI (without contrast agent and independently to time response). SOR was resection/histology (n = 2), MRI (n = 1) and follow-up 12–18 months (n = 2).

Conclusion: FNH is the second most common benign liver tumor after hemangioma. FNH is diagnosed by CEUS, CT or MRI using intravenous contrast agents. This is the first european experience demonstrating the excellent clinical value of SMI to diagnose typical FNH with spoke-wheel-like vessels. SMI is an easy to use, intuitive imaging tool without the need of contrast agent that offers a detailed visualization of small, low-velocity vessels within FNH lesions. In the presented cases, SMI was able to provide the same diagnostic imaging criteria for FNH as CEUS in the arterial phase. In contrast to SMI, CEUS and especially CT and MRI require early arterial contrast enhancement, which may be missed due to a short detection period of sometimes only a few seconds.

Disclosure: Nothing to disclose

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P0059 COMPARISON OF THE DIAGNOSTIC ACCURACIES OF MAGNETIC RESONANCE TECHNIQUE AND TRANSIENT ELASTOGRAPHY FOR EVALUATING HEPATIC STEATOSIS IN NONALCOHOLIC FATTY LIVER DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Noninvasive methods have been used for the assessment of hepatic steatosis in patients with nonalcoholic fatty liver disease (NAFLD). Magnetic resonance derived measures, such as proton density fat fraction (PDFF) and fat fraction (FF), and transient elastography based controlled attenuation parameter (CAP) of liver fat and volume are emerging as non-invasive, accurate imaging biomarkers.

Aims and Methods: We performed this systematic review and meta-analysis to compare the efficacies and accuracies between magnetic resonance technique and transient elastography for evaluation of hepatic steatosis in NAFLD patients. PubMed, the Cochrane Library, Embase and Web of science were searched to gather studies, relating to accuracies of MR technique or TE for evaluating grading of steatosis (S0-S3) diagnosed by liver biopsy. We compared the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and hierarchical summary receiver operating characteristic (HSROC) curves of these 2 methods for grading of steatosis. The clinical utilities of MR technique and TE were also evaluated.

Results: 19 articles with a total of 1558 NAFLD subjects were included. As for diagnostic accuracy of MR based PDFF, the summary sensitivities and specificities values were 0.92 (95% CI, 0.88–0.95) and 0.93 (95% CI, 0.88–0.97) for ≥ S1, 0.76 (95% CI, 0.71–0.80) and 0.88 (95% CI, 0.84–0.91) for ≥ S2, and 0.73 (95% CI, 0.68–0.78) and 0.89 (95% CI, 0.86–0.92) for ≥ S3. The HSROCs were 0.96 for ≥ S1, 0.91 for ≥ S2, and 0.89 for ≥ S3. Following a positive measurement (over the threshold value) for ≥ S1, ≥ S2, and ≥ S3, the corresponding post-test probabilities for the presence of steatosis (pretest probability was 50%) were 93%, 87% and 87%, respectively; if the values were below these thresholds (negative results), the post-test probabilities were 14%, 7%, and 7%, respectively. The diagnostic accuracy of MR based fat fraction(FF) for stage ≥ S1, the summary sensitivity was 0.92 (95% CI, 0.87–0.95), and the specificity was 0.82 (95% CI, 0.76–0.87). Besides, the HSROC is 0.9260. For diagnostic accuracy of TE-CAP detecting stage ≥ S1, ≥ S2, ≥ S3, the summary sensitivity was 0.79 (95% CI, 0.67–0.89), 0.80 (95% CI, 0.75–0.84), 0.81 (95% CI, 0.78–0.84), and the specificity was 0.83 (95% CI, 0.80–0.96), 0.74 (95% CI, 0.70–0.78), 0.66 (95% CI, 0.59–0.73), respectively. Following a positive measurement (over the threshold value) for ≥ S1, ≥ S2, and ≥ S3, the corresponding post-test probabilities for the presence of steatosis (pretest probability was 50%) were 86%, 76% and 71%, respectively; if the values were below these thresholds (negative results), the post-test probabilities were 16%, 18%, and 18%, respectively.

Conclusion: MR technique and TE both provide standardized non-invasive approaches for staging hepatic steatosis in NAFLD patients. Compared with TE based CAP, MRI derived PDFF is significantly more accurate for evaluating dichotomized grades of steatosis, especially in those obese patients, which probably offer the best diagnostic performance and may be used instead of invasive liver biopsies.

Disclosure: Nothing to disclose

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P0060 PORTAL HYPERTENSION IN CIRRHOTIC PATIENTS WITH HEPATITIS B VIRUS: DIAGNOSTIC ACCURACY OF LIVER AND SPLEEN STIFFNESS BY SHEAR WAVE ELASTOGRAPHY

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Introduction: Portal hypertension is the main cause of bleeding from ruptured esophageal and gastric varices that may lead to death. Timely and accurate diagnosis of portal hypertension is of primary importance on the choice of treatment strategies and on the judgment of prognosis. Hepatic venous pressure gradient (HVPG) has been accepted as the gold standard for evaluating portal pressure [1]. But this method is limited in clinical applications because of its invasiveness, expensiveness, high requirements for equipment and techniques, and difficulty in follow-up. To explore and verify noninvasive methods in diagnosing portal hypertension becomes a hot issue in medical research. Real-time shear wave elastography (SWE) is a newly developed technique used to evaluate tissue elasticity. Previous studies suggested that SWE has excellent performance in the diagnosis of liver fibrosis and cirrhosis in chronic hepatitis B ([2]). Moreover, SWE may be more reliable in patients with ascites than noninvasive methods. Based on previous study results, the objective of this project is to further explore the diagnostic accuracy of SWE and its derived models in assessment of portal hypertension, aiming to provide new ideas and alternatives for clinical noninvasive evaluation of portal hypertension.

Aims and Methods: To assess the diagnostic accuracy of liver and spleen stiffness by shear wave elastography (SWE) and its derived models in assessment of predicting clinically significant portal hypertension (CSPH) and severe portal hypertension (SPH).

Clinical data of 135 cirrhotic patients who underwent assessment of portal pressure and endoscopic examination before starting prophylactic treatment were consecutively collected. Liver stiffness measurement (LSM) and spleen stiffness measurement (SSM) was measured with SWE by repeated performance 5 times per patient and the average values of stiffness were collected. The correlation between LSM, SSM and hepatic venous pressure gradient (HVPG) were assessed. The diagnostic accuracy of LSM, SSM and composite scores as the liver stiffness-spleen diameter to platelet ratio score (LSPS) and the portal hypertension (PH) risk score were evaluated, and also compared with other noninvasive parameters including the aspartate-to-platelet ratio index (APRI) and the platelet count/spleen diameter ratio. CSPH and SPH were defined as a HVPG ≥ 10 mmHg and ≥12 mmHg.

Results: A total of 104 patients were eligible for analysis. CSPH and SPH were detected in 84 patients (80.7%) and 74 patients (71.2%) respectively. LSM and SSM were significantly corrected with HVPG in overall, CSPH and SPH patients ($r1 = 0.627$, 0.554 and 0.412; $r2 = 0.665$, 0.565 and 0.476, respectively; all $p < 0.001$). The AUROC of LSM, SSM and LSPS and the PH risk score was 0.72 (95% Cl, 0.49–0.95), 0.78 (95% Cl, 0.51–0.93), 0.76 (95% Cl, 0.51–0.96), and 0.73 (95% Cl, 0.55–0.88) for CSPH and 0.77 (95% Cl, 0.51–0.97), 0.79 (95% Cl, 0.55–0.94), 0.81 (95% Cl, 0.58–0.98), and 0.80 (95% Cl, 0.59–0.93) for SPH, respectively. The diagnostic performance was significantly better than that of other noninvasive parameters. The cut-off values of LSM for determining CSPH and SPH were 16.1 kPa (Sensitivity, 81%; Specificity, 80%) and 23.5 Kpa (Sensitivity, 83%; Specificity, 81%), respectively. The cut-off values of SSM for determining CSPH and SPH were 25.3 kPa (Sensitivity, 83%; Specificity, 79%) and 33.4 Kpa (Sensitivity, 82%; Specificity, 80%), respectively.

Conclusion: In cirrhotic patients with hepatic B virus, LSM and SSM and composite scores by SWE is a reliable non-invasive diagnosis tool to predict CSPH and SPH.

Disclosure: Nothing to disclose

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P0061 PREDICTIVE FACTORS OF HEPATIC ENCEPHALOPATY AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT - TEN YEARS OF EXPERIENCE OF A PORTUGUESE CENTER

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Introduction: Many complications can occur during Transjugular Intrahepatic Portosystemic Shunt (TIPS) implantation procedure. However, the most relevant clinical complication is hepatic encephalopthy (HE).
Aims and Methods: The aim of this study was to assess TIPS indications, sucess rates and related complications. The secondary goal was to identify predictive factors of HE after TIPS.
We present a restrospective unicenter cohort study from October 2007 to January 2018 including patients undergoing TIPS procedure on a Portuguese referral center. Portal pressure gradients before and after TIPS were only recorded from January 2015.
Results: 180 patients were included (76.1% male; mean age 55.03 ± 10.99 years (21–79 years)). Portal pressure gradients were recorded in 61 patients.
Primary liver disease was alcoholic in 59.44%, alcoholic/viral in 15%, viral in 11.1% and due to other causes in 10.56%. The indications for TIPS were: refractory ascitis (52.78%), recurrent upper gastrointestinal bleeding (17.78%), acute upper gastrointestinal bleeding (11.1%), hepatic hydrothorax (0.56%) and Budd-Chiari syndrome (0.56%). 17.22% of the patients had more than 1 indication for TIPS procedure.
Technical success rate was 91.67% (n = 165). Hemodynamic success rate (since January 2015) was 82.86% in patients with refractory ascitis and 100% in patients with upper gastrointestinal bleeding.
3.33% had immediate TIPS-related complications: hemoperitoneum (1.11%); haemorrhagic shock (0.56%); porto-biliary fistula (0.56%); cervical haematoma (0.56%) and anestesia complications (0.56%).
After TIPS, 49.44% (n = 89) patients with refractory ascitis had improved and 5.56% (n = 10) patients had a rebleending episode. HE after TIPS was seen in 44.4% (n = 80) of the patients (26.7% newly installed, 13.3% maintained and 4.4% worsened). It was found that patients with HE "de novo" or worsened were older (58.2 vs. 53.6, p = 0.09).
Higher severity scores (MELD and Child-Turcotte-Pugh) and non-sclerosis hemostasis were not associated with a higher occurrence of HE (p > 0.05). However, a portal pressure gradient ≤5mmHg demonstrated a higher risk of HE (10/16 Vs 13/45, p = 0.017).
Conclusion: The success rates were over 80%. HE was a frequent complication. Older age and portal pressure gradient≤5mmHg were associated with a higher risk of HE after TIPS.
Disclosure: Nothing to disclose

P0062 INTER-OBSERVER REPRODUCIBILITY OF VTQ (ARFI TECHNIQUE) FOR THE EVALUATION OF FOCAL LIVER LESIONS STIFFNESS

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Introduction: Several studies showed that VTQ (Virtual Touch Quantification) provides additional information regarding FLLs stiffness and it is useful when differentiating between malignant and benign FLLs.
Aims and Methods: We aimed toevaluate inter-observer reproducibility of a point shear wave elastography- pSWE [using Acoustic Radiation Force Impulse Quantification (ARFI)]: VTQ (Siemens) for the evaluation of focal liver lesions stiffness.
We performed a prospective study including 44 patients diagnosed with focal liver lesions (FLLs) after an ultrasound examination admitted to the Department of Gastroenterology of SCJUT between January 2017-December 2017: 23 men (52.3%) and 21 women (47.7%), mean age 65.3 ± 11.1 years. A total of 48 FLLs were examined.
Elastographic measurements (EM) were obtained in 48 FLLs using VTQ (Siemens). 2 examiners with different levels of experience in ultrasound-based elastography, performed EM using VTQ on each subject: 10 measurements in the liver parenchyma and 10 measurements in each focal liver lesion. Medians and interquartile ranges (IQRs) were calculated (m/s). We used the interclass correlation coefficient (ICC) with 95%b lower and upper limits of agreement (LOA) to assess the inter-observer reproducibility of VTQ.
Results: A total of 48 lesions were evaluated. The lesions were: 32/48 (72.7%) hepatocellular carcinomas, 7/48 (14.5%) hemangiomas, and 9/48 (18.7%) metastases. The total mean values obtained were: 1.62 m/s in HCCs, 2 m/s in hemangiomas and 2.62 m/s in metastases. The agreement between the novice and the experienced examiner was excellent: 0.950 (95% CI: 0.91–0.972).
Conclusion: The excellent ICCs for the median values show that ARFI technique with VTQ for evaluating FLL stiffness is a reproducible method and could provide significant complementary information regarding the tissue stiffness, useful for the differential diagnosis of focal solid liver lesions.
Disclosure: Nothing to disclose

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P0063 RECTUS ABDOMINIS ULTRASOUND MAY DETECT SARCOPENIA AND PREDICT SURVIVAL IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Sarcopenia may affect patients with liver cirrhosis. It is associated with a poorer quality of life and higher morbidity and mortality.
Aims and Methods: We aimed to evaluate the value of ultrasound measured psoas major (PM) and rectus abdominis (RA) thickness in predicting survival of patients with liver cirrhosis**.** 61 patients were included in a prospective study in a 16-month period and followed-up for at least 6 months. Sarcopenia was assessed using surrogate parameters - handgrip strength (HGS), mid-arm muscle circumference (MAMC) and SGA (subjective global assessment) score.
Results: There were 40 men, with a mean age of 58.03 ± 10.8 years. 26.22% of patients were Child-Pugh A, 45.9% B and 27.86% C. Patients were followed-up for 11.9 ± 5.63 months.
Mean RA (mRA) was 8.73 ± 2.57mm. RA thickness moderately correlated with MAMC (r = 0. 596, p < 0.0001) and HGS (r = 0.515, p < 0.0001) and decreased with increasing SGA class (A 10.6 ± 2.8mm, B 8.3 ± 1.9mm, C 6.5 ± 1.9mm, p < 0.0001).
Survival at 6 months was independently predicted by MELD-Na score (OR 1.305, p = 0.005). Survival during follow-up was independently predicted by mRA (HR 0.701, p = 0.011, AUROC 0.732) and ascites (HR 1.876, p = 0.026, AUROC 0.732). A cut-off of mRA less than 6.75mm had 50% sensitivity and 93% specificity to predict mortality in patients with liver cirrhosis.
Conclusion: As a surrogate marker of sarcopenia, ultrasound measured rectus abdominis muscle may predict survival in patients with liver cirrhosis.
Disclosure: Nothing to disclose

P0064 TRUE SEVERITY OF LIVER STEATOSIS AND FIBROSIS IN TYPE 2 DIABETES MELLITIUS PATIENTS

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Introduction: Prevalence of type II diabetes has significantly increased in the last decade.
Type II diabetes and nonalcoholic fatty liver disease (NAFLD) are frequently associated.
Aims and Methods: The aim of the present study was to assess the severity of liver fibrosis and steatosis in a cohort of type II diabetic patients, using non-invasive methods: Transient Elastography (TE) and Controlled Attenuation Parameter (CAP) before and after the CAP adjustment algorithm was applied. The study included 576 type II diabetic patients, who were prospectively randomized. All were evaluated by means of TE and CAP (FibroScan EchoSens). A cut-off value of 10.5 kPa [1] was used to define clinically relevant fibrosis (F≥3). We used the following cut-off values [2]: for S2 (moderate steatosis) - 255 dB/m, and 290 dB/m for S3 (severe steatosis) - We corrected the CAP values according to the presence of diabetes (we deducted 10 dB/m) and according to the degree of obesity (we deducted 4.4 dB/m for each BMI > 25 kg/m^2 and added 4.4 dB/m for each BMI < 25 kg/m^2) [1, 3].
Results: Out of 576 diabetics screened, we excluded those with associated viral hepatitis, those with an AUDIT-C score ≥8 and those with unreliable LSM. The final analysis included 403 subjects (59.3% women, BMI = 31.6 ± 6 kg/m^2) with reliable LSM obtained using both probes. Moderate and severe steatosis by means of CAP was found in 18.9% and 61.5% cases respectively. After correction, we found moderate steatosis in 22.1% cases and severe steatosis in 52.6%

cases. We found no significant differences regarding the proportion of patients with moderate steatosis after the algorithm was applied (18.9 vs. 22.1%, $p = 0.26$), but we found significant differences regarding the proportion of severe steatosis, (61.5% vs. 52.6%, $p = 0.01$). Clinically relevant fibrosis was detected by means of TE in 13.6% (55/403) of subjects.
Conclusion: In type 2 diabetes patients it is necessary to use an algorithm for correction in order to avoid overestimation of the degree of steatosis and fibrosis.
Disclosure: Nothing to disclose

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P0065 SEGMENTAL DISTRIBUTION OF HEPATOCELLULAR CARCINOMA CORRELATES WITH MICROVASCULAR INVASIONS IN LIVER EXPLANTS (UNDERGOING TRANSPLANTATION)

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Introduction: The microvascular invasion (MVI) in hepatocellular carcinoma (HCC) patients is a poor prognostic factor for survival after liver transplantation and/or resection. Any correlation between MVI and segmental location of HCC has yet to be studied.
Aims and Methods: Our aim is to evaluate the location of HCC and its correlation with the presence of microvascular invasion, recurrence of HCC and portal vein thrombosis (PVT) in explanted liver. Another objective of the study is to assess the treatment history (ablation or transarterial chemoembolization (TACE)) and size of the tumor with respect to the risk of MVI.
This is a single-center, retrospective chart review, including 98 patients with the age of 18 years and older who had liver transplantation in our institute between 2012 and 2017. We reviewed the radiological images of the HCC, the pathological findings of the explanted liver and the follow up imaging after transplantations.
Results: 98 patients with the diagnosis of HCC underwent liver transplantation between 2012 and 2017. The mean age of the cohort was 63 ± 8.2. Males represented 75% of the cohort and 25% were females. Caucasian race was representing 75% of the cohort. The average MELD score was 13.5+/- 6.5. The most common etiology of cirrhosis was chronic hepatitis C virus infection followed by alcohol abuse and non-alcoholic steatohepatitis (NASH) with percentages of 50%, 23% and 10% respectively. Microvascular invasion was found in 16% of the patients while recurrence of HCC and PVT was found in 6% and 17% of the cohort respectively.
MVI was found in 10 single HCC and 6 multifocal HCC. Right sided HCC had more MVI when compared to the left and multilobar HCC with percentages of 11%, 2%, 3% respectively.
Localization of HCC in segment 8 was associated with the highest percentage of MVI when compared to all other segments. The risk of MVI in segment 8 was 3.5 times higher than the risk of the other segments ($p = 0.002$) while no vascular invasion was found in segments 1, 3 and 5. The risk of vascular invasion in the untreated HCC is 3 times the risk in treated HCC ($p = 0.03$).
[Table 1]

HCC	Microvascular invasion	Odd ratio	P-value
Single	10	1.5	0.3
Multifocal	6	0.6	0.3
Size > 2 cm	10	0.4	0.6
Segment 4	1	1.3	0.6
Segment 6	2	2	0.19
Segment 8	6	3.5	0.002
Segment 2	1	1.3	0.7
Treated	6	0.3	0.03
Untreated	10	3.0	0.03

Conclusion: Our data indicate that the risk of microvascular invasion is higher in segment 8 HCC and in the untreated HCC. The size and the number of the HCC were not associated with an increased risk of microvascular invasion.
Disclosure: Nothing to disclose

P0066 TRANSIENT ELASTOGRAPHY AS A PREDICTOR OF DE NOVO HEPATOCELLULAR CARCINOMA (HCC) DEVELOPMENT IN CIRRHOTIC PATIENTS WITH CHRONIC HEPATITIS C TREATED WITH DIRECT ACTING ANTIVIRAL DRUGS (DAAS)

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Introduction: Hepatocellular carcinoma is a common health burden in cirrhotic patients with HCV infection. New direct-acting antivirals substantially improved the cure rate to above 90%. However, cancer risk persists even after 10 years of viral cure. Several risk-predictive host factors e.g., advanced liver fibrosis, older age, co-morbid metabolic diseases such as diabetes, persisting hepatic inflammation, and elevated alpha-fetoprotein were associated with HCC development. Transient Elastography is a widely available non-invasive marker of fibrosis which can be a reliable method of fibrosis assessment and risk stratification.
Aims and Methods: We aimed to evaluate Liver stiffness measurement by transient elastography as a predictor of HCC development after direct acting antiviral drugs (DAAs).
All patients with HCV related fibrosis who did FibroScanTM before treatment with DAAs were included retrospectively. Liver, renal function tests, CBC, INR, alpha-fetoprotien, abdominal ultrasonography, Triphasic CT, and FibroScanTM were performed at the National Liver Institute, Menofia University from January 2015 to December 2016. Patients who had a Transient Elastography measurement before treatment with DAAs were included and divided into 2 groups; Group (I) patients who developed de novo HCC and Group (II) are those who did not developed HCC after DAAs.
Results: Patients who developed de novo HCC after DAAs (group I, 30 patients) had higher serum AST levels (68.3 ± 38.2 vs. 48.7 ± 32.4 U/L), lower platelet count (131.5 ± 55.6 vs. $179.5 \pm 69.8 \times 10^3$ /μL) and older age (59.5 ± 6.4 vs. 51.3 ± 10.5 years) than patients who did not develop HCC (group II, 90 patients) with $p < 0.05$. Group I patients had a statistically significant higher liver stiffness measurement (LSM) by FibroscanTM (32.1 ± 10.7 vs. 15.5 ± 11.5 kPa, $p = 0.001$) than patients who did not develop HCC. With a cutoff of 18.5 kPa being the most predictive value of de novo HCC development after treatment of chronic HCV infection with DAAs (90.0% sensitivity, 80.0% specificity, 55.0% PPV, 97.3% NPV, 80.0% accuracy).
Conclusion: The measurement of liver stiffness by FibroScanTM could be a reliable method for risk stratification and prediction of de novo HCC development after DAAs in cirrhotic patients.
Disclosure: Nothing to disclose

P0067 SERUM PEROXIREDOXIN - 3 AS A USEFUL BIOMARKER FOR DETECTION OF HEPATOCELLULAR CARCINOMA

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Introduction: HCC is a major type of primary liver cancer and one of the most frequent human malignant neoplasms. It is estimated to cause more than a quarter of a million deaths each year throughout the world. The increased prevalence of HCC is related to the prevalence of hepatitis B virus and hepatitis C virus infections. Because of the very high prevalence of HCV in the Egyptian population, it accounts for most chronic liver disease and HCC cases.
Aims and Methods: This study was conducted to verify the reliability of serum peroxiredoxin-3 (PRDX-3) as a marker for diagnosis of HCC
The study included 20 patients with liver cirrhosis (cirrhotic group) and 20 patients with liver cirrhosis and HCC (HCC group) from Menoufia University Hospitals (Egypt) and 10 healthy volunteers as a control group. They underwent physical examination and laboratory investigations (CBC, liver profile {ALT, AST, albumin, bilirubin, PT %}, blood urea, serum creatinine, AFP and serum peroxiredoxin-3 (PRDX-3)). Abdominal ultrasonography was done for all patients. HCC is further confirmed by triphasic CT.
Results: AFP level of HCC group (846.7 ± 820.2 ng/dl) was significantly higher than cirrhotic group (17.1 ± 14.1 ng/dl) and controls (4.5 ± 1.1 ng/dl) ($p = 0.0001$). Serum PRDX-3 level of HCC group (285.1 ± 127.8 ng/dl) was significantly higher than cirrhotic group (120.4 ± 72.6 ng/dl) and controls (46.9 ± 19.1 ng/dl) ($p = 0.0001$). Serum PRDX-3 in cirrhotic group was significantly higher than that of controls ($p = 0.0001$).
At a cut off value of 162 ng/ml, serum PRDX3 showed a high AUC of (0.877) with sensitivity of 84.2%, specificity of 79.8%, compared to AUC of AFP (0.721) with sensitivity of 70.1%, specificity of 60%. The combined use of PRDX3 and AFP raised the sensitivity to 90% and the specificity to 84% with diagnostic accuracy of 91.2%. There was positive correlation between PRDX3 and serum AFP level ($r = 0.88$ and $p = 0.0001$) and the focal lesion size ($r = 0.61$ and $p = 0.004$).
Conclusion: PRDX-3 is more sensitive and more specific than AFP in diagnosis of HCC. Serum PRDX-3 level could be a valuable marker for detection of HCC in patients with liver cirrhosis.
Disclosure: Nothing to disclose

P0068 MODIFIED ALBI-T SCORE AS PROGNOSTIC MODEL IN THE EVALUATION OF PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Introduction: ALBI score eliminates the need for the subjective variables required in the CTP grade. The addition of tumor characteristics from TNM classification resulted in ALBI-T score. ALBI grade 2 showed a wide range of patients, Ogasawara sub classification of ALBI grade 2 classifies patients more precisely.
Aims and Methods: We accrued data from the HCC clinic at National Liver Institute, Menoufia University. We had access to a data set of a cohort of 1910 patients diagnosed with HCC and fulfilled the inclusion criteria. Patients were followed up from the time of diagnosis to the date of death or date of data collection if they remained alive. Modified ALBI-T was obtained through using new grading of ALBI score (grade 1 to 4 instead of grade 1 to 3) obtained through Ogasawara sub-classification of ALBI grade 2 and using it in calculating ALBI-T score. We compared our score to other scoring systems as CTP, TNM, BCLC, ALBI, PALBI, ALBI incorporated BCLC and ALBI-T scores.
Results: For 1910 patients, the mean age was 57 years, 1575 were males. At presentation, 50.6% were CTP A, 36.1% were CTP B and 13.4 % were CTP C. Most of the patients were ALBI grade 2 (63.2%), 17.8 % were ALBI grade 2A while 45.5% were ALBI grade 2B. ALBI grade 1 & 3 were 12% & 24.7% respectively. The overall median survival was 13 months; the median survival was better in patients with ALBI grade 1 than ALBI 2 & 3 (28.6, 14 and 5.8 months respectively, $p < 0.001$). Moreover, the median survival for ALBI grade 2A patients was better than ALBI 2B (18.6 vs. 13 months respectively, $p < 0.001$). ALBI-T grades 0 & 1 patients had better median survival than those of ALBI-T grades 2, 3, 4 & 5 (42, 24.4, 17, 8.9, 5 and 3 months respectively ($p < 0.001$)). On adding the ALBI sub classification proposed by Ogasawara, the modified ALBI-T showed significant improvement in the median survival of modified ALBI-T grades 2, 3, 4, 5 and 6 to be 28.6, 20.9, 13.9, 8 and 4 months respectively. On comparing our model to CTP, TNM, ALBI, BCLC, ALBI (modified), PALBI, ALBI based BCLC and ALBI-T, it showed significantly better AUC (0.818 vs. 0.643, 0.620, 0.709, 0.713, 0.719, 0.734, 0.749 and 0.803, respectively).
Conclusion: Modified ALBI-T classifies patients with HCC more precisely than other scoring systems.
Disclosure: Nothing to disclose

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P0069 THE ALBI AND P-ALBI GRADES PREDICT SURVIVAL IN PATIENTS WITH HEPATOCELLULAR CARCINOMA UNDERGOING TRANSARTERIAL CHEMOEMBOLIZATION (TACE)

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Introduction: The prognosis of hepatocellular carcinoma is influenced by severity of liver disfunction. Child-Pugh (CPS) and MELD scores have considerable limitations.
Recently the prognostic value of albumin-bilirubin (ALBI) [1] grade has been evaluated in patients undergoing HCC treatment with different modalities, but not specifically in patients undergoing TACE [2]. Moreover, the pALBI grade, that includes platelet count, is a surrogate marker of portal hypertension [3].
Aims and Methods: ALBI and pALBI are proposed to be objective scores of liver function reserve which could adequately stratify patient survival.
The aim of this research is to study the role of ALBI and pALBI in predicting outcome for HCC patients who underwent transcatheter arterial chemoembolization (TACE).
We retrospectively evaluated the prognostic significance of ALBI and pALBI in patients undergoing TACE recorded in the Ita.Li.Ca. database, and compared it with other prognostic systems, including MELD, CPS, hepatoma arterial-embolization prognostic (HAP) and mHAPII.
Results: 2283 TACE performed in 1012 consecutive patients between January 2008 and December 2016 were evaluated. Patients had a median MELD of 9 and belonged to all BCLC stages; 1168 TACE were perfomed in BCLC-A, 696 in BCLC-B and 419 in BCLC-C stage. Median overall survival in the whole population was 33.9 months.
Considering all TACE procedures, irrespective of the BCLC stage, the ALBI grade and pALBI grade were significant predictors of overall survival ($p = 0.001$ and $p < 0.0001$ respectively), similar to the HAP and the mHAP scores ($p < 0.0001$). When patients in different BCLC stages were considered, ALBI was a significant predictor of OS only in BCLC-C ($p < 0.001$) patients treated with TACE, pALBI was a significant predictor of OS in BCLC-B ($p = 0.001$) and BCLC-C ($p < 0.001$) similarly to HAP and mHAPII.
Similar data were obtained when only the first TACE procedure was considered in each patient (total of 901 patients, 460 BCLC-A, 259 BCLC-B and 182 BCLC-C). Considering all BCLC stages, ALBI was a significant predictor of overall survival ($p = 0.001$) similar to the pALBI, HAP and mHAPII scores ($p = 0.003$). When different BCLC stages were considered, ALBI, pALBI and HAP were significant predictors of OS in BCLC-C ($p = 0.008$, $p = 0.003$ and 0.008 respectively), whereas mHAPII was not significant. PALBI was also a significant predictor of OS in BCLC-B ($p = 0.005$).
Conclusion: ALBI and pALBI offer additional simple and objective methods of assessing liver function in HCC and may be useful for selecting patients more likely to survive after TACE, especially ALBI in those belonging to the BCLC -C stage whereas pALBI in BCLC-B and BCLC-C stage.
Disclosure: Nothing to disclose

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P0070 HCC RECURRENCE AFTER DAA TREATMENT IN HCV PATIENTS

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Introduction: The debate on the matter of HCC recurrence risk and its aggressiveness in patients who have a history of previously and successfully treated HCC underwent DAAs treatment is still open.
Aims and Methods: The present real-life multicenter, prospective study aims to investigate the impact of new DAAs therapies in HCV patients with a previous successfully treated HCC, in terms of neoplastic recurrence. From March 2015 to March 2017, 101 consecutive HCV patients with prior HCC underwent DAAs treatment were enrolled. The assessment of neoplastic recurrence was used as primary outcome, while a secondary outcome was the evaluation of baseline characteristics predicting HCC recurrence.
Results: 83% of patients were in Child-Pugh class A, and 89% had a history of HCC BCLC stage 0/A, while 35% of patients had a prior HCC recurrence. 91% of the patients achieved SVR. The median time between the HCC 1st diagnosis and DAAs-starting was 17.2 months (range 10.1–37.2), while the median time from the last successful HCC treatment to DAAs starting was 10 months (range 5.8–16.6). 31 HCC recurrences were observed from DAAs-starting in a median observational follow-up of 24.7 months (range: 2–36.9). The cumulative rate of recurrence was 20.5/100 person-year (95% C.I. 13.9–29.0). The 6-, 12- and 24-months HCC recurrence rates from the last HCC treatment were 1%, 8.9% and 25.6%, respectively. Higher BMI (HR 1.27, 95% C.I. 1.05–1.52), lower age (HR 0.93, 95% C.I. 0.87–0.98) and DAAs treatment failure (4.17, 95% C.I. 1.23 - 14.29) were significantly associated with higher risk of HCC recurrence, both at univariate and at Cox multivariate analysis.
Conclusion: Patients without HCC recurrence are characterized by lower BMI, older age and higher SVR rate. These data suggest that the absence of well-known HCC risk factors reduces the HCC recurrence rate also in patients underwent DAAs.
Disclosure: Nothing to disclose

P0071 EVALUATION OF SERUM ENDOGLIN LEVEL AS A NEW DIAGNOSTIC BIOMARKER FOR HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular carcinoma is the most common primary malignant tumor of the liver. It occurs most commonly on top of a cirrhotic liver which in Egypt is prevalence is due to chronic HCV infection. Diagnosis of HCC at earlier stages improves patient outcomes. Currently, the most commonly used methods for screening and diagnosing HCC are ultrasound imaging and serum α-fetoprotein (AFP) concentration measurements, but the diagnostic value of AFP is recently challenged due to its low sensitivity and specificity.

Aims and Methods: The aim of the study is to evaluate the value of serum endoglin as a noninvasive biomarker in diagnosis of HCC versus serum AFP in liver cirrhosis patients.

The study was conducted upon 90 subjects who were divided into 3 groups: group I included 40 patients with liver cirrhosis and hepatocellular carcinoma, group II included 30 patients with liver cirrhosis without HCC, group III had 20 healthy subjects as controls. Group I was also divided into 2 subgroups, Group Ia represents patients with AFP less than 200ng/ml and Group Ib represents patients with AFP more than 200ng/ml. For all participants, thorough clinical examination, blood picture, liver function tests, HCV antibody, HBsAg, alpha fetoprotein (AFP), and serum endoglin were performed. Abdominal ultrasound, abdominal triphasic computed tomographic (CT) scan.

Results: In this study, the serum levels of Endoglin and alpha fetoprotein were highest in patients of group I with HCC compared to those with liver cirrhosis and the control groups with significant difference. Serum AFP and Endoglin was found to be positively correlated with number of hepatic focal lesions. However, it did not increase significantly with tumour size, vascular invasion. At a cut off value 220ng/ml, the diagnostic sensitivity and specificity of AFP for selective detection of HCC over the cirrhotic group was 67.5% and 100% respectively. At a cut off value 1125pg/ml the diagnostic sensitivity and specificity of Endoglin for selective detection of HCC over the cirrhotic group was 90% and 76.67% respectively. When combining both markers together the sensitivity increased to 100% with a specificity of 100%.

Conclusion: Serum Endoglin is a promising tumor marker that may be used with serum AFP as noninvasive technique to aid diagnosis of HCC.

Disclosure: Nothing to disclose

P0072 THE EFFECT OF DIRECT ACTING ANTIVIRALS ON THE OCCURRENCE AND RECURRENCE OF HEPATOCELLULAR CARCINOMA: META-ANALYSIS OF 1438 PATIENTS

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Introduction: Previous reports suggested an unexpected high rate of hepatocellular carcinoma (HCC) occurrence and recurrence following antiviral treatment using direct acting antiviral (DAA).

Aims and Methods: We aim to synthesis evidence about effect of DAA on the occurrence and recurrence of HCC.

A compute literature search for PubMed, Cochrane CENTRAL, EMBASE, Web of Knowledge, and SCOPUS was carried out. We included prospective cohort studies and clinical trials that the reported the rate of occurrence or recurrence of HCC following DAA treatment in patients with HCV. Data were extracted and analyzed using Open-Meta (Analyst) software for windows. Rates were pooled as relative risk (RR) in a random-effect model using Mantel Haenzel (M-H) method.

Results: Seven prospective cohort studies were included in the present review with a total of 1438 HCV patients. The pooled HCC occurrence rate in the DAA group was 2.7% (95% CI [0.015, 0.038]). The pooled HCC recurrence rate in the DAA group was 13.6% (95% CI [0.059, 0.214]); while the two-arms meta-analysis showed that the DAA group was associated with less risk of HCC recurrence compared to the control group (RR = 0.55, 95% CI [0.32, 0.96], p = 0.04). Pooled effect estimates did not differ significantly after subgrouping the patients according to DAA regimens. All pooled analyses were homogenous.

Conclusion: The present meta-analysis showed that the rate of HCC occurence or recurrence following DAA regimens is low.

Disclosure: Nothing to disclose

P0073 PROGNOSTIC VALUE OF ALBUMIN BILIRUBIN SCORE AND ALBUMIN BILIRUBIN RATIO IN HEPATOCELLULAR CARCINOMA PATIENTS TREATED WITH TRANS-ARTERIAL CHEMOEMBOLIZATION

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Introduction: Albumin bilirubin score (ALBI) is a recently reported, simpler, more objective, and evidence-based alternative to the Child-Pugh (CP) score and Barcelona clinic liver cancer (BCLC) for prediction of survival and prognosis in hepatocellular carcinoma (HCC). Albumin bilirubin ratio is a novel method for detection of early recurrence of HCC after management.

Aims and Methods: This study aimed to validate prognostic value of both albumin bilirubin score and albumin bilirubin ratio in hepatocellular carcinoma patients treated with conventional transarterial chemoembolization (cTACE). The study enrolled 78 HCC patients with BCLC stage (A,B) underwent cTACE, all of them have complete response (CR) according to mRECIST criteria. ALBI score was measured before cTACE using this equation - $0.085\times$ (albumin g/l) $+ 0.66 \times \log$ (bilirubin µmol/l) while the ratio between albumin (g/l) and bilirubin (µmol/l) was mathematically calculated before TACE. Follow-up of the patients was done every 6 months for 36 months using dynamic imaging, liver, kidney functions and AFP.

Results: Early HCC recurrence (within the first 6 months) was observed in 28 patients, ALBI score was significantly associated with early tumor recurrence (p = 0.001). Albumin Bilirubin ratio also was significantly associated with early tumor recurrence (p = 0.001). The Roc curve for ALBI score for detection of early recurrence of HCC after cTACE (at cut off value 0.637, sensitivity is 100% and specificity is 77%), for Albumin Bilirubin ratio (at cut off value 0.885, sensitivity is 95.2% and specificity is 71.4%). Both ALBI score and albumin bilirubin ratio were significantly positively correlated with Child Pugh score, BCLC staging and model for end stage liver disease (MELD) score (p = 0.001).

Conclusion: ALBI score and albumin bilirubin ratio could be used as prognostic indices in HCC management and help in assessing early recurrence of HCC following TACE with high sensitivity and good specificity in comparison to other well-known scores like BCLC and Child -Pugh scores.

Disclosure: Nothing to disclose

P0074 DYNAMIC DETERMINANTS OF PORTAL HYPERTENSION ARE IDENTIFIED BY HISTOLOGICAL COLLAGEN PROPORTIONATE AREA ESTIMATIONS

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Introduction: Portal hypertension is determined both by 'static' fibrosis and 'dynamic' hemodynamic components. The correlation of fibrosis area and portal pressure has not been systematically assessed in different animal models and in human liver disease of different etiologies. Thus, we evaluated the correlation of collagen-proportionate area (CPA) with portal pressure (PP) in animal models and with hepatic venous pressure gradient (HVPG) in patients with cirrhosis.

Aims and Methods: Carbon tetrachloride (CCl_4) or bile duct ligation (BDL) models were used to mimic toxic or biliary cirrhosis in rats, respectively. Portal pressure was measured by direct cannulation of the portal vein. Patients underwent HVPG measurements and transjugular liver biopsy. Liver samples were stained by chrome-aniline-blue (CAB) or picro-sirius-red (PSR) and CPA was quantified by ImageJ software.

Results: Portal pressure correlated with CPA both in BDL ($R = 0.844$, $p < 0.001$) and in CCl_4 ($R = 0.866$, $p < 0.001$) animals. The 'linear fitting' curve was steeper in BDL ($PP = 2.303*CPA + 4.045$) as compared to CCl_4 ($PP = 1.520*CPA + 4.794$). Animals outside the 75% confidence interval of the expected PP (based on CPA) might have pronounced 'dynamic' components, e.g. in endothelial dysfunction, splanchnic blood flow or portosystemic shunting. Similarly, in (n = 18) patients, HVPG correlated with CPA ($R = 0.339$, $p = 0.17$) yielding a 'predicted' HVPG (mmHg) of $0.663*CPA + 11.8$. In patients with 25% higher HVPG as expected by the CPA-formula, we recorded higher vWF-Ag (368 ± 3 vs. $233 \pm 50\%$; $p = 0.048$), IL6 (23 ± 8 vs. 8 ± 4 ng/L; p = ns), and bile acids (34 ± 18 vs. 7 ± 3 µmol/L; p = ns) than in patients with 25% lower HVPG as expected. More patients will be presented at congress.

Conclusion: CPA as the 'static' component of PHT correlates with PP/HVPG, with model-specific and etiology-dependent correlation estimates. Outliers to this curve imply profound alterations of 'dynamic' components of PHT, such as endothelial dysfunction, significant collateralization, bacterial translocation or a deranged gut-liver axis. Identification of outliers refines the assessment of vascular and hemodynamic dysfunction and may allow for personalized therapy of PHT.

Disclosure: Nothing to disclose

P0075 PRONOSTIC FACTORS IN PATIENTS WITH PORTAL CAVERNOMA: RESULTS OF A PROSPECTIVE COHORT OF 131 CASES

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Introduction: The portal cavernoma (PC) follows a chronic thrombotic occlusion of the portal vein. PC is rare event and scanty data are available on its incidence of thrombotic recurrence, complications of portal hypertension, survival and causes of death and no data are available to identify those patients in which lifelong anticoagulation is necessary to prevent recurrent thrombosis.

Aims and Methods: The aim of the study was to analyze the long-term prognosis of patients with PC.

The study was prospective and follow-up study of patients initially managed for portal cavernoma from January 2008 to June 2017. Patients with cirrhosis, cancer or Budd Chiari syndrome were excluded. Portal hypertension was managed according to Baveno V recommendations. Anticoagulant therapy has been indicated according to current recommendations. All recurrent thrombosis, gastrointestinal bleeding, adverse events of anticoagulant therapy and death were registered.

Results: In this study 131 patients were included and followed up for a median time of 51.5 months. Of the 131 patients, 69 were men and 62 women, with a median age of 46.2 (23–81) years. PC was an incidental finding in 25 (19%) patients; 46 (35.2%) patients presented with abdominal pain; 60 (45.8%) patients presented with bleeding from portal hypertensive sources. Esophageal and/or gastric varices were present at diagnosis in 78 (59.5%) patients. Prothrombotic disease was identified in 75 (57.2%) patients. Among the factors identified, the most common were chronic myeloproliferative disease (CMD, 25.2%) and protein S deficiency (14.9%). 95 (72.5%) patients received long-term anticoagulation therapy. During the follow-up, 91 patients had no hemorrhagic or thrombotic events. The incidence rate of esophageal varices was 25%; 15 (11.4%) patients suffered from 23 episodes of gastrointestinal bleeding with no deaths. 6 patients had ascites and 15 patients had symptomatic cholangiopathy effectively treated with UDCA. New venous thrombotic episodes occurred in 11 (8.4%) patients of which 71% were in the splanchnic area. There was no case of occurrence or recurrence of intestinal infarction under anticoagulation therapy. 5 patients had latent CMD progression and 1 patient died of acute myeloid leukemia. No serious bleeding or death related to anticoagulant treatment was registered. Survival rates at 1, 3, and 5 yr were 100%, 99.2%, and 97.6%, respectively.

Conclusion: The long-term prognosis of patients with portal cavernoma is good, 70% of patients have a stable evolution. The combination of anticoagulants and the treatment of portal hypertension is effective in preventing thrombotic recurrence and management of bleeding complications.

Disclosure: Nothing to disclose

P0076 SGC STIMULATION AND PDE5 INHIBITION DECREASE SINUSOIDAL RESISTANCE AND REDUCE FIBROSIS IN RATS WITH BILIARY CIRRHOSIS

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Introduction: Dysfunctional nitric oxide (NO) and cGMP signalling results in increased intrahepatic resistance in cirrhotic portal hypertension (PHT). PHT contributes to major complications such as variceal bleeding or ascites. Currently medical treatment of PHT is limited to non-selective beta-blockers, while there is no available treatment for liver fibrosis. We investigated the soluble guanylyl cyclase (sGC) stimulator riociguat (RIO) and activator cinaciguat (CINA) and phosphodiesterase-5 inhibitor tadalafil (TADA) in bile duct ligated (BDL) rats.

Aims and Methods: Male Sprague-Dawley rats underwent BDL or sham-operation. Starting 1 week after surgery, RIO (0.5mg/kg), CINA (1mg/kg), TADA (1.5mg/kg) or vehicle (VEH) were gavaged for 3 weeks. Portal pressure (PP), mean arterial pressure, heart rate and splanchnic/portal blood flow were measured. Liver fibrosis, hepatic inflammation and hepatic cGMP levels were assessed.

Results: Cirrhotic BDL-VEH rats showed significant increase in PP (13.07 ± 0.97mmHg) compared to healthy controls. In BDL animals RIO (9.96 ± 0.7mmHg, $p = 0.021$) and TADA (10.27 ± 0.86mmHg, $p = 0.050$) treatment decreased PP without affecting systemic hemodynamics. Intrahepatic vascular resistance was reduced by RIO (2.86 ± 0.25 vs. 4.85 ± 0.54mmHg/min*mL, $p = 0.005$). Hepatic hydroxyproline content was reduced by RIO and TADA treatment (RIO:350 ± 30µg/g, $p = 0.003$; TADA: 282 ± 50µg/g, $p = 0.003$ vs. BDL-VEH: 503 ± 20µg/g liver), whereas fibrotic chrome-aniline-blue stained area decreased only by RIO ($2.14 \pm 0.3\%$ vs. $4.15 \pm 0.53\%$, $p = 0.011$). Both, RIO and TADA therapy decreased transaminases AST (RIO: −36%, $p < 0.001$; TADA: −24%, $p = 0.006$) and ALT (RIO: −32%, $p = 0.035$; TADA: −27%, $p = 0.053$). In line, BDL-RIO rats presented less hepatic *Il6* expression (−56%, $p = 0.053$), indicating a reduction of necroinflammation. Furthermore, hepatic cGMP levels were significantly increased by RIO, but not by TADA or CINA. In cirrhotic BDL rats, 1mg/kg CINA caused weight loss, hypotension and increased lactate levels.

Conclusion: The sGC stimulator riociguat and the PDE5 inhibitor tadalafil showed beneficial effects in cirrhotic rats by reducing liver fibrosis and decreasing portal hypertension. High dosing of sGC activators such as 1mg/kg cinaciguat may be associated with toxicity in cirrhosis.

Disclosure: BK, KP, LD, SA, SP, BD, BA, SJ, PBK, SM, ZK, RUN, TM, RT, SP have nothing to disclose This study has been financially supported by a grant from Boehringer Ingelheim.

P0077 SUBCLINICAL PORTAL HYPERTENSION: RESULTS AND CONCORDANCE OF DIFFERENT MEANS OF NON-INVASIVE DIAGNOSIS

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Introduction: The diagnosis of portal hypertension at a subclinical stage is important because of major prognostic and therapeutic consequences. In the latent stage, non-invasive imaging and endoscopic exploration play a major role in the positive diagnosis. The aim of this work is to study the concordance between Esophagogastroduodenoscopy (EGD) and non-invasive imaging examinations in the positive diagnosis of infra-clinical portal hypertension.

Aims and Methods: This is a retrospective study that included all patients with infra-clinical portal hypertension syndrome between January 2010 and August 2017. A clinical or latent infra-clinical portal hypertension is referred to any elevation of pressure in the portal system which is not complicated with digestive hemorrhage. Data collection was done from patients' medical records. All patients included in the study had EGD and x-ray examination by abdominal ultrasound (+ doppler) or abdominal CT scan.

Results: 183 patients were included in the study. There were 102 men and 81 women. The average age was 58 [15–81 years]. The syndrome of portal hypertension was secondary to cirrhosis in the majority of cases (90.7%), a portal cavernoma in 11% of the cases, a Banti syndrome in 2 patients and a tumor of the head of the pancreas in a patient. The main etiologies of cirrhosis were viral hepatitis B (33.3%) and C (16.7%), autoimmune origin (4.2%) and nonalcoholic steatohepatitis (8.3%). EGD revealed signs of oesophageal varices, gastric varices and or hypertensive gastropathy in 87.4% of cases. Signs revealed by radiological examinations were splenomegaly (79.2%), portosystemic diversion pathways (33.3%), portal trunk dilatation (50%) and portal flow reversal (54%). The concordance between the existence of signs of endoscopic portal hypertension and the radiological abnormalities that identify the portal hypertension syndrome was: 65% for splenomegaly, 52% for portosystemic diversions, 68% for portal dilatation and 59% for reversing the portal flow.

Conclusion: Consistent with the results of previous studies, concordance between endoscopy and imaging data in the diagnosis of portal hypertension remains moderate. All the interest lies in facing these 2 diagnostic methods to increase the chances of diagnosing portal hypertension at an early stage and avoid its complications.

Disclosure: Nothing to disclose

P0078 A MULTICENTER RANDOMIZED TRIAL OF LASER VERSUS ELECTROHYDRAULIC LITHOTRIPSY FOR DIFFICULT BILE DUCT STONES

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Introduction: Firstly, difficult bile duct stones were removed by mechanical lithotripsy. But, if this failed, the electrohydrulic (EHL) or laser lithotripsy (LL) could be performed.

Aims and Methods: We performed the first prospective randomized controlled study to compare the efficiency and safety of LL and EHL in multicenter of South Korea.

Between 2014 and 2016, a total of 122 patients who underwent LL or EHL was enrolled from 12 centers. All patients had failed to remove stones by conventional endoscopic stone extraction method including mechanical lithotripsy because huge stone, inaccessible major duodenal papilla, or intrahepatic bile duct (IHD) stone. For laser lithotripsy, we used holmium laser technology. Main outcome measures included complete stone clearance, procedure times and post-procedure complications.

Results: 31 patients received LL and 33 received EHL. Those in the LL treatment were older, had longer procedure times (EHL33.3 ± 13.8 min, LL 47.9 ± 25.7 min, p = 0.006). There were no significant differences in stone size (EHL 15.0 ± 7.6 mm, LL 13.1 ± 4.4 mm, p = 0.235), number of sessions (EHL 2.4 ± 1.1, LL 3.0 ± 1.6, p = 0.113), stone location between the 2 treatment groups. Rate of complete clearance (EHL 90.9%, LL 96.8%, p = 0.333) and complications (EHL 15.2%, Holmium 19.4%, p = 0.656) were not different between the groups. Main complications included bleeding (n = 3), infection (n = 7), and pancreatitis (n = 1), although there were no differences in complications between the 2 treatments, and no severe complications were observed. Recurrence rate was 22.6% (14/62), although no differences were seen in either LL or EHL treatment groups (EHL 57.1%, Holmium 42.9%, p = 0.638). IHD stone was significantly associated with recurrence compared to common bile duct (CBD) stones (Odds ratio = 1.957, 95% confidence interval = 1.017–3.767, p = 0.045).

Conclusion: Although both LL and EHL were safe and effective in the treatment of refractory CBD stones or intrahepatic stones, LL had longer procedure. However, the number of session was not different. Further large comparative studies are warranted

Disclosure: Nothing to disclose

P0079 LONG-TERM OUTCOME OF ENDOSCOPIC PAPILLARY LARGE-BALLOON DILATION FOR BILE DUCT STONES

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Introduction: Endoscopic papillary large-balloon dilation (EPLBD) has been reported to be safe and effective for large, multiple common bile duct (CBD) stones. However, long-term outcome of EPLBD for such difficult stones has not been sufficiently determined.

Aims and Methods: The aim of this study was to evaluate long-term outcome of EPLBD for CBD stones. 102 consecutive patients who had undergone endoscopic CBD stone removal with EPLBD, which was defined as papillary dilation with a balloon having a diameter ≥ 12 mm between October 2011 and December 2015 were identified using a prospectively maintained database. Patients with previous history of surgical choledochoduodenostomy or endoscopic papillectomy, those with benign biliary stricture, and those in whom stones were not completely removed were excluded for evaluation of long-term outcome. Postal or telephone surveys were conducted for patients who did not undergo periodical follow-up. Patients who rejected or inappropriately replied to the survey were also excluded. The main outcome measurement was the recurrence rate of CBD stones after complete stone removal with EPLBD during a follow-up. Risk factors for such recurrence were secondarily analyzed. In addition, other complications in the biliary system, such as acute cholecystitis and acute non-calculous cholangitis, and the patient survival period were analyzed.

Results: Complete stone removal with EPLBD was achieved in 99 patients (96.1%). After elimination according to the above-mentioned criteria, 93 patients were finally included in the retrospective analyses for long-term outcome. The mean follow-up period after the successful procedure was 33.7 ± 16.6 months. CBD stones recurred in 16 patients (17%) during the follow-up period. The mean time to recurrence was 12.7 ± 12.7 months. Univariate analyses revealed that a large CBD diameter, multiple stones, and a large stone size were significant risk factors for stone recurrence. Multivariate analysis using the cox proportional hazard model indicated that a large CBD diameter was the only significant risk factor for the recurrence (hazard ratio, 1.25 [95% confidence interval, 1.04–1.50], p = 0.019). Acute cholecystitis and acute non-calculous cholangitis were observed in 5 (5%) and in 3 (3%) patients, respectively. In the 19 patients (20%) who died during follow-up, the causes of death did not involve biliary events.

Conclusion: The long-term outcome of EPLBD for CBD stones, including stone recurrence, acute cholecystitis, and acute cholangitis, was found to be acceptable. A large CBD diameter was the independent risk factor for stone recurrence.

Disclosure: Nothing to disclose

P0080 BILIRUBIN LEVEL AT ADMISSION AS PREDICTOR OF CONCOMITANT CHOLEDOCHOLITHIASIS IN PATIENTS WITH ACUTE CHOLECYSTITIS AND RATE OF READMISSION FOR BILIARY COMPLICATIONS IN PATIENTS WITH DELAYED SURGERY FOR SUSPECTED BILIARY DUCT OBSTRUCTION

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Introduction: Laparoscopic cholecystectomy (LC) is the gold standard treatment in acute cholecystitis (AC). Concomitant choledocholithiasis incidence is 4–20%. Confirming choledocholithiasis often delays LC and leads to initial conservative management of the acute episode. Biliary endoscopic sphincterotomy and bile duct clearance, followed by LC is actually the most common treatment, although the appropriate management of these patients still remain controversial.

Aims and Methods: The aim of this study was to identify admission and maximum bilirubin levels in patients with AC and its capability to predict the presence of concomitant choledocholithiasis. The second aim was to assess the rate of readmissions for biliary complications in these patients treated conservatively due to the suspect of choledocholithiasis.

Data was retrospectively collected from hospitalization medical reports between June 2015 and October 2017 at Virgen Macarena University Hospital. Tokyo guidelines criteria were used for AC diagnosis and American Asociation for Gastroenteroly (ASGE) criteria for assessing high risk suspect of choledocholithiasis (common duct stone in abdominal ultrasound (US), bilirubin > 4 mg/dL, bilirubin > 1.8 with bile duct dilatation in US and/or cholangitis). Patients under 18 years old, benign or malignant biliary ducts stenosis, previously abnormal liver function tests, previous hepatobiliary surgery, gastrectomy and/or cholecystostomy were excluded. Data were analyzed using SPSS software.

Results: 88 patients with AC were included. 59% were male, ASA score II and III were the most common (31.8 and 37.5% respectively). Delayed programed LC was performed in 64 patients (72.7%). Surgery was ruled out on 19 patients (21%). Only 5 underwent LC on the acute episode (5.7%). Choledocholithiasis was confirmed in 39.8% of cases either with US or abdominal magnetic resonance. In patients with normal biliary ducts in US, admission and maximum bilirubin levels were significantly higher when concomitant cholecholithiasis was present (table 1). The bilirubin level at admission found to be predictor for choledocholithiasis was 7.1mg/dL (sensitivity 80% and specificity 81.6%), OR 1.8 [IC 95%(1.1–2.9); p = 0.14], AUC = 0.87 [IC 95%(0.75–0.98), p = 0.008]. Median time of Hospitalization days was 9.5 (IC 95% 8.77–14.28). Median time for programmed cholecystectomy was 68 days (IC 95% 59.29–109.22) for 44 patients, while 20 patients were still waiting for cholecystectomy 4 months after the acute episode. Readmission for biliary complications was observed in 24.1% of patients who didn't undergo LC on the acute episode (second episodes of AC, cholangitis and biliary acute pancreatitis were reported), 3 of them required urgent surgery.

Conclusion: In the majority of patients with AC, surgical intervention was delayed due to the suspicion of concomitant choledocholithiasis. However, in less than 40% of cases the diagnosis was confirmed and the requirement of endoscopic treatment was needed. This resulted in a readmission rate for biliary complications higher than 20% in patients treated conservatively.

Admission Bilirubin cutoff found to be predictor of common biliar duct obstruction in this study was higher than established on ASGE guidelines. Considering that the appropriate management of this patients could be different according to this findings, more prospective studies should be formed.

Disclosure: Nothing to disclose

P0081 LONG-TERM OUTCOME OF ACUTE ACALCULOUS CHOLECYSTITIS TREATED BY NON-SURGICAL MANAGEMENTS

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Introduction: Although cholecystectomy is generally recommended in acute acalculous cholecystitis (AAC), non-surgical managements can be considered in patients with high risk of surgery and some recent studies showed favorable outcomes of non-surgical management for AAC. The aim of this study was to analyze the long-term outcome of AAC patients treated by non-surgical managements.

Aims and Methods: We retrospectively analyzed 93 patients diagnosed as AAC between January, 2007 and April, 2014. They were divided into two groups; non-surgical group (n = 43) and surgical group (n = 50). Non-surgical managements included percutaneous transhepatic gallbladder drainage (PTGBD, n = 26) and antibiotics alone (n = 17). Non-surgical group was surveyed for more than 3 years after treatment.

Results: The mean age and the incidence of cerebrovascular accident were significantly higher in non-surgical group than surgical group (70.0 ± 10.8 vs. 65.4 ± 11.1, p = 0.047 and 25.6% vs. 8%, p = 0.026, respectively). No statistical difference regarding the mean hospital stay (9.9 days vs. 8.9 days) and mortality (2.3% vs. 2.0%) was found between two groups, whereas surgical group had a significantly higher incidence of post-treatment complications than non-surgical group (18% vs. 2.3%, p = 0.018). During a mean follow up period of 5.5 years for non-surgical group, AAC was recurred in 4 (9.3%) patients. Of those 4 patients, 3 patients underwent cholecystectomy and one was treated with antibiotics alone, and no recurrence-related death occurred. There was no difference

in recurrence rate between PTGBD and antibiotics only groups (7.7% vs. 11.8%). 2 patients underwent prophylactic cholecystectomy during non-symptomatic period after non-surgical managements.
Conclusion: Recurrence occurred in 9.3% of patients with AAC treated with non-surgical managements and the treatment outcome of non-surgical group was not inferior to that of surgical group. Further studies are needed to clarify role of non-surgical managements in patients with AAC.
Disclosure: Nothing to disclose

P0082 PREVALENCE OF FUNCTIONAL GASTRO-INTESTINAL DISEASES IN PATIENTS WITH UNCOMPLICATED CHOLECYSTOLITHIASIS; A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Cholecystolithiasis and functional gastrointestinal diseases (FGID) are both highly prevalent in the industrialised world. There are over 1.8 million ambulatory visits for symptomatic cholecystolithiasis in the United States. Incorrect assignment of abdominal symptoms may lead to inappropriate cholecystectomies with subsequent lack of benefit. We conducted a systematic review and meta-analysis to determine the prevalence of FGID in patients with uncomplicated cholecystolithiasis.
Aims and Methods: We searched MEDLINE, EMBASE and Web Of Science to identify studies reporting the prevalence of FGID in adults (≥18 years) with uncomplicated cholecystolithiasis. Pooled prevalences and 95% confidence interval (CI) were calculated. Subgroup analyses were performed according to diagnostic criteria used and for dyspepsia and irritable bowel syndrome (IBS) separately.
Results: Of the 1,696 studies evaluated, 11 reported the prevalence of dyspepsia and IBS in a total of 5,069 cholecystolithiasis patients. The pooled prevalence of FGID was 66.8% (95% CI 40% - 89%); 72.7% (95% CI 56% - 87%) for dyspepsia and 42.5% (95% CI 3% - 91%) for IBS. There were no statistically significant differences between diagnostic criteria.
Conclusion: This study finds that 67% of patients with cholecystolithiasis have FGID. In the United States this comprises 1.2 million patients. This is a concern, as these patients are at risk of cholecystectomy that will not benefit them. Extra measures to exclude FGID as a cause of abdominal symptoms, prior to cholecystectomy, is warranted.
Disclosure: Nothing to disclose

P0084 VALIDATION OF TOKYO GUIDELINE 2013 FOR TREATMENT OF ACUTE CHOLECYSTITIS BY REAL-WORLD DATA

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Introduction: The Tokyo guideline 2013 indicated emergency cholecystectomy was one of the most important and early treatment options for acute cholecystitis. However, surgical intervention is not necessarily indicated in the patients with advanced ages. Therefore, in this communication, we evaluated percutaneous transhepatic gallbladder aspiration (PTGBA), percutaneous transhepatic gallbladder drainage (PTGBD) and the administration of antibiotics alone as an option for the treatment for acute cholecystitis.
Aims and Methods: From 2010 January to 2015 December, in the period of 6 years, 120 patients with acute cholecystitis were treated at our institution. The data from these patients were retrospectively analyzed.
Results: Of these 120 cases, 84 underwent PTGBA, 28 PTGBD, and 8 were administered antibiotics alone. None of the 120 needed urgent (''early'') cholecystectomy and all patients were discharged without mortality. In only 3 of the 84 patients, cholecystitis was not controlled by PTGBA. PTGBD was performed in these 3 cases.
Long-term follow-up of the patients was conducted in all cases. Of the 120 cases, 111 had gall bladder stones initially, while 9 had none at the time of presentation. Of these 111 patients with gall bladder stones, 67 underwent elective cholecystectomy, while 45 did not. Of the 67 patients who underwent elective cholecystectomy, 2 developed choledocholithiasis. Of the 45 patients who did not undergo elective cholecystectomy, 3 developed choledocholithiasis and 2 developed acute cholecystitis. The incidences of choledocholithiasis and acute cholecystitis did not significantly differ between the 2 groups ($p = 0.19$).
Conclusion: Despite the recommendation in the Tokyo Guideline 2013, emergency cholecystectomy was not needed in any of our patients with acute cholecystitis. Acute cholecystitis can be successfully treated with PTGBA or PTGBD, which are simple procedures with good short- and long-term safety; we highly recommend these procedures for patients with acute cholecystitis, especially in the elderly population.
Disclosure: Nothing to disclose

P0085 PRACTICE PATTERNS FOR THE MANAGEMENT OF CONCOMITANT GALLSTONES AND CHOLEDOCHOLITHIASIS

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Introduction: Patients with concomitant gallstones and common bile duct (CBD) stones should have endoscopic retrograde cholangiopancreatography (ERCP) followed by cholecystectomy.
Aims and Methods: We studied the success rate of ERCP, and recurrent choledocholithiasis in those who did and did not have cholecystectomy post-ERCP. All patients, diagnosed with CBD stones on imaging between September 2015 and July 2017, and had subsequent ERCP + sphincterotomy, were retrospectively included in this study. Data was collected from medical notes.
Results: 126 patients underwent ERCP for stone extraction. CBD was cannulated in 94%. 20% had normal ERCP. 92 patients (80%) had CBD stones at ERCP. 58 (63%) had complete stone extraction with 1 ERCP (76%), 2 ERCPs (19%), >2 ERCPs (5%). 19 (21%) were lost to follow-up or deemed unfit for repeat ERCPs. 13 (14%) were still undergoing regular ERCPs. 2 (2%) had surgical CBD exploration.
Only 41% (29/71) underwent cholecystectomy post-ERCP. 93% (27/29) remained CBD stone-free at a mean follow-up of 1 year (5 - 23 months). In the 59% (42/71) who did not have cholecystectomy post-ERCP, 95% (40/42) remained CBD stone-free at a mean follow-up of 1 year (1 - 24 months). 5% developed new CBD stones requiring another ERCP.
Conclusion: 95% with choledocholithiasis achieve CBD stone clearance with 1-2 ERCPs. Cholecystectomy post-ERCP was not performed in 60%. Choledocholithiasis-free survival was comparable at 1 year in patients who did and did not have a cholecystectomy post-ERCP. This suggests strong benefits from sphincterotomy alone, however cholecystectomy would still be necessary to prevent cholecystitis, biliary colic, cholangitis or biliary pancreatitis.
Disclosure: Nothing to disclose

P0086 PREVALENCE AND RISK FACTORS OF CHOLELITHIASIS IN CROHN'S DISEASE

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Introduction: Cholelithiasis occurs in patients with Crohn's disease more frequently than in a healthy population. The cause of this difference has not been satisfactorily explained, nor its risk factors.
Aims and Methods: The aim of our study was to determine the prevalence of cholelithiasis in CD patients, to compare prevalence with a control group and to analyze the risk factors of cholelithiasis. We performed a monocentric retrospective case-control study. The cohort consisted of all CD patients who underwent abdominal ultrasound from January 2007 to January 2018 at the IBD Center of the 5th Department of Internal Medicine in Bratislava. The control group consisted of patients, who underwent ultrasound at the same department because of dyspepsia and were age and gender matched. Medical records were reviewed and patients demographics, behavior, localisation, duration and number of flare of CD, number and type of bowel resections, number and length of total hospitalization, number of total parenteral nutrition treatments and presence of cholelithiasis and its characterization were noted. An univariate and a multivariate analysis were performed using logistic regression analysis (with cholelithiasis as the dependent variable). Prevalence and odds ratios were calculated with their 95% confidence intervals.
Results: The study cohort consisted of 238 CD patients and 238 controls. The prevalence of cholelithiasis in CD group was 12.6% and 9.2% in control group (RR 1.36, $p = 0.24$). In the univariate analysis, we observed cholelithiasis association with multiple risk factors such as - age, age at CD diagnosis, inflammatory versus aggressive disease behaviour, duration of disease, abdominal resection, number of intestinal resections, length of ileal resection, number of corticosteroid treatments, hospitalizations and total parenteral nutritions. The age (OR 1.077, 95% CI 1.043–1.112, $p < 0.001$) and the number of total parenteral nutritions (OR 1.812, 95% CI 1.131–2.903, $p = 0.013$) were determined as independent risk factors for cholelithiasis in CD patients by multivariate analysis.
Conclusion: The prevalence of cholelithiasis in our CD patient population reached 12.6%, which was not significantly higher than in the control group. We identified the age of patient and the number of parenteral nutritions as the independent risk factors of cholelithiasis in CD patients.
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00–17:00
Pancreas I - Hall X1____

P0087 P8 DEFICIENCY LEAD TO ELEVATED PANCREATIC BETA CELL MASS BUT DOES NOT CONTRIBUTE TO INSULIN RESISTANCE IN MICE FED WITH HIGH-FAT DIET

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Introduction: Nuclear Protein 1, Transcriptional Regulator gene (NUPR1, p8) was firstly described to be overexpressed in acute pancreatitis and encodes a ubiquitous nuclear and cytoplasmic stress protein. Analysis of insulin sensitivity and glucose tolerance in p8 haplodeficiency and p8-knockout mice revealed counterintuitive results. Thus, we analyzed glycemic control of p8 in mice fed with standard (SD) and high-fat diet (HFD).
Aims and Methods: $p8^{-/-}$ mice and wild type ($p8^{+/+}$) littermates were used to study glucose homeostasis. We determined glucagon (immunohistochemistry) and insulin levels (ELISA) from isolated pancreatic islets and analyzed beta cell mass. In addition, hyperinsulinemic- euglycemic glucose clamp technique, i.p. glucose tolerance test (ipGTT), i.p. insulin tolerance test (ipITT) and metabolic chamber analysis over 72 hours were performed in SD (4% fat) and HFD (55% fat) groups.
Results: $p^{8-/-}$ mice showed no differences in glucagon content but higher levels of insulin in pancreatic islets upon glucose stimulation compared to wildtype littermates. p8 deficiency resulted in elevated beta cell mass but was not associated with increased insulin resistance in ipGTT or ipITT in both SD and HFD groups. Glucose clamp tests also revealed no evidence of association of p8 deficiency with insulin resistance. Metabolic chamber analysis showed equal energy expenditure in $p8^{-/-}$ mice and wildtype animals.
Conclusion: Complete p8 depletion may contribute to glucose metabolism by means of stress-induced insulin production and beta cell mass. Nevertheless, p8 knockout showed no impact on insulin resistance in SD and HFD fed mice.
Disclosure: Nothing to disclose

P0088 HISTOLOGICAL ANALYSIS OF THE OBESTATIN/G-PROTEIN COUPLED RECEPTOR 39 (GPR39) SYSTEM IN HUMAN PANCREAS

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Introduction: Obestatin, a 23-amino acid peptide encoded by the ghrelin gene, and the GPR39 receptor were reported to be involved in the control of mitogenesis of gastric cancer cell lines. Our data strongly suggest the involvement of the obestatin/GPR39 system in the pathogenesis and/or clinical outcome of human gastric adenocarcinomas and highlight the potential usefulness of GPR39 as a prognostic marker in gastric cancer. Although this system has been described in the rat endocrine pancreas, its exact expression and function in human pancreas has not been assessed yet.
Aims and Methods: The aim of the present study was to determine the expression levels of the obestatin/GPR39 system, both in healthy and diseased human pancreas.
The tissue samples of human healthy pancreas (n = 3), chronic pancreatitis (CP, n = 3) and pancreatic ductal adenocarcinoma (PDAC, n = 3) were obtained from the Biobank of our centre. The expression of obestatin and GPR39 was evaluated by immunohistochemistry and immunofluorescence.
Results: In healthy pancreas, obestatin was exclusively expressed in the ghrelin endocrine cells of the pancreatic islets, whereas GPR39 expression in the pancreatic endocrine cells was much less intense. GPR39 expression was mainly confined to the exocrine pancreas (acinar cells) and to some HSP47 positive cells (stellate cells). In serial sections of the CP samples, GPR39 is expressed in the GFAP positive cells, the stellate cells, localized in the fibrosis area. For the PDAC tissues, an aberrant GPR39 expression was observed in the cancer cells as well as in the stellate cells (alpha-SMA positive cells) of the surrounding fibrotic area. The tumour area is negative for obestatin.
Conclusion: The expression of the obestatin/GPR39 system found in healthy pancreas indicates a potential role of this system in the regulation of the exocrine pancreas, as well as in the regeneration of this organ. Similar to its role in the stomach, GPR39 might be involved in the regulation of enzyme secretion. Obestatin/GPR39 expression in pathological conditions (CP and PDAC) might suggest the implication of this system in the pathogenesis of CP and human pancreatic adenocarcinoma. Similar findings were described by our group in gastric cancer, in which in addition, GPR39 expression was shown to be closely and directly related to proliferation and poor prognosis.
Disclosure: Nothing to disclose

P0089 OBESTATIN PROMOTES MIGRATION AND INVASSION OF ACTIVATED HUMAN PANCREATIC STELLATE CELLS

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Introduction: There is evidence that the mature adult pancreas has the ability to regenerate, similar to the liver, although to a lesser extent. Studies in animal models confirmed the plasticity and regeneration of both exocrine and endocrine pancreatic cells. Pancreatic stellate cells (PSC) play a major role in pancreas regeneration after partial pancreatectomy. Obestatin, a peptide derived from preproghrelin, and its receptor GPR39 have been described in the endocrine pancreas. Recent studies showed that exogenous administration of obestatin accelerates the recovery of ischemia/reperfusion-induced or cerulein-induced acute pancreatitis in rats.
Aims and Methods: Based on the previous background, the main objective of the present study was to evaluate the regulatory function of the obestatin/GPR39 system in the human pancreatic stellate cells RLT-PSC.
The immunocytochemical expression of the obestatin/GPR39 system in the activated human pancreatic stellate cells RLT-PSC was evaluated. The effect of the exogenous administration of obestatin on the phosphorylation of key signalling targets of this system (Akt and ERK1/2), proliferation, migration, invasion, epithelial-mesenchymal transition (EMT) and agiogenesis was evaluated.
Results: The obestatin/GPR39 system was expressed in the activated RLT-PSC cells. Obestatin administration (100 nM) activated the targets previously described in the signalling pathway of this system: Akt and ERK1/2 (6.29 ± 1.47, $p = 0.025$ and $0.50 \pm 0.00\%$, $p = 0.002$; respectively). Moreover, obestatin stimulated the proliferation of this cells in an autocrine/paracrine manner ($32.10 \pm 14.69\%$; $p = 0.038$), as well as migration ($16.32 \pm 5.96\%$; $p = 0.018$) and invasion ($86.76 \pm 0.141\%$; $p < 0.001$). This system also regulates characteristic markers of the EMT: E-cadherin (-0.39 ± 0.11, $p = 0.014$), N-cadherin (0.41 ± 0.17, $p = 0.014$), vimentin (6.29 ± 1.47, $p = 0.005$), β-catenin (0.82 ± 0.45, $p = 0.014$); and of the angiogenesis: VEGF (0.59 ± 0.08, $p = 0.009$), expressed as fold of control.
Conclusion: The obestatin/GPR39 system was expressed in the RLT-PSC cells. This system regulated the proliferation, migration and invasion of these cells, as well as the expression of EMT and angiogenesis markers. These data reveal the potential role of this system on the recovery of the injured pancreas via the regulation of the activated pancreatic stellate cells, accordingly to the regenerative and/or protector role previously described for obestatin in the pancreas.
Disclosure: Nothing to disclose

P0090 THE RELATIONSHIP BETWEEN CHOLECYSTOKININ SECRETION, INSULIN RELEASE AND PANCREATIC [^{11}C]METHIONINE UPTAKE IN PATIENTS AFTER PARTIAL PANCREATICODUODENECTOMY

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Introduction: The uptake of [^{11}C]methionine ([^{11}C]MET) is associated with pancreatic endocrine and exocrine activity such as insulinogenic index and pancreatic digestive enzyme release. However, studies that examine both, the impact of endocrine and exocrine function, on methionine uptake of the pancreas are rare. Cholecystokinin (CCK), a trigger of pancreas secretion is altered after operations that accelerate gastric emptying, such as gastrectomy. Similarly insulin release is modified due to elevated glucose plasma concentrations and via GLP-1. The purpose of this study was to shed light on the relationship between the secretion of CCK, insulin release and [^{11}C]MET uptake in subjects having undergone pancreaticoduodenectomy (PD).

Aims and Methods: 19 tumor-free survivors after PD (age mean ± SD: 61 ± 8.7 yr; 10 male, 9 female) were given a mixed meal. Plasma CCK, insulin and glucose concentrations were measured before and at 10, 20, 30 and 60 minutes after ingestion. Simultaneously 800 MBq of [^{11}C]MET were administered and the activity (maximum tissue standardized uptake values [SUVmax]) over the pancreas was measured using PET-CT at 15, 30 and 60 minutes after injection. Beta cell function was calculated from basal plasma glucose and insulin concentrations. Area under the curve [AUC] was calculated for insulin, CCK and SUVmax (methionine uptake).
Results: CCK AUC_{30} ($R^2 = 0.26$, $p = < 0.05$), beta cell function ($R^2 = 0.54$, $p < 0.01$) and insulin AUC_{60} ($R^2 = 0.66$, $p < 0.01$) correlated with the SUVmax AUC_{60}. Multivariate analysis revealed CCK, basal beta cell function and postprandial insulin (AUC_{60}) concentrations as significant independent predictors of [^{11}C]methionine uptake ($R^2 = 0.84$, $p < 0.01$, Table 1, Figure 1).
[Table 1. Multiple linear regression on the dependent variable 'methionine SUVmax AUC60' in patients after PD (R2 = 0.84, p < 0.01)]
Conclusion: The association between CCK secretion, beta cell function and postprandial insulin release with pancreatic [^{11}C]MET uptake might suggest the representation of digestive enzyme and insulin metabolism. Further studies are needed to evaluate the relative impact of exocrine and endocrine pancreatic function on the uptake of this tracer.

Variable	*Estimate*	*Standard error*	*p-value*
Intercept	3.33	76.36	0.9658
Betas cell function	1.73	0.57	0.0094
Insulin AUC60 (mU/l x min)	0.07	0.02	0.0014
CCK AUC30 (pmol/l x min)	0.72	0.33	0.0457

[Table 1. Multiple linear regression on the dependent variable 'methionine SUVmax AUC60' in patients after PD (R2 = 0.84, p < 0.01)]
Disclosure: Nothing to disclose

P0091 INFLUENCE AND ROLE OF RAMP1 ON THE INNATE IMMUNE RESPONSE DURING ACUTE PANCREATITIS

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Introduction: Previous research suggests an important role of the CGRP pathway as modulator of innate immune response in mice. The CGRP receptor incorporates 2 important subunits: the receptor activity-modifying protein 1 (RAMP1) and the calcitonin receptor-like receptor (CRLR). It is known, that CGRP can directly influence immune-cells and their capacity of producing inflammatory cytokines. By using a RAMP1 full-body knockout mouse model ($RAMP^{-/-}$) we examined the role and function of the CGRP receptor in the acute phase of caerulein-induced pancreatitis.
Aims and Methods: In order to generate acute pancreatitis we performed hourly injections of caerulein for a period of 8h in our $RAMP1^{-/-}$ and control mice. Analysis was performed at 8h, 24h, 2 days and 7 days post caerulein treatment. To compare the severity and extent of inflammation in $RAMP1^{-/-}$ and wild-type mice, histological analyses including immunohistochemistry were performed. Additionally, cytokine levels were assessed using real-time PCR. For improved characterization serum-levels of LDH and Lipase were measured.
Results: $RAMP1^{-/-}$ mice showed higher ratio between pancreas-weight and body-weight ($p = 0.018$), increased tissue edema ($p = 0.0071$) and higher amount of F4/80 positive cells ($p = 0.0245$) 8h after caerulein injection, as compared to wild-type mice. Furthermore, overall infiltration of immune-cells at 24h was markedly increased in $RAMP1^{-/-}$ mice ($p < 0.0001$) and composed predominantly of MPO positive cells ($p < 0.0001$) without any difference in the number of CD8 and CD4 cells. Cleaved caspase 3 positive cells were markedly increased in $RAMP1^{-/-}$ mice at 24h post caerulein injection ($p = 0.0025$) compared to wild-typ mice. In addition, higher amount of CCL3 and IL-1β in $RAMP1^{-/-}$ mice was observed in the real-time PCR.
Conclusion: Using a murine $RAMP1^{-/-}$ model, this study underlines the essential role of the CGRP receptor as central modulator of the innate immune response in acute pancreatitis. Mice lacking RAMP1 showed increased inflammation and edema particularly in the early phase of acute pancreatitis.
Disclosure: Nothing to disclose

P0092 CLINICAL STUDY OF IMPROVEMENTS IN PANCREATIC BLOOD FLOW AS MEASURED BY PERFUSION COMPUTED TOMOGRAPHY IN PATIENTS WITH SEVERE ACUTE PANCREATITIS AND ADMINISTERED RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN

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Introduction: Pancreatic circulation failure due to disseminated intravascular coagulation (DIC) is a significant factor in determining the severity of pancreatitis. Pancreatic circulation failure affects walled-off necrosis (WON) caused by pancreatic ischemia/necrosis. A study has shown that patients with severe acute pancreatitis (SAP) administered recombinant human soluble thrombomodulin (rhTM) exhibit significant improvements in coagulation anomalies and inhibited WON development [1]. Perfusion-computed tomography (PCT), an advanced imaging technique for evaluating blood circulation in SAP, can accurately diagnose the development of pancreatic ischemia/necrosis in the early stages of SAP. PCT can also be used to predict the severity of acute pancreatitis [2].
Aims and Methods: This study applies PCT to investigate whether rhTM improved pancreatic blood flow (PBF) in cases of SAP involving pancreatic ischemia/necrosis.
We retrospectively analyzed 27 SAP patients with pancreatic ischemia/necrosis treated from January 2015 to January 2018 at Osaka Saiseikai Nakatsu Hospital. All patient data was gathered from an electronic database. The 27 SAP patients were divided into two groups: SAP patients with DIC treated with rhTM (380 U/kg for 30 minutes, once daily: the rhTM(+)DIC(+) group, 14 patients) and without DIC and not treated with rhTM (DIC(-) group, 13 patients). To determine a diagnosis of pancreatic ischemia, we measured PBF with PCT within 48 hours and set a criterion of 25% or greater reduction of PBF in a region of 1 cm^2 or larger compared to normal pancreatic parenchyma. We assessed the extent of pancreatic ischemia based on the ratio of ischemic pancreatic PBF/normal pancreatic PBF. We calculated the PBF ratio, APACHE II, SOFA, JPN prognostic factor (by the Japanese severity scoring system), and JAAM DIC scores within 48 hours of hospitalization and again on the seventh day of hospitalization (day 7).
Results: The background data for the subjects is as follows: mean age of 62.6 years; male/female ratio: 18/9; cause: 11 alcohol, 5 gallstone, 6 idiopathic, 3 cases of ERCP, 2 other, and 1 fatality. In the Revised Atlanta Criteria, the rhTM(+)DIC(+) group was significantly severe: the rhTM(+)DIC(+) group vs. DIC(-) group (7 severe/6 moderate vs. 1 severe/9 moderate). We found no differences in SOFA scores between the two groups as of the time of hospitalization (i.e., rhTM(+)DIC(+) vs. DIC(-): 3.8 ± 2.1 vs. 2.8 ± 2.4). However, we found significant differences with respect to the prognostic factor (3.5 ± 1.6 vs. 1.8 ± 1.3), mean APACHE II scores (12.5 ± 5.8 vs. 8.2 ± 4.1), and JAAM DIC scores (3.7 ± 1.5 vs. 1.9 ± 1.3) ($p < 0.05$). PBF ratios within 48 hours of hospitalization did not differ between the rhTM(+)DIC(+) and DIC(-) groups: 0.560 ± 0.144 vs. 0.673 ± 0.241. The PBF ratio for rhTM(+)DIC(+) group was significantly higher (0.760 ± 0.218) on day 7 ($p < 0.01$). The PBF ratio for the DIC(-) group without rhTM treatment failed to improve (0.670 ± 0.119) on day 7. The PBF ratio for the rhTM(+)DIC(+) group on day 7 was significantly higher than for the DIC(-) group (0.760 ± 0.218 vs. 0.670 ± 0.119) ($p < 0.05$). WON occurred in 12 cases (44.4%).
Conclusion: Since pancreatic ischemia is defined as a reduction in PBF of 25% or more, we considered ischemia in many of the patients meeting this criteria was reversible. Although the symptoms in the rhTM(+)DIC(+) group were significantly worse, improvements in the PBF ratio were significantly better. Since rhTM improved coagulation anomalies, we considered it may improve PBF ratios. rhTM offers a new therapeutic option in treating pancreatic ischemia.
Disclosure: Nothing to disclose

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P0093 ALCOHOL CONSUMPTION AND SMOKING SYNERGIZE WITH EACH OTHER AND INCREASE THE RISK OF LOCAL COMPLICATIONS IN ACUTE PANCREATITIS

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Introduction: Both alcohol consumption and cigarette smoking have been reported to have harmful effects on the pancreas. These addictions very often go together, therefore careful investigations are crucially needed to understand their independent/synergic effects on the pancreas.
Aims and Methods: To examine the clinical effects of alcohol consumption and/or smoking in patients with acute pancreatitis (AP).
A total of 1435 adult patient were enrolled from 2012 to 2017 with the diagnosis of AP in 28 healthcare centres by the Hungarian Pancreatic Study Group. Specific questionnaires for AP including information on cigarette smoking and alcohol consumption were used, whereas detailed clinical data such as the results of laboratory parameters and imaging, the course and the outcome of AP episodes were collected.
Results: 692 (48.32%) of the patients were non-drinkers and non-smokers (ND-NS). 615 of the patients were drinkers (D) (43.0%). 279 (45.4%) of the drinkers did not smoke (D-NS), whereas 336 (54.6%) of them were smokers (D-S) as well. The age of onset was 61.1y in the ND-NS group, 55.1y in the D-NS and 46.3y in the D-S group. The female/male ratio was 0.6 in the ND-NS group, 3.15 in the D-NS and 5.99 in the D-S group. Drinking alone had no effect on the BMI (ND-NS: 28.2, D-NS: 28.2), but smoking in addition to drinking decreased it (D-S: 25.7). Concerning the parameters on admission the ND-NS, D-NS and D-S groups were as follows: amylase (U/L): 1310 ± 1351, 1009 ± 1194, 737 ± 1237; lipase (U/L): 3233 ± 4911, 2617 ± 3350, 2035 ± 6617; CRP (mg/L): 53 ± 77, 51 ± 72, 63 ± 80; WBC (G/L): 13 ± 5.5, 13.3 ± 6.4, 13.6 ± 5.7. Smoking had synergic effect with drinking on local complications (ND-NS: 34.4%, D-NS: 37.5%, D-S: 44.1%) such as necrosis (8.8%, 11.0%, 11.5%), development of pseudocyst (9.0%, 9.2%, 13.3%) and fluid collection (28.3%, 31.3%, 35.5%). The percentage of moderate AP copied the same pattern (24.9%, 26.8% and 31.9%). We could see no difference in mortality and the rate of severe AP. Drinking and smoking together also elevate the risk for acute recurrent pancreatitis (ARP). 18.9% of the patients had ARP in the ND-NS, 23.5% in the D-NS, whereas 31.9% in the D-S groups.
Conclusion: Drinking and smoking together results in the onset of pancreatitis 15 years earlier, in addition it elevates the risk for recurrence of the disease. Drinking and smoking synergize with each other and increase the rate of local complications.
Disclosure: Nothing to disclose

P0094 IMPACT OF VISCERAL ADIPOSITY ON SEVERITY OF ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is a sudden inflammation of the pancreas. The early evaluation and accurate prediction of AP severity is vital, as severe cases require intensive care treatment. It is well established that obesity is a risk factor for AP and increases the incidence of systemic complication, motality. However, the relationship between visceral adiposity and acute pancreatitis has not been fully examined.
Aims and Methods: This study is to explore the predictive significance of visceral adipose tissue (VAT) and visceral adipose tissue /skeletal muscle tissue ratio (VAT/SMT ratio) for the prognosis in AP patients. After 1:2 propensity score matching, a total of 306 patients were enrolled in the analysis from 2010 to 2017. Visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and skeletal muscle tissue (SMT) were measured via unenhanced computed tomography (CT). They were calculated by Cox proportional hazards models.
Results: VAT and VAT/SMT ratio were significantly higher in the moderate SAP and SAP groups than those in the MAP group (both p values < 0.001). ICU transfer, AP severity, systemic complications and prognostic scores (Acute Physiology and Chronic Health Evaluation II [APACHE-II] score ≥ 8, Ranson's score ≥ 3, Bedside Index of Severity in Acute Pancreatitis [BISAP] score ≥ 3, the systemic inflammatory response syndrome [SIRS] score ≥ 2) were significantly related to the value of VAT and VAT/SMT ratio in the AP patients. The multivariate adjusted HR for VAT and VAT/SMT ratio in the relationship between body parameters and AP mortality were 1.042 (95% CI, 1.019–1.066) and 7.820 (95% CI, 1.978–30.917), respectively. Compared with other prognostic scores, VAT demonstrated the highest AUC (0.943, 95% CI, 0.909–0.976) among independent predictors.
Conclusion: VAT and VAT/SMT ratio play a prognostic role in AP patients.
Disclosure: Nothing to disclose

P0095 ABDOMINAL ADIPOSITY AND ECTOPIC FAT PHENOTYPES ASSOCIATED WITH THE PRESENCE OF DIABETES AFTER ACUTE PANCREATITIS

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Introduction: The adverse effects of excess body fat, in particular abdominal adiposity, and ectopic fat deposition during the course of acute pancreatitis (AP) are well established. Emerging studies indicate a high frequency of diabetes after AP, but the role of excess abdominal adiposity in post-pancreatitis setting is not completely understood. Moreover, the associations between abdominal adiposity and ectopic fat phenotypes and pancreatitis-related factors (aetiology, severity) in individuals after AP have never been studied.
Aims and Methods: The aim was to investigate phenotypic differences in distribution of abdominal adipose tissue and ectopic fat between individuals after AP (with and without diabetes) using magnetic resonance imaging (MRI). The secondary aim was to determine pancreatitis-related factors associated with abdominal adiposity and ectopic fat phenotypes. A total of 84 individuals who had been diagnosed prospectively with AP were included in this study. They were recruited after an average time of 28 months since last episode of AP and were categorised into 'diabetes' and 'no diabetes' groups, in line with the American Diabetes Association guidelines.[1] 28 normoglycaemic healthy volunteers were also recruited. Using 3 Tesla (T) MAGNETOM Skyra MRI scanner (SIEMENS, Erlangen, Germany), abdominal adiposity [(visceral fat volume (VFV), subcutaneous fat volume (SFV), visceral-to-subcutaneous fat volume ratio (V/S ratio)], and ectopic fat [liver fat percentage (LF%), pancreatic fat percentage (PF%)] phenotypes were quantified. The differences in abdominal adiposity and ectopic fat phenotypes between the groups were compared using analysis of variance. Linear regression analysis was used to investigate the association between pancreatitis-related factors and the studied phenotypes in unadjusted and adjusted (accounting for age and sex) models.
Results: Of the abdominal adiposity phenotypes, VFV was significantly higher in the diabetes (2715.3 ± 1077.6 cm^3) as compared with no diabetes (1983.2 ± 1092.4 cm^3) and healthy (1126.2 ± 740.4 cm^3) groups ($p < 0.001$). Moreover, V/S ratio was significantly higher in the diabetes (0.97 ± 0.27) as compared with no diabetes (0.68 ± 0.42) and healthy (0.52 ± 0.34) groups ($p = 0.001$). Of the ectopic fat phenotypes, PF% was significantly higher in the diabetes ($10.2 \pm 1.2\%$) as compared with no diabetes (9.2 ± 1.7 %) and healthy (7.9 ± 1.9 %) groups ($p < 0.001$). Other studied phenotypes did not differ significantly between the groups. C-reactive protein levels during hospitalization for AP were associated with significantly increased VFV in unadjusted ($\beta = 3.32$; 95% CI, 1.68, 4.96; $p < 0.001$) and adjusted ($\beta = 2.71$; 95% CI, 1.24, 4.19; $p < 0.001$) models. Biliary aetiology of AP was associated with a significantly increased PF% in adjusted model ($\beta = 0.67$; 95% CI, 0.01, 1.33; $p = 0.047$).
Conclusion: The findings of this study show, for the first time, that individuals after an episode of AP have abnormal adiposity phenotypes, particularly increased visceral fat and pancreatic fat depots. Further, these depots are significantly associated with the presence of diabetes after AP. Levels of C-reactive protein during hospitalisation for AP are significantly associated with VFV whereas biliary aetiology of AP is significantly associated with PF%.
Disclosure: Nothing to disclose

Reference

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P0096 DIETARY FAT PATTERNS AND OUTCOMES IN ACUTE PANCREATITIS

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Introduction: Lipolysis of adipocyte triglycerides by pancreatic lipases resulting in the release of free Fatty Acids (FA) seem to be an important factor in the pathogenesis of local and systemic complications in acute pancreatitis (AP). In this setting, several basic and clinical studies suggest that unsaturated FA (UFAs) are associated to a more severe AP, while saturated FA (SFAs) are less toxic. We speculated that differences in dietary fat patterns are associated to different composition of fat storages, and thus to a different frequency of complications and death in AP.
Aims and Methods: Our aim was to investigate whether different patterns of fat intake are associated to worse outcomes in AP. We used data from the Atlantis project, a 23-center prospective nation-wide Spanish database aiming to investigate the determinants of morbidity and mortality in acute pancreatitis. Dietary fat patterns (fat intake, proportion of fats, SFAs, mono and polyunsaturated UFAs) from different regions of Spain were retrieved from the ANIBES (Anthropometry, Intake and Energy Balance in Spain) cross-sectional study using a nationally representative sample of the Spanish population. Outcome variables were: necrotizing pancreatitis (pancreatic gland and/or peripancreatic fat necrosis), persistent organ failure (POF) and mortality. Variables addressing fat intake were divided according to their median value into low and high intake. Univariate (Chi-square) and multivariate (binary logistic regression) analysis were performed. The variables included on the multivariate analysis model were: Charlson comorbidity index >3 (includes also age), alcohol etiology, gender, obesity and recurrent AP; adjusted Odds Ratio (aOR) were calculated.
Results: 1,655 episodes of AP were analyzed. Etiology was biliary in 60%, 54% of the patients were male, AP was associated to necrosis in 17%, to persistent organ failure (POF) in 7% and mortality was 4%. On univariate and multivariate

analysis, a high SFA intake was independently associated to a lower risk of necrosis [15 vs. 19%, aOR 0.746 (0.570–0.978), p = 0.034], a lower risk of POF [5 vs. 9%, aOR 0.550 (0.367–0.822), p = 0.004] and mortality [3 vs. 6%, aOR 0.548 (0.329–0.914), p = 0.021].
Conclusion: Our study suggests that a high saturated fatty acid intake is associated to improved outcomes in acute pancreatitis, resulting in a 50% lower risk of persistent organ failure and mortality.
Disclosure: Nothing to disclose

P0097 BODY-MASS INDEX CORRELATES WITH SEVERITY AND MORTALITY IN ACUTE PANCREATITIS - A META-ANALYSIS

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Introduction: During the past decades, obesity rates have increased sharply. As there is a growing number of cases in which acute pancreatitis (AP) is accompanied by obesity, we found it clinically relevant to investigate how body-mass index (BMI) affects the outcome of the disease.
Aims and Methods: Our aim was to quantify the association between subgroups of BMI and the severity and mortality of AP. A meta-analysis was performed using the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols. 3 databases (PubMed, EMBASE and Cochrane Library) were searched for articles containing data on BMI, disease severity and mortality rate of AP. English-language studies from inception to 19 June 2017 were checked against our predetermined eligibility criteria. The included articles reported all AP cases with no restriction on the etiology of the disease. In severity analyses we only involved studies that classified AP cases according to the Atlanta Criteria. Odds ratios (OR) and mean differences (MD) were pooled using the random effects model by the DerSimonian-Laird estimation and displayed on forest plots. The meta-analysis was registered in PROSPERO under number: CRD42017077890.
Results: Altogether 19 articles were included in our meta-analysis, containing data on 9,997 patients. Severity: The subgroup analysis shows a direct association between AP severity and BMI. BMI < 18.5 compared to normal BMI (18.5–25) seems to increase the risk of severe AP (OR = 1.89, 95% CI = 0.52–6.87, p = 0.336), however this result is not significant. Patients with a BMI > 25 have an almost 3 times increased risk for a severe AP (OR = 2.87, 95% CI = 1.90–4.35, p < 0.001) in comparison to normal BMI. The mean BMI of patients with severe AP is notably higher than of the non-severe group (MD = 1.79, 95% CI = 0.89–2.70, p < 0.001). Mortality: Death rates of AP patients are the highest in the underweight and obese subgroups. A BMI < 18.5 carries an almost 2-fold increase in risk of mortality (OR = 1.82, 95% CI = 1.32–2.50, p < 0.001) in comparison to normal BMI. However, the chance of mortality is almost equal in the normal BMI and BMI 25–30 subgroups. A BMI > 30 results in a 3 times higher risk of mortality in comparison to a BMI < 30 (OR = 2.89, 95% CI: 1.10–7.36, p = 0.026).
Conclusion: Our new findings confirm that a BMI 25–30 increases the risk of severe AP, but not mortality, while a BMI > 30 increases both the risks of severe AP and mortality. A BMI < 18.5 carries an almost 2 times higher risk of mortality in AP.
Disclosure: Nothing to disclose

P0098 GENERAL AND ADIPOSE TISSUE-SPECIFIC INSULIN RESISTANCE AFTER AN EPISODE OF ACUTE PANCREATITIS

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Introduction: Emerging evidence indicates that individuals after an episode of acute pancreatitis (AP) are at an increased risk of developing metabolic derangements, in particular new-onset prediabetes or diabetes after AP.[1] The link between general obesity and insulin resistance (IR) was established decades ago, however the impact of body fat distribution on IR has gained attention only recently and is not completely understood. In the setting of AP, the association between abdominal obesity and IR, and a comprehensive assessment of various IR indices in post-pancreatitis setting, is lacking.
Aims and Methods: The aim of this study was to investigate associations between abdominal obesity and IR (general and adipose tissue-specific) in patients after AP independent of the effect of covariates including diabetes mellitus, and to determine the relative accuracy of several indices of IR in characterising abdominal obesity. Patients were eligible for this cross-sectional study if they were previously admitted with a primary diagnosis of AP, established prospectively. Fasting venous bloods were collected to measure glucose, insulin, free fatty acids, glycerol, adiponectin (AD), omentin (OM), and vaspin(VAS). The IR indices - homeostasis model assessment of IR (HOMA-IR), adipose tissue IR (Adipo-IR), insulin*glycerol (IG) index, HOMA-AD, HOMA-OM, and HOMA-VAS were calculated. Abdominal obesity was defined according to the National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines.[2] Modified Poisson regression was conducted, with statistical model adjusting for patient-, metabolic-, and pancreatitis-related risk factors. Areas under the receiver operating characteristic (ROC) curve were calculated to compare the relative accuracy of the studied indices followed by determination of agreement between the two new indices (HOMA-OM, HOMA-VAS) and HOMA-IR.
Results: Of the 92 individuals recruited, 41 had abdominal obesity. The median (interquartile range) time since AP was 24 (7 - 46.5) months. Insulin resistance indices HOMA-IR, IG index, HOMA-OM, and HOMA-VAS were significantly associated with abdominal obesity, both in unadjusted and adjusted models (Table 1). Area under ROC curves for HOMA-IR was 0.698 (95% CI, 0.591, 0.791; p < 0.001), for IG index was 0.695 (95% CI, 0.585, 0.791; p < 0.001), for HOMA-OM was 0.756 (95% CI, 0.648, 0.845; p < 0.001), and for HOMA-VAS was 0.735 (95% CI, 0.625, 0.827; p < 0.001). There was a good agreement between observed HOMA-IR values and values obtained from HOMA-OM (p = 0.733) and HOMA-VAS (p = 0.595).
Conclusion: Individuals with abdominal obesity after AP have a significantly higher IR, independent of diabetes and other covariates. Visceral adipose tissue specific adipokines, omentin and vaspin, hold promise for future clinical investigation of tissue-specific IR.
[Associations between the indices of insulin resistance and abdominal obesity]
Disclosure: Nothing to disclose

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Insulin resistance indices	Models	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P-trend
HOMA-IR	Unadjusted	1.00 (reference)	3.49 (1.10, 11.00)	4.67 (1.55, 14.09)	4.38 (1.43, 13.41)	**0.003**
	Adjusted	1.00 (reference)	3.39 (1.01, 11.35)	5.11 (1.56, 16.71)	5.93 (1.73, 20.30)	**0.001**
Adipose tissue-IR	Unadjusted	1.00 (reference)	0.57 (0.25, 1.30)	1.00 (0.52, 1.91)	1.05 (0.56, 1.97)	0.411
	Adjusted	1.00 (reference)	0.56 (0.24, 1.28)	0.86 (0.45, 1.64)	1.13 (0.47, 2.75)	0.424
Insulin*glycerol index	Unadjusted	1.00 (reference)	1.00 (0.38, 2.60)	2.33 (1.11, 4.89)	2.16 (1.02, 4.61)	**0.011**
	Adjusted	1.00 (reference)	1.18 (0.44, 3.21)	2.19 (1.06, 4.52)	2.89 (1.21, 6.89)	**0.014**
HOMA-Adiponectin	Unadjusted	1.00 (reference)	1.40 (0.53, 3.68)	2.00 (0.83, 4.81)	2.32 (0.99, 5.42)	0.156
	Adjusted	1.00 (reference)	1.72 (0.60, 4.99)	2.32 (0.96, 5.60)	2.52 (1.00, 6.35)	0.180
HOMA-Omentin	Unadjusted	1.00 (reference)	2.80 (0.86, 9.09)	3.85 (1.26, 11.80)	4.55 (1.52, 13.61)	**0.005**
	Adjusted	1.00 (reference)	2.81 (0.92, 8.63)	4.68 (1.54, 14.27)	5.20 (1.67, 16.26)	**0.006**
HOMA-Vaspin	Unadjusted	1.00 (reference)	1.14 (0.41, 3.16)	2.00 (0.83, 4.81)	3.00 (1.35, 6.68)	**0.004**
	Adjusted	1.00 (reference)	1.09 (0.42, 2.84)	2.10 (0.93, 4.74)	3.12 (1.38, 7.03)	**0.009**

P0099 COMBINATION OF HEPARANASE INHIBITORS AND ASPIRIN DRAMATICALLY AMELIORATES ACUTE PANCREATITIS IN AN ANIMAL MODEL

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Introduction: Acute pancreatitis (AP) is one of the most common diseases in gastroenterology. However, neither the etiology nor the pathophysiology of the disease is fully understood and no specific or effective treatment has been developed. We previously showed that heparanase (Hpa) appears to play an important role in the pathogenesis of AP and that Hpa inhibitors significantly reduced the severity of the AP in an animal model. Aspirin has also been demonstrated to inhibit Hpa activity both *in vivo* and *in vitro*. We hypothesize that a combination of Hpa inhibitor and aspirin can ameliorate AP more efficiently than each drug alone.
Aims and Methods: The current study examines whether combination of Aspirin with PG545 or Roneparstat (SST0001), 2 inhibitors of Hpa, exerts superior pancreato-protective effect in cerulein-induced AP in mice, vs each compound alone.
Heparanase-overexpressing transgenic mice (Hpa-TG) and wild-type (WT) BALB/c mice (n = 7–8) were intraperitoneally injected with either cerulein (50 mg/kg, 5 times, at 1 hour apart) or vehicle, with or without either PG545 (0.4 mg/mouse, kind gift of Dr. Edward Hammond, Zucero Therapeutics, Brisbane, Queensland, Australia), Roneparstat (2 mg/mouse, kind gift of Dr. Alessandro Noseda, Leadiant Biosciences S.A., Mendrisio, Switzerland), Aspirin (250 mg/kg) or combination of both drugs. The animals were sacrificed 24 hours following the induction of pancreatitis. The severity of AP and architectural structure changes were evaluated by serum pancreatic enzyme (amylase and lipase) levels, inflammatory cytokines, pancreatic edema index (determined by organ-to-animal weight ratio), tissue inflammatory response (determined by immune-histopathological analysis) and autophagy response (determined by electron microscopy and immunohistochemistry staining).
Results: Cerulein-induced AP in WT mice was associated with significant rises in the serum levels of amylase (X2.5) and lipase (X4). These increases were characterized by elevated levels of amylase and lipase, enhancement of pancreatic edema index, tissue inflammation, and autophagy response. All types of responses to administration of cerulein were profoundly exaggerated in Hpa-TG mice that over-express heparanase, as was evident by 6- and 8-fold increases in amylase and lipase levels, respectively. Importantly, pretreatment with Aspirin, PG545 or Roneparstat reduced pancreatic inflammatory response, autophagy, and amylase and lipase serum levels in both WT and Hpa-Tg mice. Noteworthy, combination of Aspirin with either PG545 or Roneparstat completely abolished AP at the biochemical, inflammatory and histological levels in both subgroups of animals.
Conclusion: Administration of either Aspirin or Hpa inhibitor exerts protective effect against Cerulein-induced AP. Interestingly, combination of Aspirin and Hpa inhibitors completely abolished AP, providing a rational basis for the treatment of this clinical setting
Disclosure: Nothing to disclose

P0101 CENTRALIZED CARE OF ACUTE PANCREATITIS SIGNIFICANTLY IMPROVES ITS OUTCOMES

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Introduction: In this observational study, we investigated whether specialized care improves outcomes of acute pancreatitis (AP).
Aims and Methods: Consecutive patients admitted to 2 university hospitals with AP between 01.01.2016.–31.12.2016. were enrolled in this study (group A: specialized center, group B: general medical care). Data on demographic characteristics, etiology, severity, mortality and quality of care (enteral nutrition and antibiotic use) of AP were extracted from the Hungarian Acute Pancreatitis Registry. Independent sample t-test, Mann-Whitney test, Chi-squared or Fisher test were used for statistical analyses. Costs of care were calculated and compared in the 2 models of care.
Results: There were 355 patients enrolled between 01.01.2016 and 31.12.2016., 195 patients in the specialized center (group A) and 160 patients in the general medical hospital (group B). There was no difference in the mean age (57.02, +/−17.16 vs. 57.31, +/−16.50, p = 0.872) and sex ratio (56% males vs. 57% males, p = 0.837) between group A and B; allowing comparison without selection bias. Group A had lower mortality (n = 2, 1.03% vs. n = 16, 6.25%, p = 0.007), more patients received enteral feeding (n = 179, 91.8%, vs. n = 36, 22.5%, p < 0.001), less patients were treated with antibiotics (n = 85, 43.6% vs. n = 123, 76.9%, p = 0.001) and the median length of hospitalization was shorter (Me 6, IQR 5-9 vs. Me 8, IQR 6-11, p = 0.02). Costs of care were 25%less in group A.
Conclusion: Our data suggests that treatment of AP in specialized centers improves its mortality, the quality of care, the length of hospitalization and reduces the costs of care.
Disclosure: Nothing to disclose

P0102 GENISTEIN INHIBITS THE ACTIVATION OF PANCREATIC STELLATE CELLS BY PI3K/AKT/MTOR SIGNALING PATHWAY

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Introduction: In 1998, pancreatic stellate cells (PSCs) were firstly characterized by stelliform cells in pancreas. In healthy pancreas, PSCs are inactive and accompanied by lipid droplets that contain vitamin A. As the response of inflammation of injury, they were awakened from their inactive phenotype into highly proliferative myofibroblast-like cells with extracellular matrix components (EMCs) expressions and α-smooth muscle actin (α-SMA) positive.
In pancreatic ductal adenocarcinoma (PDAC) and chronic pancreatitis (CP), it is the activated PSCs that deposit collagen fibers and contribute to the progression of pancreatic fibrosis. Therefore, the in-depth study of the processes involved in PSCs activation is of critical importance for the development of effective therapeutic approaches for pancreas related diseases. Any agents which can inhibit the activation of PSCs could become potential candidates for treatment strategies in PDAC and CP.
Genistein a kind of isoflavonoid. In many reports, soy production shows potential efficacy to reduce the risk of osteoporosis, cardiovascular disease, and cancer. And genistein also has the antioxidant activity. A recent study showed that genistein can suppress the ROS-induced hypersensitivity.
Many studies have demonstrated that oxidative stress (OS) exists in CP and PDAC proven by reduced sustains antioxidant (AO) capacity and increased levels of products of OS in patients with CP and PDAC.
Genistein has the antioxidant activity, however, whether genistein can affect the activation of PSCs remains unclear until now. Hence, in this study, we aimed to explore the effect of genistein applied to the processes of PSCs activation. Our research can provide more groundwork for genistein related clinical treatment strategies of pancreas disease.
Aims and Methods: Pancreatic stellate cells (PSCs) have a vital role in pancreatic fibrosis accompanied by pancreatic ductal adenocarcinoma (PDAC) and chronic pancreatitis (CP). Any agents which can affect the activation of PSCs could become potential candidates for treatment strategies in PDAC and CP. Our aim was to explore the effect of genistein in the processes of PSCs activation.
Isolated PSCs from C57BL/6 mouse were treated with various dosages of genistein. Effect of genistein on autophagy, senescence and oxidative stress, as well as the activation of PSCs were analyzed by immunocytofluorescent staining, quantitative real time RT-PCR, western blotting, SA-β-galactosidase staining, malondialdehyde and reactive oxygen species (ROS) assay. Chronic pancreatitis animal model was also established to identify the anti-fibrotic effect of genistein by HE, Masson and Red sinus staining.
Results: Expression of α-smooth muscle actin, LC3II and Beclin1 levels were significantly reduced in genistein treatment groups. Meanwhile, compared with the control group, significant differences in the expression of desmin, P62, p-PI3K, p-AKT and p-mTOR levels in genistein treatment groups were found. Moreover, genistein affected the secretion of extracellular matrix components for PSCs. Few SA-β-gal positive cells were found in genistein-treated groups. A significant decrease in ROS positive cells and malondialdehyde levels were observed after exposure to genistein. The HE, Masson and Red sinus staining showed that there was less ECM production in genistein group.
Conclusion: Our finding suggests that genistein inhibits the activation of PSCs by suppressing autophagy through activating the PI3K/AKT/mTOR signaling pathway. Genistein may act as a therapeutic agent in PSC-related pathologies and/or anti-fibrotic approaches.
Disclosure: Nothing to disclose

P0103 DIAGNOSIS, TREATMENT AND LONG-TERM OUTCOMES OF AUTOIMMUNE PANCREATITIS IN SWEDEN

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Introduction: Autoimmune pancreatitis (AIP) is a pancreatic inflammatory process characterized by a strong inflammatory cell infiltration and 2 histopathological distinct subtypes: type 1 and type 2. Diagnosis is often challenging and requires a combination of clinical, laboratory and imaging data. AIP can mimic pancreatic tumors leading to unnecessary resections if not correctly diagnosed. Short and long-term outcomes of AIP have been poorly investigated so far and no big series has been previously reported from Sweden.

Aims and Methods: We aimed to determine clinical presentation together with short and long-term outcomes of AIP in Sweden.
This was a single-center, retrospective, cohort study of patients with histologically confirmed or highly probable diagnosis of AIP according to ICDC criteria. Clinical/radiological characteristics, type of treatment and its outcomes were collected and analyzed. T-test was used for statistical analysis.
Results: 71 patients with AIP (87.3% with type 1), were evaluated at Karolinska University Hospital between 2004 and 2018; 49.2% males, mean age 49.2 years (range 44.7–53.8). Among them, 28.1% were histologically confirmed, 35.2% presented with jaundice, 22.5% with acute pancreatitis, 39.4% had non-specific symptoms such as weight loss or abdominal pain, 40.8% displayed other organ involvement (OOI). Radiologically, 40.5% displayed a focal mass, 36.2% a focal pancreatic enlargement, 27.5% a sausage-like pattern, 27.5% signs of acute pancreatitis, 10.1% of chronic pancreatitis. In total 58 patients (81.6%) underwent treatment comprising different medications: 46 (79%) cortisone, 7 (12.0%) azathioprine, 5 (8.6%) other immunosuppressive drugs. 26 (36.6%) underwent biliary stenting and 12 (16.9%) surgery due to suspicion for pancreatic malignancy. All (100%) of patients treated with cortisone, displayed a clinical response. After a mean follow-up of 46.7 months, 97.1% of patients were alive, 92.6% were in clinical remission, 70% displayed a radiological complete response, 89.6% were treatment-free. None developed pancreas cancer but 1 patient (1.4%) developed mucinous cystic neoplasm (MCN) with high-grade dysplasia and was therefore successfully operated. 59.3% of patients developed pancreatic exocrine insufficiency (PEI) of which 76.4% had a severe form (fecal elastase-1 < 100 μg/g) and 23.8% of patients developed diabetes mellitus (pancreatic endocrine insufficiency) of which 73.3% requiring insulin.
Conclusion: AIP is a challenging disease for diagnosis and treatment. Cortisone treatment is generally successful and provides clinical remission in the large majority of patients ($>90\%$). In the further course of the disease, a considerable number of patients develop PEI (up to 60% of pts) and diabetes (up a quarter of pts). Only a quarter of patients exhibit the characteristic ''sausage-like''pancreas, approximately 40% had a focus mass that can be misdiagnosed as pancreatic malignancy.
Disclosure: Nothing to disclose

P0104 DEFICIENCY OF FAT-SOLUBLE VITAMINS, MINERALS AND TRACE ELEMENTS IN PATIENTS WITH CHRONIC PANCREATITIS OF DIFFERENT ETIOLOGY

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Introduction: Malnutrition with deficiencies of fat-soluble vitamins and trace elements are well-known consequences of maldigestion and poor absorption of nutrients, and have been frequently identified in patients with pancreatic exocrine insufficiency (PEI).
The prevalence of abnormal laboratory nutritional markers in chronic pancreatitis has been investigated in several studies, but most of them were restricted to patients with alcoholic chronic pancreatitis (CP) and had limitations due to the small number of studied patients. We are presenting results of the largest study so far comparing markers of malnutrition in relation to different etiological groups of CP.
Aims and Methods: We performed a retrospective analysis of medical records of patients with CP. Etiology of CP was determined according to M-ANNHEIM classification. The following demographic, clinical and demographic parameters were analyzed: age, gender, smoking (pack years), consumption of alcohol (units per day/years), fecal elastase-1 (FE1), albumin, calcium, magnesium, iron, triglyceride, cholesterol, hemoglobin, vitamin A, vitamin E, vitamin D and zinc.
Results: Altogether, 226 patients were included in the analysis: 131 (58.0%) male and 95 (42.0%) female, mean age 51.8 ± 17.9 years (range 18–89). The different etiologies of CP comprised: autoimmune ($n=69$; 30.5%), alcohol ($n=65$; 28.8%), efferent duct factors ($n=19$; 8.4%), hereditary ($n=26$; 11.5%), smoking ($n=20$; 8.8%) and idiopathic ($n=27$; 12.0%). FE1 was normal (FE1$>$ 200mg/g) in 83 (41.7%) patients. Mild to moderate PEI (FE1: 100–200mg/g was found in 22 (11.1%) of patients and severe PEI (FE1$<$ 100mg/g) in 94 (47.2%) of patients. Prevalence of deficiencies in serum nutritional panel was as follows: vitamin D 51.3%, albumin 34.2%, zinc 26.0%, hemoglobin 15.8%, cholesterol 14.1%, cobalamin 11.0%, iron 10.5%, vitamin A 8.3%, vitamin E 6.9%, magnesium 5.7%, folate 4.4%, triglycerides 1.1% and calcium 0%, with no statistical significant differences between nutritional deficiencies and different etiologies of CP. Factors associated with low zinc values were age >70 years ($p=0.003$) and current smoking status. ($p=0.02$). Factors associated with low vitamin D levels were age >60 years ($p=0.03$), male gender ($p=0.05$), insulin treated diabetes mellitus ($p=0.05$) and severe PEI ($p=0.05$). In patients in whom bone-mineral density was performed, 21 (24.1%) of patients had osteopenia and 9 (10.3%) osteoporosis.
Conclusion: A large number of CP patients exhibits signs of malnutrition with vitamin deficiencies. Deficiencies of fat-soluble vitamins, minerals and trace elements appear not to be related to CP etiology. Noteworthy, more than a third of patients with CP exhibit osteopenia or osteoporosis.
Disclosure: Nothing to disclose

P0105 PREDICTION OF PANCREATIC ATROPHY AFTER STEROID THERAPY USING EQUILIBRIUM CONTRAST CT IMAGING IN AUTOIMMUNE PANCREATITIS

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Introduction: Previous reports showed pancreatic atrophy 6 months after the beginning of steroid therapy was associated with diabetes control worsening and incidence of new onset of diabetes in patients with autoimmune pancreatitis (AIP). However, predictor for pancreatic atrophy after steroid therapy at the diagnosis of AIP remains unknown.
Aims and Methods: We aimed to evaluate the role of equilibrium computed tomographic (CT) imaging for the prediction of pancreatic atrophy 6 months after steroid therapy
33 steroid treated AIP patients, who underwent CE-CT examinations before and after steroid therapy, were included in this study during December 2005 to October 2015. CT attenuation (Hounsfield units [HU]) values in noncontrast (NC) and equilibrium phase (EP) images were measured by placing 3 regions of interest (ROIs) from the pancreas swelling at the diagnosis of AIP. The incidence of the pancreatic atrophy after steroid therapy was estimated by the following 3 parameters in CE-CT before steroid therapy: 1) HU values in NC images; 2) HU values in EP images; and 3) subtracted HU values between NC and EP images. The relationship of each HU value with the degree of thickness of pancreatic body ($<$ 10mm, 10–15mm, $<$ 15mm) was also investigated. Pancreatic atrophy 6 months after steroid therapy was defined to be present when the width of the pancreatic body was less than 10 mm.
Results: Pancreatic atrophy was observed in 11 patients and not in 22 patients after the steroid therapy. Pancreatic atrophy was not associated with the thickness of pancreatic body on CE-CT before steroid therapy, other organ involvement, pattern of pancreas swelling (diffuse/focal) and serum IgG4 levels. The HU values in EP and subtracted HU values in AIP with atrophy were significantly higher than those without atrophy (113.2 ± 16.1 vs. 100.0 ± 11.8, $p=0.01$, 70.7 ± 18.0 vs. 57.8 ± 13.9, $p=0.03$). Thickness of pancreatic body after steroid therapy was also associated with HU values in EP and subtracted HU values (less than 10mm: 10–15mm: more than 15mm 113.2 ± 16.1 105.6 ± 9.2: 92.7 ± 10.9, $p=0.002$, 70.7 ± 18.0: 63.6 ± 11.7: 50.4 ± 13.5, $p=0.01$).
Conclusion: Equilibrium contrast CT imaging at the diagnosis of AIP would be a potential predictor for pancreatic atrophy after steroid therapy. The use of other therapies, such as immune-modulating agents, might be recommended for those patients.
Disclosure: Nothing to disclose

P0106 INCIDENTAL FINDINGS OF FATTY PANCREAS ON COMPUTED TOMOGRAPHY ASSOCIATED WITH IMPAIRED BONE METABOLISM

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Introduction: Fatty pancreas (FP) is an increasingly recognised entity associated with obesity and the metabolic syndrome. It correlates with non-alcoholic fatty liver disease (NAFLD) and progression to cirrhosis. It is hypothesised that a similar process exists resulting in chronic pancreatitis, fibrosis and pancreatic exocrine insufficiency (PEI) with associated malnutrition-related complications; such as vitamin D deficiency and impaired bone metabolism.[1–3] FP as a cause of PEI has not been thoroughly assessed, with published studies largely comprising case reports.[4–5]
Aims and Methods: This study assessed the relationship between FP and PEI, by examining the correlation with impaired bone metabolism. Cases were identified by a search of computed tomography (CT) reports from January 1st, 2010 to June 30th, 2017 at Melbourne Health, using keywords of FP and its synonyms; including pancreatic lipomatosis, fatty replacement or infiltration of the pancreas, lipomatous pseudo-hypertrophy of the pancreas, and pancreatic steatosis.[6] Controls were identified using keywords of normal pancreas. All images were reviewed by a radiologist to confirm CT report diagnoses. Retrospective clinical data was obtained from existing medical records and pathology. Data of interest included features of impaired bone metabolism, namely osteopenia and osteoporosis. Patients without available medical records were excluded. Cases and controls were assessed for baseline characteristics, including gender and age. Outcomes of impaired bone metabolism were assessed as categorical variables and statistical analysis undertaken on identified trends. Chi-square test for independence was used with a statistical significance level of $p < 0.05$; Fisher's exact test was used for small sample sizes with a statistical significance level of $p<0.05$. Sub-analyses were completed to remove confounding variables of age and gender.

Results: 133 cases and 117 controls were identified. There were no statistically significant differences in gender distribution or age between the cohorts. Both groups comprised 59% males. The mean age of cases and controls was seventy-75 years and 76 years respectively [case range 43–99 years; control range 42–94 years; p = 0.15]. There was a statistically significant difference in impaired bone metabolism, present in FP cases and controls in 41.4% and 20.5% respectively [OR 2.73, RR 2.02]. This difference was independent of gender [males OR 3.53, RR 2.65; females OR 2.28, RR 1.63] and age greater than 65 years [total OR 2.83, RR 2.02; males OR 3.44, RR 2.53]; women greater than 65 years demonstrating a positive trend without statistical significance [OR 2.19, RR 1.56].
Conclusion: The study showed a statistically significant relationship between incidental FP and impaired bone metabolism with a RR of 2.02. This was independent of gender and increased age, except with women greater than 65 years of age showing a positive trend but no statistical significance. This suggests that FP is not a benign finding and is associated with PEI. Recognising these patients is of clinical importance, as early detection and treatment of PEI will improve the associated morbidity and mortality.
Disclosure: Nothing to disclose

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P0107 METABOLIC BONE DISEASE IN CHRONIC PANCREATITIS; A SINGLE-CENTRE EXPERIENCE

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Introduction: Chronic pancreatitis is associated with metabolic bone disease which increases the risk of fragility fractures. The National Institute of Clinical Excellence (NICE) guidance recommends that all patients aged 50 or over should be considered for DEXA scanning if at risk (1). Previous data has shown underutilisation of DEXA scanning in this population despite increased risk of osteoporosis. The aim of this study was to assess compliance with metabolic bone assessment in patients with chronic pancreatitis, assess the prevalence of abnormal DEXA scans and the impact of this assessment on appropriate management.
Aims and Methods: Retrospective analysis of outpatient coding for ''chronic pancreatitis'' was performed over a 2-year period. Patient demographics, aetiology of chronic pancreatitis, prescription of pancreatic enzyme replacement therapy (PERT), vitamin D levels, DEXA scan result, history of fractures and bone protection medications were noted. Univariate and multivariable analysis were performed to explore why DEXA scanning was not performed as well as factors associated with abnormal scans. The impact of DEXA scanning on prescription of bone protection was also assessed.
Results: 134 chronic pancreatitis patients (mean age 57.6 years, 88 males) were included with aetiology recorded as alcohol (n = 68), idiopathic (n = 52), hypertriglyceridaemia (n = 5), autoimmune (n = 4), hereditary (n = 3), anatomical (n = 1) and biliary (n = 1). 102/134 (76.1%) had vitamin D levels tested of which 82/104 (78.8%) were low. 62/134 (46.3%) had been sent for DEXA scanning of which 8 results were unavailable, 19 (30.6%) were normal, 24 (38.7%) showed osteopenia and 11 (17.7%) osteoporosis. 46/62 (74.2%) who had a DEXA scan were on bone protection compared to 30/72 (41/7%) who did not have a DEXA scan (p = 0.002). Lack of DEXA scanning was associated with female sex (adjusted OR 0.22, 95% CI 0.09–0.57, p = 0.0017) and not requiring PERT (adjusted OR 0.44, 0.20–0.95, p = 0.035). Not requiring PERT was also independently associated (protective) with abnormal DEXA scan results (adjusted OR 0.17, 95% CI 0.03–0.98, p = 0.047). 76 patients were prescribed bone protection of which 11 were on bone protection and 10 had a DEXA scan. 21/134 (15.7%) had a previous fracture of which 10 had DEXA scanning. 8/10 were on bone protection compared to 2/11 who had not had a DEXA scan (p = 0.03).
Conclusion: Despite a high prevalence of metabolic bone disease, less than half of chronic pancreatitis patients were assessed. Those not requiring PERT and females were less likely to have a DEXA. Interestingly, DEXA scanning was significantly associated with appropriate prescription of bone protection. Whether a standardised proforma would improve rates of metabolic bone assessments needs to be studied.
Disclosure: Nothing to disclose

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P0108 DIFFERENCES IN IMAGING STUDY BETWEEN LOCALIZED AUTOIMMUNE PANCREATITIS AND PANCREATIC CANCER: A MATCHED CASE-CONTROL STUDY

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Introduction: Although the differential diagnosis between autoimmune pancreatitis (AIP) and pancreatic cancer (PC) is important in clinical settings, it is difficult to distinguish PC and localized type AIP which mimics PC in clinical presentation. However, the difference in imaging study between them has not been fully discussed.
Aims and Methods: The aim of this study was to compare the imaging findings between localized AIP and PC. 81 patients were diagnosed as AIP by International Consensus Diagnostic Criteria (ICDC) from April 2007 to October 2017, and 22 of them who showed the focal enlargement in parenchymal imaging were analyzed retrospectively (Group AIP; definitive 18, probable 4). During the same period, 191 patients were diagnosed as PC after surgical resection, and 44 of them were selected as a control (Group PC) in this study. To minimize the selection bias, the patients in Group PC was extracted by 1: 2 ratio optimal matching, which was adjusted for age, gender, mass location, tumor size using propensity score. Measured outcomes were the findings of contrast enhanced CT, MRCP, and EUS. The statistical evaluations were conducted using Mantel-Haenszel test.
Results: Median ages of Group AIP and PC were 69 (range, 49–80) and 71 (range, 49–82) years old, respectively. The male to female ratios of them were 15: 7 and 28: 16. The mass location of the patients in Group AIP was pancreatic head in 11 and body/tail in 11 while that of the patients in Group PC was pancreatic head in 22 and body/tail in 22. Median tumor sizes of them were 21 (range, 5–40) and 23 (range, 10–23) mm. On CT imaging, the rates of the patients with a low attenuation lesion in arterial phase or apparent capsule like rim were not different between Group AIP and PC (95% vs. 98%; 9% vs. 2%). However, a high attenuation lesion as compared to normal pancreatic parenchyma in equilibrium phase was observed more in the patients of Group PC (27% vs. 55%, p = 0.029). More than 4mm of main pancreatic duct (MPD) dilation was also noticed more in the patients in Group PC (27% vs. 64%, p = 0.008). MRCP was carried out to 19 patients of Group AIP and matched 30 patients of Group PC. Among them, MPD stricture at the lesion was observed in 84% of Group AIP and 80% of Group PC. However, MPD stricture apart from the lesion was also indicated in 53% of Group AIP and 7% of Group PC, which showed a significant difference between them. As for EUS, the significant differences were not present in the findings regarding the boundary or echogenicity of the lesion. However, hyperechoic foci inside the lesion was observed more in the patients of Group AIP (91% vs. 7%, p < 0.007).
Conclusion: While a high attenuation tumor in equilibrium phase or more than 4mm of MPD dilation on CT were observed more frequently in PC, specific findings of AIP were the MPD stricture apart from the lesion on MRCP and presence of hyperechoic foci inside the lesion on EUS.
Disclosure: Nothing to disclose

P0109 THE FIRST DEFINITION FOR EARLY CHRONIC PANCREATITIS

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Introduction: Early diagnosis of chronic pancreatitis (CP) is important in order to stop the disease progression in time. Unfortunately, neither definitions nor biomarkers of early CP are available. It has been reported that acute recurrent pancreatitis (ARP) can lead to CP, therefore, the number of previous attacks or ARP-associated parameters may be suitable for characterizing early CP.
Aims and Methods: The main aim of this study is to identify biomarkers which are significantly different in acute pancreatitis (AP), ARP, and CP. Another aim

is to understand the modifying effect of the number of acute episodes which could be considered as early CP. The Hungarian Pancreatic Study group has built up a prospective register of subjects with AP. In the last 6 years, precise clinical data were collected from 1435 patients. In this study, data on the number of episodes from 1315 patients with high data accuracy were analyzed.
Results: In our cohort, 983 (74.75%), 270 (20.53%), 62 (4.72%) patients had a single episode of AP, ARP, and CP, respectively. In the ARP group, 173 patients (64.07%) had 2 episodes, 43 (15.93%) had 3 episodes, 24 (8.89%) had 4 episodes, and 30 (11.11%) had 5 or more episodes. 13 biomarkers were significantly different in the first attack of AP and CP. The significant difference between AP and CP disappeared after the second episode of AP concerning 8 biomarkers (gender, age, biliary etiology, alcohol consumption, pseudocyst development, gammaGT, amylase, and red blood cell count), as did after the third episode concerning 3 biomarkers (biliary etiology, body mass index, ASAT) as did after the fourth and fifth episodes concerning 2 biomarkers (ALAT and smoking). As an average, the significant differences between AP and CP disappeared from 2.63 attacks. The average number of acute episodes of patients with pre-existing morphological alterations of the pancreas (CP group) was 4.77.
Conclusion: A definition of early CP may be 3 or more previous attacks of AP without chronic morphological alterations in the pancreas.
Disclosure: Nothing to disclose

P0110 HYPERTHERMIA ENHANCES SENSITIVITY OF PANCREATIC CANCER SW1990 CELLS TO GEMCITABINE THROUGH ROS/JNK SIGNALING

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Introduction: Pancreatic cancer (PC) is a highly aggressive cancer. Gemcitabine (GEM) is a standard chemotherapy of advanced pancreatic cancer, but the efficacy still needs to be improved. Therefore, a more effective therapeutic method needs to be further explored.
Aims and Methods: The purpose of this study is to investigate the effect of hyperthermia on GEM anti-tumor activity and explore its underlying mechanism. In this study, PC cell line SW1990 was treated with hyperthermia at a temperature of 42°C. MTT assay was performed to evaluate cell proliferation, and Annexin V-FITC/PI assay was carried out to confirm the effect of hyperthermia on GEM-induced apoptosis. To further investigate the mechanism of hyperthermia enhancing GEM-induced apoptosis in PC cells, Western blot analysis was performed to detect protein levels of survivin, c-Jun-N-terminal kinase (JNK) and its phosphorylation (p-JNK), and flow cytometry assay was used to detect the generation of reactive oxygen species (ROS).
Results: Mild hyperthermia at 42°C increased effectively the inhibition of GEM on cell proliferation and GEM-induced apoptosis in PC SW1990 cells, and displayed an increased S-phase arrest and downregulated anti-apoptosis protein Bcl-2 expression and upregulated pro-apoptosis protein Bax, cleaved caspase-3 and cleaved caspase-9 expressions. Further, we found that hyperthermia led to a rapid generation of reactive oxygen species (ROS) and substantial activation of c-Jun-N-terminal kinase (JNK). And the introduction of ROS and JNK inhibitors suppressed hyperthermia-induced apoptosis in GEM-treated cells, suggesting that hyperthermia increased GEM cytotoxicity in PC SW1990 cells by inducing apoptosis via ROS/JNK signaling.
Conclusion: Hyperthermia is able to enhance sensitivity of pancreatic cancer SW1990 cells to gemcitabine through ROS/JNK signaling.
Disclosure: Nothing to disclose

P0111 FAS SPECIFICALLY MEDIATES NEURAL INVASION IN PANCREATIC CANCER

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Introduction: Pancreatic cancer (PCa) cells have a notorious affinity to nerves. This neural invasion markedly worsens the prognosis of PCa patients. Identifying and targeting the specific molecular mediators of NI may thus have key implications for the future therapy of PCa. In the present study, we analyzed the transcriptome of neuro-invasive genetically induced PCa mouse models and validated the role of an identified mediator in human tissues and cells.
Aims and Methods: Cancer cells from the neuro-invasive Ela1-TGFalpha;p53lox/lox (TPC) mouse model were compared to Ptf1a-Cre;LSL-KrasG12D; p53lox/lox (KPC) cancer cells for difference in their mRNA profile via microarray analyses. The identified mediators were tested for their expression in 7 different human pancreatic cancer cells lines via immunoblotting and QRT-PCR, and in human neural invasion lesions via immunostaining.
Results: TPC cancer cells cells exhibited increased expression for the Fas receptor of the tumor necrosis factor (TNF)/TNF- receptor family, when compared to KPC cancer cells. All the 7 tested human PCa cell lines expressed Fas, yet at varying levels. The Fas protein content of the human PCa cell lines SU86.86 and T3M4 correlated to their *in vitro* neuro-invasive potential. In human PCa tissues, nerve-invading PCa cells exhibited a greater Fas immunoreactivity than cancer cells that were distant to nerves.
Conclusion: Fas may serve as a specific mediator of neural invasion in PCa. Targeting Fas in preclinical studies will further elucidate its actual role for tumor progression.
Disclosure: This abstract has also been submitted for presentation at the 2018 meeting of the European Pancreatic Club

P0112 PANCREATIC CANCER CELLS ENRICH PHOSPHO-PAXILLIN IN THEIR FILOPODIA DURING NEURAL INVASION

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Introduction: Neural invasion (NI) is a leading cause of local recurrence, neuropathic pain sensation in pancreatic ductal adenocarcinoma (PDAC) and is encountered in up to 100% of PDAC cases. The changes that occur in the cytoskeleton of neuro-invasive PDAC cells have, however, never been analyzed.
Aims and Methods: Human PDAC cells and dorsal root ganglia (DRG) neurons isolated from newborn C57BL/6 mouse were suspended in a 3D migration assay and monitored via Apotome-supported digital time-lapse microscopy. The density and length of cancer cell filopodia were quantified with the FiloQuant® software, and the expression of phospho-paxillin was measured and compared between the neuron-facing migration front and control front. Cancer cells were treated with DRG supernatants, and the expression of phospho-paxillin was determined by Western Blotting. Tumor specimens obtained from 18 PDAC patients were immunostained against phospho-paxillin, and the phospho-paxillin content of cancer cells around nerves was compared to cancer cells that were in no contact with nerves.
Results: In the 3D-migration assays, the neuron-facing tumor cells acquired a typical morphological change of their cytoskeleton. In particular, phalloidin stainings shows that cancer cells migrating towards DRG exhibited a more polygonal shape with a consequent increase of their cell volume. The density and length of filopodia were increased, and the filopodia exhibited a specific enrichment of phospho-paxillin in the migration front, when compared to the back front. Accordingly, phospho-paxillin expression was increased in tumor cells around nerves when compared to tumor cells away from nerves in human PDAC tissues. After treatment of PDAC cell with DRG supernatants, the phospho-paxillin expression was prominently enhanced in PDAC cells.
Conclusion: Neuro-invasive PDAC cells exhibit highly characteristic alterations in their cytoskeletal conformation and specifically enrich phospo-paxillin in their filopodia.
Disclosure: This abstract has also been submitted for presentation at the 2018 meeting of the European Pancreatic Club.

P0113 PANCREATIC STELLATE CELLS AUGMENT NEURAL INVASION IN PANCREATIC CANCER

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Introduction: Neural invasion is one of most unfavorable prognostic factors in pancreatic cancer (PCa). Neural invasion in PCa is particularly frequent in desmoplastic tissue areas. Pancreatic stellate cells (PSC) emerged in recent years as the main actor for the generation of pancreatic fibrosis in PCa. Thus, here, we investigated whether pancreatic stellate cells (PSC) can augment neural invasion in PCa.
Aims and Methods: Mouse PSC (mPSC) were isolated from C57BL/6 mouse, KPC (LSL-$Kras^{G12D/+}$; LSL-$Trp53^{flox/flox}$; $p48^{+/Cre}$) and TPAC (Ela-TGFalpha; $p53^{flox/flox}$; $p65^{flox/flox}$; $p48^{+/Cre}$) mice and cultivated under hypoxia, stimulated with TGFbeta, or left untreated as controls. The levels of PSC activation markers was determined by Western Blotting and qRT-PCR. For 3D-migration assays, mouse PCa cells alone or in mixture with mPSCs were placed next to murine dorsal root ganglia (DRG) neurons and observed via digital time-lapse microscopy. Furthermore, different ratios of tumor cell-mPSC co-cultures were confronted with DRG in the 3D-migration assay. Tumor cells were treated with mPSC supernatants and their viability was determined via the MTT assay.
Results: After treatment of mPSCs with recombinant TGFbeta or 12 hrs of hypoxia, the expression of α-SMA and vimentin was increased, both at mRNA level and protein level. In the 3D-migration assays, mPSC exhibited a similar affinity to DRG neurons, which was comparable to the affinity of cancer cells to neurons. Importantly, when cancer cells were mixed together with mPSCs, the migration of the mixture to DRG neurons was prominently increased when compared to their affinity in mono-culture. Here, the tumor cell viability was markedly higher after their treatment with mPSC supernatants.
Conclusion: TGFbeta-activated PSC augment the viability and particularly the neuro-affinity of PCa cells and accelerate their migration to neurons. PSC may be among the key promoters of neural invasion in PCa.
Disclosure: This abstract has also been submitted for presentation at the 2018 meeting of the European Pancreatic Club.

P0114 GLYOXALASE-I: A NOVEL TARGET FOR PANCREATIC CANCER?

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the most frequent gastrointestinal cancers and the 4th leading cause of cancer-related death. Despite several new developed anti-cancer drugs, the survival rates in advanced stages remain disappointing. Thus, innovative therapeutic approaches are urgently needed.
On molecular levels, oxidative stress (ROS) is important for the development and progression of PDAC. Amongst others, the highly reactive compound methylglyoxal (MGO) is an important source for ROS. MGO is a by-product of glycolysis and mainly detoxified by Glyoxalase-I (Glo-I). Overexpression of Glo-I has been shown in different tumours and linked to multi drug resistance in cancer therapy. So far, the impact of Glo-I in PDAC has not been elucidated. Thus, we analysed the role of Glo-I for proliferation, migration and colony formation in PDAC.
Aims and Methods: Expression of Glo-I was determined in 7 PDAC cell lines (BxPC3, Capan-1, Capan-2, CFPAC, HS776T, MiaPaca-2 and Panc-1) via immunocytochemistry (DAB-staining) by means of Cytospin centrifugation. Analysis of cell proliferation (Wst-assay), migration (scratch assay) and colony formation (clonogenic assay) was performed in all cell lines and correlated to Glo-I expression.
Results: HS776T and MiaPaca-2 cells showed highest expression of Glo-I. Capan-2 and CFPAC revealed low Glo-I staining intensity whereas BxPC3, Capan-1 and Panc-1 indicated average Glo-I expression. Interestingly, HS776T and MiaPaca2 also showed highest rates of proliferation and colony formation but not migration. In contrast, Capan-2 and CFPAC revealed minor proliferation and colony formation but only CFACP indicated high cell migration. Proliferation, migration and colony formation of BxPC3, Capan-1 and Panc-1 was at average levels.
Conclusion: Glo-I is expressed in all examined PDAC cell lines. High expression of Glo-I was positively correlated with proliferation and colony formation but not migration. Ongoing studies analysing the effects of Glo-I-knockdown, -overexpression and pharmacologic inhibition will further elucidate the role of Glo-I for PDAC.
Disclosure: Nothing to disclose

P0115 PANCREATIC ULTRASOUND ELASTOGRAPHY AND ITS CLINICAL USE IN PREDICTING THE RISK OF PANCREATIC FISTULAS AFTER PANCREATIC RESECTION

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Introduction: A soft texture of pancreatic remnant is one of the most important risk factors recognized for the development of clinical relevant post-operative pancreatic fistula (CR-POPF) after pancreatic resection. Several authors tried to make an objective assessment of pancreatic texture with preoperative scores or with the use of ultrasound elastography; for this latter, controversial results are reported.
Aims and Methods: The aim of the study is to evaluate pancreatic stiffness by shear-wave elastography in patients affected by pancreatic tumor compared to healthy volunteers, and to evaluate its predictive value for CR-POPF. Pancreatic elastography was performed in both groups. Differences in shear-wave elastography (SWE) were then assessed. Pre-operative SWE was compared with a pre-operative risk score for CR-POPF in patients undergoing surgery. A linear regression analysis was performed to evaluate predictive variables associated with CR-POPF.
Results: Ninety subject who underwent pancreatic elastography were consecutively enrolled. No differences were found in SWE (mean and SD, m/s) between healthy volunteers and patients affected by pancreatic neoplasm (1.33 ± 0.31 Vs 1.26 ± 0.30, $p = 0.337$). At multivariate linear regression only male gender was associated with a softer pancreas at SWE (OR 0.74, CI 0.55–0.98, $p = 0.035$). Considering 45 patients suitable for secondary end-point, the presence of a soft pancreas assessed by manual palpation (OR 61.21; CI 2.14->1000; $p = 0.016$) and the increasing of pre-operative risk score (OR 1.72; CI 1.01–2.96; $p = 0.049$) were the only predictors of CR-POPF. SWE seemed to be lower in patients who developed CR-POPF compared to patients who experienced a normal post-operative course (OR 0.01; CI 0.01–1.33; $p = 0.065$).
Conclusion: The pancreatic stiffness of the remnant pancreas of patients with pancreatic neoplasm is the same as healthy controls. A soft pancreas and an increasing pre-operative risk score were associated with CR-POPF. SWE showed a trend in predicting CR-POPF.
Disclosure: Nothing to disclose

P0116 A PROSPECTIVE, RANDOMIZED, MULTICENTER CLINICAL TRIAL COMPARING 25-GAUGE AND 20-GAUGE PROCORE NEEDLES FOR ENDOSCOPIC ULTRASOUND-GUIDED SAMPLING OF SOLID PANCREATIC LESIONS

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Introduction: Core biopsy needles have been developed for endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB). However, the properties of needle gauge on diagnostic outcomes of solid pancreatic lesions remain unknown.
Aims and Methods: This trial compared obtaining rates of histologic cores from solid pancreatic lesions with EUS-FNB using 20- and 25-gauge (G) ProCore biopsy needles. In a prospective randomized multicenter clinical trial, patients with solid pancreatic lesions underwent EUS-FNB with either 20G or 25G ProCore biopsy needles. The obtaining rates of histologic core, overall diagnostic accuracy, and complications were compared between two groups.
Results: In total, 88 patients (48 men, mean age 65.7 years) were enrolled. There were no significant differences between 2 groups in demographic characteristics. The obtaining rate of histologic cores in 20G ProCore needle group (41/45, 91.1%) was significantly higher compared with 25G ProCore needle group (32/43, 74.4%, $p = 0.037$). However, there were no significant differences in overall diagnostic accuracy between 20G (40/45, 88.9%) and 25G (35/43, 81.4%, $p = 0.322$). There were no procedure-related adverse events in both groups.
Conclusion: In total, 88 patients (48 men, mean age 65.7 years) were enrolled. There were no significant differences between 2 groups in demographic characteristics. The obtaining rate of histologic cores in 20G ProCore needle group (41/45, 91.1%) was significantly higher compared with 25G ProCore needle group (32/43, 74.4%, $p = 0.037$). However, there were no significant differences in overall diagnostic accuracy between 20G (40/45, 88.9%) and 25G (35/43, 81.4%, $p = 0.322$). There were no procedure-related adverse events in both groups.
Disclosure: Nothing to disclose

P0117 CLINICOPATHOLOGICAL FEATURES OF PANCREATIC DUCTAL ADENOCARCINOMA CONCOMITANT WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

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Introduction: Although intraductal papillary mucinous neoplasms of the pancreas (IPMNs) have been recognized as precursor lesions for pancreatic cancer, it has been reported to be associated with pancreatic ductal adenocarcinoma (PDAC) that does not occur from IPMN lesions (concomitant PDAC, C-PDAC). However, the occurrence rate of C-PDAC and clinicopathological features of C-PDAC have not been clarified in comparison to other types of pancreatic adenocarcinoma.
Aims and Methods: This study was performed to elucidate the clinicopathological features of C-PDAC. Of the 438 patients histologically confirmed to have pancreatic invasive adenocarcinoma by using resected specimens, EUS-FNA, or endoscopic biopsy at our center between January 1985 and December 2016, 91 patients with C-PDAC were included in this study and retrospectively analyzed. Accompanying IPMN was diagnosed by using resected specimens in 47 resection cases and by using imaging examinations in 44 non-resection cases. The outcome measurements were defined as (1) the rate of C-PDAC patients among all PDAC patients (C-PDAC + PDAC without IPMN) and (2) the clinicopathological features of C-PDAC (group A, $n = 47$) in comparison to those of PDAC without IPMN (group B, $n = 105$) and those of invasive cancer derived from branch duct IPMN (group C, $n = 27$) in resected cases.
Results: The percentage of C-PDAC was 29% (47/160) in resection cases and 16% (44/278) in non-resection cases. There was no statistical difference in all factors investigated, such as age, sex, history of acute pancreatitis or diabetes mellitus, pathological stage, and survival period after surgical resection, between groups A and B. Between groups A and C, the pathological stages (stage IA, 6% vs. 33%, $p = 0.004$) and survival period after surgery (mean, 1368 vs. 2567 days, $p = 0.044$) were significantly different. As to morphological findings on the accompanying IPMN in groups A and C, there was significant difference in the cyst size (17.1 ± 10.6 mm vs. 44.1 ± 21.0 mm, $p < 0.001$), multifocal

prevalence (60% vs. 15%, $p < 0.001$), existence of mural nodules (11% vs. 63%, $p < 0.001$), and the histological subtype (gastric type, 88% vs, 44%). The cyst size of the largest IPMN lesion was < 20 mm in 66% of the patients in group A, whereas it was ≥ 20 mm in all patients in group C.
Conclusion: PDAC which was not derived from IPMN was accompanied by IPMN apart from the PDAC lesion in 29% of the resection cases and 16% of the non-resection cases. There were no differences in all factors investigated, including the survival period, between PDACs with and without IPMN apart from the PDAC lesion among the resection cases. IPMNs in most cases of concomitant PDAC was multifocal with small lesion sizes, gastric subtype and without mural nodules, unlike the IPMNs in cases with invasive cancer derived from IPMNs.
Disclosure: Nothing to disclose

P0118 AN EXAMINATION OF THE USEFULNESS OF MASPIN STAINING IN EUS-FNA SAMPLES FOR PANCREATIC CANCER

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Introduction: There are many reports that KRAS and p53 were useful in improving the diagnostic yield of endoscopic ultrasound-guided fine needle aspiration biopsy (EUS-FNA) for pancreatic tumors. Nevertheless, KRAS and p53 are often negative if structurally, the tumor is anaplastic or the sample amount is small. On the other hand, Maspin which is serine protease inhibitor, is recently attracted as a new gene marker of pancreatic cancer
Aims and Methods: The aim of this study was to evaluate the usefulness of Maspin staining in histopathological diagnosis using EUS-FNA.
98 patients who were performed both Maspin and p53 staining in specimen obtained by EUS-FNA were enrolled in this study. All patients were diagnosed as the pancreatic adenocarcinoma at Dokkyo medical university hospital using EUS-FNA in the period from April 2015 to December 2017. We evaluated positive rate of Maspin and/or p53, and the relationship between immunohistochemistry and clinical factors (sex, age, location, size, tissue differentiation, rate of metastasis, Maspin positive rate, and tumor biomarker).
Results: The positive rates were 72.4% (71/98) in p53, 98.0% (96/98) in Maspin. There was no statistically significant difference between p53 positive and negative cohorts, but Maspin was positive in all cases of the p53 negative cohort. On the other hand, there was statistically significant difference between Maspin positive cohort and the negative cohort in age (70.5 vs. 53.0, $p = 0.026$) and the revel of SPAN-1 (3569 vs. 5, $p = 0.023$). In addition, p53 was positive in 2 cases where Maspin was negative.
Conclusion: The expression of Maspin was higher than p53 in pancreatic adenocarcinoma. Our study suggested that the immunostaining combined p53 and Maspin would contribute to the improvement of diagnostic yield for pancreatic tumor using EUS-FNA.
Disclosure: Nothing to disclose

P0119 DIAGNOSTIC USEFULNESS OF LOCALIZED STENOSIS OF THE MAIN PANCREATIC DUCT FOR DETECTION OF EARLY PANCREATIC CANCER

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Introduction: Although early detection of pancreatic cancer is associated with a better prognosis, it has been extremely difficult to detect. Localized stenosis of the main pancreatic duct (MPD) often indicates early pancreatic cancer, including intraepithelial cancer.
Aims and Methods: The aim of this study was to evaluate the predictive sensitivity of localized MPD stenosis for the detection of pancreatic cancer.
Among 597 patients who underwent intentional endoscopic retrograde pancreatography (ERP) between January 2008 and December 2017 at Sendai City Medical Center, those in whom ERP was performed to evaluate abnormal findings on the MPD were extracted from the prospectively maintained database. Those with multiple MPD stenoses, diffuse MPD dilation, and a mass detectable on other imaging examination, were excluded. Those with other pancreatic diseases, such as intraductal papillary mucinous neoplasm (IPMN), autoimmune pancreatitis (AIP), and definite chronic pancreatitis were also excluded. Finally, 17 patients with a single, localized stenosis in the MPD without a mass (defined as the typical MPD findings for suspicious early pancreatic cancer [TF-EPC]) were included in this study.
Final diagnosis of the etiology causing the MPD stenosis was defined as being (1) malignant or benign by histological diagnosis with a surgically resected specimen when resection was performed, (2) malignant when an obviously malignant tumor appears at the site during follow-up if resection was not performed, or (3) benign when the abnormal findings improved or did not change on imaging examinations (EUS, CT, MRI or ERP) after a 5-year follow-up without resection. If the findings were difficult to define, whether they changed or not, the patients were excluded.
The main outcome measurement was the predictive sensitivity of the TF-EPC for the presence of pancreatic cancer.
Results: Of the 9 patients who underwent surgical resection among the analyzed 17 patients, the final diagnosis of the MPD stenosis was judged as pancreatic cancer in 8 patients and as a non-neoplastic change in 1 patient. In the remaining 8 patients, the MPD stenosis was judged as being non-neoplastic by performing clinical follow-up of >5 years (mean follow-up period, 2186 ± 415 days).
Overall, the final diagnosis of the MPD stenosis with the TF-EPC was pancreatic cancer in 8 patients (47%) and a non-neoplastic change in 9 patients. In other words, the predictive sensitivity of the TF-EPC for presence of pancreatic cancer was 47%. Of the 8 patients with pancreatic cancer, 3 were diagnosed as having intraepithelial adenocarcinoma, whereas the other 5 had invasive ductal adenocarcinoma. The size of the invasive mass was less than 10 mm in all 5 patients with invasive cancer (mean diameter, 7.0 ± 0.9 mm). The sensitivity, specificity, and accuracy of cytology by using pancreatic juice obtained during ERP with cell-block preparation was 100%, 80%, and 88%, respectively.
Conclusion: MPD stenosis with typical findings for suspicious early pancreatic cancer, which was defined as a single, localized stenosis without other pancreatic diseases with no mass detectable on imaging examination, was derived from pancreatic cancer in half of the patients. Such findings were found to be useful for detecting early pancreatic cancer, although histological confirmation using pancreatic juice cytology would be necessary before surgical resection.
Disclosure: Nothing to disclose

P0120 APPROPRIATENESS OF PANCREATIC SURGERY IN HIGH-RISK INDIVIDUALS FOR FAMILIAL PANCREATIC DUCTAL ADENOCARCINOMA

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Introduction: About 5% of pancreatic ductal adenocarcinoma [PDAC] are inherited, with a deleterious germline mutation detected in $\leq$ 20% of families. Pancreatic screening in high-risk individuals (HRI) is proposed to perform early surgical treatment of malignant lesions, such as pancreatic intraepithelial neoplasia [PanIN] or intraductal papillary mucinous neoplasms [IPMN] with high-grade dysplasia, or even invasive PDAC at an early stage.
Performing surgery in HRI at the optimal time, i.e., neither too early (non-malignant lesions) nor too late (advanced PDAC), remains challenging. The outcomes of pancreatic surgery in HRI have never been properly explored.
Aims and Methods: We aimed to evaluate surgical appropriateness and explore predictive factors in screened HRI who underwent pancreatic surgery. A patient-level meta-analysis was performed on all studies reported since 1999 who included HRI defined by strict criteria and described individual screening, surgical and pathological data of operated HRI.
For each operated HRI, the highest-risk pancreatic abnormality identified at screening was classified into low-risk abnormality [LRA] (cyst with benign features) or high-risk abnormality [HRA] (cyst with worrisome features or high-risk stigmata of malignancy, solid mass and/or sample positive for malignancy). The highest malignant pathological lesion was classified into no/low malignant potential (branch-duct IPMN or PanIN with low-grade dysplasia) or potentially/frankly malignant (branch-duct IPMN or PanIN with high-grade dysplasia, main duct IPMN with low- or high-grade dysplasia or PDAC).
Surgical appropriateness was considered when potentially/frankly malignant lesions were resected. Univariate and multivariate logistic regression models of factors predictive of surgical appropriateness were performed. The variables of the multivariate model were used to establish a score and nomogram allowing the estimation of individual probability of surgical appropriateness.
Results: 13/24 studies were selected, which reported 90 HRI operated on. LRA and HRA were detected in 46.7% and 53.3% of HRI, respectively. Surgical appropriateness was consistent in 38 (42.2%) HRI operated, including 20 HRI (22.2%) with PDAC. Identification of HRA at screening was the only factor associated with surgical appropriateness at multivariate analysis ($p = 0.001$). We proposed the Beaujon score, including the identification of HRA, age $\geq$ 50 and the existence of deleterious germline mutation. The score was used to build a nomogram which predicted individual surgical appropriateness with an area under the curve of 0.81.
Survival data were available for 66 operated HRI. After a median postoperative follow-up of 29 months, 9 HRI died, including 8 who were operated on for invasive PDAC. HRI with invasive PDAC had a significantly lower overall survival (median, 35 months) compared to HRI with other pathological results ($p < 0.0001$).
Conclusion: Overall, 42.2% of HRI underwent appropriate surgery. Surgical appropriateness was higher in HRI with HRA identified at screening. We proposed the Beaujon score to help selecting the best candidates for pancreatic resection. This score requires prospective validation.
Disclosure: Pascal Hammel: Astra-Zeneca (investigator of POLO study)

P0122 PREDICTION OF LIVER METASTASIS AFTER SURGICAL RESECTION OF INVASIVE DUCTAL CARCINOMA OF THE PANCREAS BASED ON PREOPERATIVE ENDOSCOPIC ULTRASONOGRAPHY FINDINGS AND PATHOLOGICAL EXAMINATION

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Introduction: The poor prognosis after surgical resection of invasive ductal carcinoma of the pancreas (IDCP) is due to the high recurrence rate. IDCP usually recurs in the liver and at local sites, such as the pancreatic bed or adjacent structures. Notably, the survival duration among patients with liver metastasis (LM) is ≤3 years after R0 resection, even when the diameter of the IDCP is < 2 cm (pTS1). We analysed patients with pTS1 IDCP and found that the median number of invading veins within the IDCP area and the percentage of invading veins/total number of veins within the IDCP area were significantly higher in patients with than without LM [1]. However, frequent venous invasion by the carcinoma and cancer cell migration into the bloodstream had already occurred at the time of surgical resection, particularly in patients with LM. Thus, measures should be taken to avoid LM as early as possible. We have attempted to apply the results of venous invasion by the carcinoma to preoperative diagnosis, but vascular invasion could not be detected by conventional imaging. Worrisome imaging features of hepatocellular carcinoma on computed tomography and magnetic resonance imaging were recently shown to correlate with microvascular invasion and recurrence [2]. We analysed the correlations among LM, venous invasion, tumour growth patterns, and endoscopic ultrasonography (EUS) findings in patients with pTS1 IDCP.
Aims and Methods: Of 402 patients with IDCP, 21 (5.2%) had pTS1 tumours. The follow-up period among these 21 patients ranged from 6 months to 25 years. All patients underwent R0 resection. Handling of the surgical specimen and assessment of vascular permeation by the carcinoma were performed as previously described [1, 3]. Clinicopathological factors were assessed according to the Classification of Pancreatic Carcinoma (4th English edition) by the Japan Pancreas Society. The tumour growth pattern of neoplasms infiltrating surrounding tissue (INFa, expanding growth; INFc; diffusely infiltrating pattern; INFb, in between INFa and INFc) was assessed by loupe findings of the maximum cut surface of the IDCP. EUS findings were evaluated with respect to morphology.
Results: The 21 patients comprised 12 men and 9 women aged 51 to 80 years. 5 patients died of LM, and 12 patients remained alive without recurrence. The other 4 patients died of peritonitis carcinomatosa following local recurrence, subarachnoid hemorrhage, primary lung cancer, and old age, respectively. The median number of invading veins in the area of the IDCP was 5 and 2 in patients with and without LM, respectively ($p = 0.0009$), and the percentage of invading veins/total number of veins in IDCP area was 73.2% and 26.0% in patients with and without LM, respectively ($p < 0.0001$). The numbers of INFa/b/c tumours were 0/1/4 and 2/14/0 in patients with and without LM, respectively ($p = 0.0005$). Among 14 patients who underwent EUS, all 4 patients with LM exhibited nodules with a vague periphery and sunburst formation, but 7 of 10 patients without LM showed nodules with a smooth periphery ($p = 0.018$).
Conclusion: Patients with IDCP with a vague periphery as demonstrated by EUS should not only undergo surgical resection but also prepare for LM.
Disclosure: Nothing to disclose

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P0123 ROLE OF RAPID ON SITE EVALUATION (ROSE) FOR ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA) OF SOLID PANCREATIC LESIONS: "ON SITE" MULTIDISCIPLINARY TEAM IS MORE IMPORTANT THAN TECHNIQUE FOR AN ACCURATE DIAGNOSIS

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Introduction: EUS-FNA is the first-line technique for sampling pancreatic lesions. It is regarded as safe procedure but many factors influence adequacy and accuracy, among the others presence of the cytopathologist and the real time evaluation and analysis of the specimens.
Aims and Methods: This is a retrospective analysis of patients who underwent EUS-FNA for known pancreatic solid lesions before and after ROSE adoption. All consecutive EUS-FNA procedures for pancreatic lesions performed during the first year of adoption (ROSE1 group) and the following year (ROSE2 group) were compared to those performed during the previous year (pre-ROSE group). EUS was performed using a linear echoendoscope. FNA was performed using fine needles 22 or 25 Gauge diameter. Demographics, lesion location and size, number of needle passes, final diagnosis were recorded. The gold standard for diagnosis was considered histological analysis of surgical specimen, when available, or clinical and radiologic follow up compatible with neoplasia (positive) or absence of deterioration/spontaneous resolution (negative). Specimen were categorized into *diagnostic* if a final diagnosis was reported and *non diagnostic* in case of no sufficient cells or when atypia was not further classified. Adequacy (samples providing sufficient material for evaluation), diagnostic yield (rate at which a diagnosis is made), diagnostic accuracy (correspondence between cases for which a diagnosis was rendered and the gold standard) were evaluated. Aim of the study was to compare the adequacy, diagnostic yield and accuracy of EUS-FNA for solid pancreatic lesions before and after introduction of ROSE.
Results: 94 pancreatic lesions in 92 patients were enrolled (26, 30 and 38 in pre-ROSE, ROSE1 and ROSE2 groups respectively). Adequacy rate was 96.2%, 93.3% and 100% in pre-ROSE, ROSE1 and ROSE2 groups, respectively ($p = NS$). Diagnostic yield was 76.9 %, 86.7%, 92.1% and accuracy 65.4%, 76.7% and 86.8% in pre-ROSE, ROSE1 and ROSE2 groups, respectively, with significant difference between pre-ROSE and ROSE2 groups ($p < 0.5$).
Conclusion: The routine use of ROSE during EUS-FNA for solid pancreatic lesions is associated with an improvement in terms of diagnostic yield and accuracy, but it does not seem to improve the adequacy of FNA. Lack of difference during the first year of adoption of ROSE was probably due to the learning curve of the multidisciplinary team.
*[Table 1: characteristics of groups; *p < 0.5]*
Disclosure: Nothing to disclose

Abstract No: P0123

			pre-ROSE (n/%)		ROSE1 (n/%)		ROSE2 (n/%)	
number of lesions			26		30		38	
demographic	age median (range)		68 (47–82)		69 (34–84)		71 (39–85)	
	gender (F/M)		13/13		14/16		15/23	
lesions	diameter mm median (range)		27.5 (6–50)		28.5 (7–50)		30.0 (9–80)	
	localization: head-istmo-uncinate-body-tail		14-4-2-4-2	53.8-15.4-7.7-15.4-7.7	16-4-5-4-1	53.3-13.3-16.7-13.3-3.3	20-7-4-3-4	52.6-18.4-10.5-7.9-10.5
technique	needle: 22-25-22&25 Gauge		6-15-5	23.1-57.7-19.2	10-13-7	33.3-43.3-23.3	20-14-7	52.6-36.8-10.5
	n° passages (range)		3.0 (1–5)		2.5 (1–7)		2.0 (1–10)	
histopathol. diagnosis	adenoca-NET-panreatitis-normal-other-atypias-inadequate		10-2-4-4-2-4-1	38.5-7.7-15.4-15.4-7.7-15.4-3.8	21-1-2-3-0-1-2	70.0-3.3-6.7-10.0-0.0-3.3-6.7	26-3-1-5-3-0-0	68.4-7.9-2.6-13.2-7.9-0.0-0.0
adequacy	diagnostic yield	accuracy	25-20-17	96.2-76.9*-65.4*	28-26-23	93.3- 86.7-76.7	38-35-33	100-92.1*-86.8*

MONDAY, OCTOBER 22, 2018 09:00–17:00
Endoscopy and Imaging I - Hall X1____

P0124 WATER-POCKET ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL GASTRIC NEOPLASMS: A PROSPECTIVE STUDY

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Introduction: It is essential to obtain a clear view during the endoscopic submucosal dissection (ESD) to precisely dissect the appropriate submucosal layer. Some advantages of underwater techniques for gastric ESD have been reported in comparison with gas insufflation method [1, 2]. We have developed a new ESD method with the creation of a local water-pocket that provides a clear view in the dissection field. Therefore, we aimed to investigate the feasibility and safety of water-pocket ESD (WP-ESD) for superficial gastric neoplasms.
Aims and Methods: We prospectively recruited 50 patients with gastric neoplasms (early gastric cancer or gastric adenoma) between April 2017 and December 2017. Among them, 48 patients were treated with WP-ESD technique. The patients with WP-ESD were compared with 48 patients treated with standard ESD (S-ESD) who were selected by propensity score matching. The primary outcome was the ESD procedure time.
The rationale of the WP-ESD technique is that ESD procedure is carried out underneath the target lesion via a locally created water pool in the submucosal layer. First, to create a submucosal pocket, an initial incision is made approximately 2 cm proximal to the lesion. Second, the tip of the attached transparent ST hood is inserted into a small hole followed by injection of saline solution, and dissection of the submucosal layer is initiated in the water pool.
The study protocol was approved by the ethics committee of New Tokyo Hospital (IRB No. NTH 0112) and was registered in the University Hospital Medical Network Clinical Trials Registry (UMIN: 000030266).
Results: Total procedure time was significantly shorter in the WP-ESD group than in the S-ESD group (median [IQR], 27.5 [19–45] min vs. 41 [29.8–69] min; $p < 0.001$). Similarly, the dissection speed was significantly greater in the WP-ESD group than in the S-ESD group (median [IQR], 22.5 [16.8–35.3] mm^2/min vs. 17.3 [12.7–22.1] mm^2/min; $p < 0.001$). The rates of complete en bloc resection in the WP-ESD group and the S-ESD group were 97.9% and 95.8%, respectively ($p > 0.99$). The volume of saline solution used in the WP-ESD group was 205 ml (median). There were no perforations in either group.
Conclusion: WP-ESD was associated with a shorter procedure time than S-ESD. WP-ESD may provide an alternative method for resection of superficial gastric neoplasms.
Disclosure: Nothing to disclose

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P0125 CLINICAL VALUES OF DENTAL FLOSS TRACTION ASSISTANCE IN ENDOSCOPIC FULL-THICKNESS RESECTION FOR SUBMUCOSAL TUMORS ORIGINATING FROM THE MUSCULARIS PROPRIA LAYER IN THE GASTRIC FUNDUS

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Introduction: With the development and maturation of endoscopic resection, endoscopic full-thickness resection (EFTR) derived from endoscopic submucosal dissection (ESD) is gradually accepted and promoted to treat submucosal tumors (SMTs) originating from muscularis propria (MP) lays. However, there are some difficulties when EFTR is applied in the treatment of muscularis propria lesions in gastric fundus. This study intends to explore whether EFTR can be more simple, safe and effective with the traction assistance of dental floss.
Aims and Methods: From January to December in 2016, the clinical data of patients (trial group) with lesions from MP in gastric fundus undergoing EFTR with traction assistance of dental floss at Zhongshan Hospital, Fudan University were reviewed retrospectively. Control group was matched with trial group according to tumor size by 1 to 1 from January to December in 2015. The differences in tumor resection time, patient hospitalization time and complication rate were evaluated. EFTR with dental floss traction was performed as follows: During the stripping process, after removing the endoscope, an clip was tied on the tip of the dental floss, while the shorter side of the floss was cut to prevent it from affecting the field of view. The longer side of the floss was attached to the endoscope body side and was guided by an assistant.The endoscope was then reinserted, and the tumor was fastened by the clip. When the assistant pulled the dental floss, the tumor edge became clearly exposed. The tumor was then peeled away under direct visualization.
Results: There was no significant difference in the average age of the 2 groups with 24 cases respectively (58.7 ± 11.8 y vs. $56.6 + 7.9$ y, $t = 0.663$, $p = 0.511$). The statistic difference occurred when operative time was compared in 2 groups ($10.8 + 2.8$ min vs. 19.0 ± 4.7 min, $t = 7.298$, $p < 0.05$). There was no statistically significant difference in postoperative hospital stay time ($3.2 + 0.5$ d vs. $3.2 + 0.5$ d, $t = 0.291$, $p = 0.772$). In the trial group, there were 19 cases of gastrointestinal stromal tumors (both Group1) and 5 cases of leiomyoma. The control group had the same result. 2 groups of patients did not have postoperative delayed bleeding, or perforation and other complications.
Conclusion: First, dental floss traction could help expose the tumor boundaries, so that the operation field was clearer to simplify the operation process and significantly reduce the procedure time. Second, in the course of surgery, EFTR-assisted dental floss traction could better reveal the blood vessels or find bleeding blood vessels for prevention and early treatment of bleeding. Third, when the tumor was completely resected, dental floss could also prevent the tumors from falling into the abdominal cavity and help to remove the excised tumors.
Disclosure: Nothing to disclose

P0126 PURSE-STRING SUTURES USING NOVEL ENDOLOOPS AND REPOSITIONABLE CLIPS FOR THE CLOSURE OF LARGE IATROGENIC DUODENAL PERFORATIONS WITH SINGLE-CHANNEL ENDOSCOPE

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Introduction: Serious complications due to perforation restrict the development of duodenal endoscopic treatment. The key stage for remediation is the successful endoscopic closure to prevent peritonitis and the need for surgical intervention. This report presents a new simple method for the closure of large iatrogenic duodenal perforations with purse-string sutures using the novel endoloops and repositionable clips through a single-channel endoscope.
Aims and Methods: A total of 23 patients with iatrogenic duodenal perforations ≥ 1cm were retrospectively studied who were respectively treated by purse-string sutures using the novel LeCamp™ endoloops and the SureClip™ repositionable hemostasis clips with the single-channel endoscope at 4 institutes.
Results: The median maximum diameter of iatrogenic duodenal perforations was 1.65 cm (range 1.0–3.0 cm). Complete endoscopic closure of all 23 perforations was achieved. No patient had severe complications such as peritonitis. The wounds were healed and no obvious duodenal stricture was observed in all cases after 3 months.
Conclusion: Purse-string sutures using the novel endoloops and the repositionable endoclips through single-channel endoscope were feasible, effective and easy methods for the closure of large duodenal iatrogenic perforations.
Disclosure: Nothing to disclose

P0127 TO ASSESS THE ANAESTHETIC REQUIREMENTS AND MODIFICATIONS REQUIRED IN PER ORAL ENDOSCOPIC MYOTOMY (POEM) FOR SAFE PROCEDURE AND PREVENTION OF COMPLICATIONS. A RETROSPECTIVE ANALYSIS OF PROTOCOL FOR ANESTHESIA IN POEM DEVISED AT OUR CENTRE. A STUDY OF 175 CASES

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Introduction: To assess modifications in anaesthesia practices for POEM.
Aims and Methods: To assess the anaesthetic requirements and modifications required in Per Oral Endoscopic Myotomy for safe procedure and prevention of complications.
Preoperative Measures: Clear liquids and lukewarm water 24 hours before. Thorough pre anesthesia work up.
Induction of anaesthesia and intraoperative management: POEM procedures were carried out under general anaesthesia with endotracheal intubation and positive pressure ventilation to reduce the risk of capno mediastinum. One assistant is kept ready for Selliks manoeuvre and suctioning of the oral cavity if patient aspirates the fluid in the esophagus. Anaesthesia in all the patients was induced by rapid sequence method (to prevent aspiration of esophageal content). Sedation and induction was achieved by (Inj. Glycopyrrolate 0.2 mg; Midazolam 0.02 mg/kg; Propofol-1-2mg/kg; Fentanyl 100mcg; Succinylcholine 1–2 mg/kg). Atracurium (0.5 mg/kg) was used as neuromuscular block and maintenance done by N_2O+O_2+Sevoflurane (0.5–2 minimum alveolar concentration). As and when required intravenous infusion of nitro-glycerine and selective beta-blocker was used. Mechanical ventilation with pressure control mode was taken as choice method. Intraoperative screening including NIBP, ECG, and PULSE OXIMETRY & $ETCO_2$ was used. $ETCO_2$ was kept between 35–45 mm Hg by adjusting Respiratory Rate & Minute ventilation. Peak Airway pressure was observed as potential indicator for elevated intra abdominal pressure. It was tried to maintain below 35cm of H_2O by allowing low flow of CO_2 and frequent suctioning of excess CO_2 from stomach by EGD scope. Periodic assessment by palpation of upper abdomen, thorax and neck area was done to rule out capno peritoneum, capno thorax and surgical emphysema.
The tidal volume is kept low and ventilator rate is kept high to eliminate ET CO_2.
Results: Observations:
Total number of patients: **175**
Number of patients with fluid in oral cavity: **24 (13.7%)**

Number of patients who aspirated during induction of anaesthesia: 3 (1.7%). They were not required to be ventilated more than normal, but antibiotics and intensive medical support were needed in these cases.
Patients with significant rise in blood pressure intra operatively: 36 (20.5%). CO_2 flow at very low pressures was a key to avoiding this.
Patients developing high airway pressures: **16 (9.1%)**. Usually airway pressures are kept in between 20–30 cms of H2O. Airway pressures more than 40 cms of H_2O had capno thorax. They were hyperventilated and the airway pressure controlled.
Patients with symptomatic capno peritoneum/capno thorax: **3 (1.7%).** 2 needed needle decompression and 1 intercostal drain.
Patients with insignificant capno peritoneum: **108 (61.7%).** Noted on gastrografin study after 24 hours. No management needed.
Patients with post-operative pain: **140 (80%).** Controlled with tramadol and paracetamol.
Conclusion: For induction of anaesthesia in POEM, initial ventilation before intubation should not be used.
We have to be prepared for managing aspiration.
Aggressive blood pressure monitoring and maintenance is a must. Nitro glycerine and beta blockers are very useful for this.
Low tidal volume and high ventilatory rate are essential to eliminate ET CO_2.
Keen observation of ET CO_2 and persistent clinical assessment is mandatory to detect surgical emphysema and capno thorax and peritoneum. Manage these immediately.
Analgesics are required post operatively in majority.
Disclosure: Nothing to disclose

P0128 SAFETY OF PROPOFOL-BASED SEDATION WITHOUT ENDOTRACHEAL INTUBATION DURING ENDOSCOPIC SUBMUCOSAL DISSECTION IN THE ESOPHAGUS AND STOMACH

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Introduction: Endoscopic submucosal dissection (ESD) in the upper gastrointestinal tract is mostly performed in patients under general anesthesia with endotracheal intubation, especially when the estimated procedure time is likely to exceed two hours [1]. The reasons for using general anesthesia are continuous airway protection, less respiratory problems or interruptions during the procedure and therefore lower complication rates [2]. However, general anesthesia leads to longer post-procedural hospital stay [3]. Anesthetic complication rates for general anesthesia reported in the literature are up to 18.9% [2]. Analgo-sedation using propofol is favorable due to its appropriate sedation level, short half-life and rapid recovery period [4]. We hypothesized that ESD can be safely performed with analgo-sedation using propofol and remifentanil without endotracheal intubation instead of general anesthesia. The aim of this study is to report on the endoscopic and anesthetic complication rates of ESD with propofol sedation.
Aims and Methods: Retrospective cohort study of patients who underwent esophageal or gastric ESD in a tertiary referral center in the Netherlands between October 2013 and February 2018. All patients were sedated by intravenous administration of propofol until the required level of sedation was achieved according to the Ramsey Sedation Scale (score 4 to 5). Remifentanil infusion was started until the required level of analgesia was achieved. Vital signs were continuously monitored during the procedure in the endoscopy room. Primary endpoints were the rates of intra-procedural endoscopy and anesthesia related complications, secondary endpoints were 30-days post-procedural complication rates and the endotracheal intubation conversion rates.
Results: We included 86 patients with a median age of 70 years (range 24–91). 34 ESDs were carried out in the esophagus, 51 in the stomach and 1 in the duodenal bulb. Median lesion size was 25 mm (range 8–120). Median procedure time was 100 minutes (range 15–510). En bloc resection was performed in 77 patients (89.5%), piecemeal resection in 1 patient (1.2%). In 7 patients (8.1%), the procedure was discontinued and no histology was obtained due to muscular invasion ($n = 5$) or bleeding ($n = 2$). In 1 patient (1.2%), ESD was converted to endoscopic mucosal resection due to bleeding. Early cancer was found in 72/79 patients (91.1%). In 2 patients (2.3%), an intra-procedural endoscopic complication occurred; both bleeding. In 14 patients (16.3%), a post-procedural complication occurred; 5 bleeding (5.8%), 6 retrosternal pain (7.0%), 2 dysphagia (2.3%), 1 stomach pain (1.2%). In 2 patients (2.3%) an intra-procedural anesthetic complication occurred; 1 coughing and in 1 patient hypotension and desaturation ($SpO2 < 90$) occurred. Due to hypotension, desaturation and extended duration of the procedure (>5 hours), this patient was converted to endotracheal intubation. In 2 patients (2.3%), a minor post-operative anesthetic complication occurred; 1 nausea and 1 atrial fibrillation. 42 patients (48.8%) were discharged the same day. 38 patients (44.2%) were discharged the following day (29 logistical reasons, 9 medical reasons). In 6 patients, hospital stay was >2 days. Longer hospital stay was not related to anesthesia and no patients were readmitted for anesthesia-related complications.
Conclusion: Propofol-based analgo-sedation without endotracheal intubation is safe for ESD procedures in the esophagus and stomach with low complication rates and short hospital stay.
Disclosure: Nothing to disclose

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P0129 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ESOPHAGEAL NEOPLASIA PROXIMAL TO THE PREVIOUS ESD SCAR

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Introduction: Endoscopic submucosal dissection (ESD) is a standard treatment for early stage esophageal neoplasia. However, because the residual mucosa after ESD retains a high potential for development of metachronous neoplasia, recurrence sometimes develops proximal to a previous ESD scar. Such lesions are predictably difficult to treat with ESD due to severe submucosal fibrosis.
Aims and Methods: In the absence of prior reports, we evaluated the clinical outcomes of esophageal neoplasia located proximal to a previous ESD scar. This was a retrospective observational study in a single institution. Between May 2004 and March 2016, 549 consecutive patients with 927 esophageal lesions were treated with ESD. The initial or largest lesion was the target in patients with multiple lesions. The primary treatment outcomes were resectability and adverse events of esophageal neoplasia located proximal to a previous ESD scar (recurrent group). These patients were compared with cases of primary esophageal ESD (primary group). Secondary outcomes were factors predictive of esophageal perforation. Perforation was defined as a visible hole in the esophageal wall, exposing the mediastinal space. Multivariate logistic regression and the generalized estimating equation were used for statistical analysis, and inverse probability of treatment weighting (IPTW) with propensity scores was used to reduce selection bias between the groups.
Results: A total of 545 primary cases and 29 recurrent cases were evaluated. Age, antithrombotic use, macroscopic appearance, lesion size, clinical invasion depth, and treatment device significantly differed between the groups. En bloc and complete (R0) resection rates in the recurrent group were lower than those in the primary group (79.3% vs. 98.3%, $p < 0.01$ and 75.9% vs. 93.4%, $p < 0.01$). Perforations occurred more frequently in the recurrent group than in the primary group (10.3% vs. 2.0%, $p = 0.03$). However, these could be treated with endoscopic closure and conservative management. Rates of delayed bleeding and stricture were similar between the groups. A lesion located proximal to a previous esophageal ESD scar was an independent predictive factor for perforation, following adjustment for lesion size and circumference using multivariate logistic regression analysis (odds ratio (OR) = 10.37, 95% confidence interval (CI): 2.15–49.94, $p = 0.004$). IPTW methods showed similar results (OR = 6.78, 95% CI: 1.40–32.98, $p = 0.018$). Limitations of this study were the small sample size and data from a single center.
Conclusion: ESD for esophageal neoplasia located proximal to a previous ESD scar was difficult to completely resect and increased the likelihood of perforation. Large centers with surgeons specialized in treating the esophagus may be recommended for ESD of such lesions.
Disclosure: Toshio Watanabe, Tetsuya Tanigawa, and Yasuhiro Fujiwara - Faculty member of a course sponsored by EA pharma Co., Ltd. yasuhiro Fujiwara was supported by grants or donations from Ono.

P0130 USEFULNESS OF DEMARCATION OF EARLY GASTRIC CANCERS AFTER *HELICOBACTER PYLORI* ERADICATION BY MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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Introduction: Early gastric cancer after *Helicobacter pylori* (*Hp*) eradication is difficult to demarcate. Previous studies have reported that gastric cancers after *Hp* eradication show unclear demarcation in 41.7–44% of these lesions [1,2]. However, the capacity of magnifying endoscopy with narrow-band imaging (M-NBI) to demarcate early gastric cancer after *Hp* eradication has not been evaluated enough. The magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G) is a new uniform diagnostic system for gastric cancer by means of M-NBI in Japan [3].
Aims and Methods: In this study, we compared the usefulness of M-NBI using MESDA-G for demarcation of early gastric cancer between the *Hp*-eradicated

group and the *Hp*-infected group. Among 492 cases of early gastric cancer who underwent endoscopic resection in our hospital between April 2013 and February 2018, the following lesions were excluded: special type gastric carcinoma (gastric adenocarcinoma of the fundic gland type [n = 27], gastric adenocarcinoma with enteroblastic differentiation [n = 4], and gastric carcinoma with lymphoid stroma [n = 2]), remnant gastric carcinoma (n = 6), *Hp*-uninfected gastric carcinoma [n = 20], lesions in which M-NBI has not been performed [n = 2], and lesions without details of *Hp* eradication (190). The remaining lesions were classified into of the *Hp*-eradicated group (n = 92) and the *Hp*-infected group (n = 149). Moreover, all cases of the 2 groups were classified into 3 histological subgroups according to Lauren classification; pure intestinal-type/pure diffuse-type/mixed-type. We compared the clinicopathological factors (age, sex, tumor location, tumor size, macroscopic type, invasion depth, lymphatic invasion, venous invasion, horizontal margin, vertical margin, non-neoplastic epithelium, adenocarcinoma with low-grade atypia) and endoscopic findings (the range of mucosal atrophy, demarcation line, microvascular pattern, microsurface pattern).

Results: The *Hp*-eradicated group was subclassified into 81 cases of pure intestinal-type and 11 cases of mixed-type. There was no case of pure diffuse-type in *Hp*-eradicated group. The *Hp*-infected group was subclassified into 131/5/12 cases of pure intestinal-type/pure diffuse-type/mixed type. In comparison between pure intestinal-type of the 2 groups, significantly smaller tumor size (12.5 ± 8.8 mm vs. 16.4 ± 11.4 mm, $p < 0.05$), more depressed lesion (elevated/flat/depressed = 15/3/63 vs. 60/2/69, $p < 0.01$), milder mucosal atrophy (C-1, 2/C-3, O-1/O-2, 3 = 11/30/40 vs. 8/30/93, $p < 0.01$), higher non-neoplastic epithelium covering rate (25/81, 30.9% vs. 19/131, 14.5%, $p < 0.01$) were observed in *Hp*-eradicated group than in the *Hp*-infected group. Although DL (+) cases were significantly less in *Hp*-eradicated group than in the *Hp*-infected group, DL was detected in most cases in both groups (76/81, 93.8% vs. 130/131, 99.2%%, $p < 0.05$). Furthermore, DL was detected in all cases of mixed-type in both groups. Whereas, there were small number of DL (+) cases in pure diffuse-type in the *Hp*-infected group (2/5, 40%).

Conclusion: M-NBI with MESDA-G can identify the DL in most patients with pure intestinal-type and mixed-type of early gastric cancer after *Hp* eradication.

Disclosure: Nothing to disclose

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P0131 RISK FACTORS FOR ACUTE BLEEDING AND DELAYED BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION IN PATIENTS WITH EARLY GASTRIC CANCER

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Introduction: Few studies have classified risk factors according to the onset time of bleeding after endoscopic submucosal dissection (post-ESD bleeding).

Aims and Methods: We studied 1767 consecutive lesions in patients who underwent ESD for early gastric cancer from December 2006 through June 2016. Patients who had a remnant stomach or a reconstructed gastric tube were excluded. Post-ESD bleeding was classified into acute bleeding (0 to 5 days after ESD) and delayed bleeding (6 or more days after ESD), and the risk factors for each type of bleeding were compared.

Results: Post-ESD bleeding occurred in 150 (8.5%) of 1767 lesions. Bleeding was acute in 129 lesions (7.3%) and delayed in 21 (1.2%). Acute post-ESD bleeding was frequently associated with lesions located in the distal stomach, expanded indications or non-indicated lesions, a specimen diameter of ≥40 mm, and antithrombotic therapy. Delayed post-ESD bleeding was often associated with lesions located in the proximal stomach, hemodialysis, and antithrombotic therapy. Among 334 lesions in patients who received antithrombotic therapy, post-ESD bleeding occurred in 47 lesions (14.1%). Independent risk factors for post-ESD bleeding were a specimen diameter of ≥40 mm and treatment with 2 or more antithrombotic agents.

Conclusion: Acute post-ESD bleeding and delayed post-ESD bleeding were associated with different clinical characteristics. Antithrombotic therapy is a risk factor for post-ESD bleeding in both the acute and delayed phases.

Disclosure: Nothing to disclose

P0132 EFFICACY OF ORAL MIXTURE OF HYDROCORTISONE SODIUM SUCCINATE AND ALUMINUM PHOSPHATE GEL FOR THE PREVENTION OF RESTENOSIS AFTER ENDOSCOPIC BALLOON DILATION(EBD) FOR BENIGN ESOPHAGEAL STRICTURE

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Introduction: The medical management of benign esophageal strictures consists of lifelong antireflux measures and periodic mechanical esophageal dilation. Repeat EBD is usually required over long period to resolve the stricture, which makes quality of life in the patients drastically decreased. We explore an innovative strategy with oral mixture of hydrocortisone sodium succinate and Aluminum phosphate gel for prevention of the restenosis after EBD and evaluate the efficacy of this mixture in single center of Beijing, China.

Aims and Methods: 32 patients who were diagnosed with benign esophageal strictures were included in this study. They were divided into 2 groups chronologically: 12 patients underwent EBD with no preventative treatment for restenosis (EBD alone group) were in control group and 20 patients received oral mixture of hydrocortisone sodium succinate and aluminum phosphate gel for restenosis (OHA group) were in treatment group. Patients in OHA group started with mixture of hydrocortisone sodium succinate 50mg and aluminum phosphate gel 20g, qid for 2weeks and continued with a gradually tapering OHA dose on the second day post-EBD. Patients in EBD alone group were treated by conventional method. Esophagogastroduodenoscopy (EGD) was performed on demand whenever patients complained of dysphagia. Among those cases, EBD was performed again when patients experienced persistent dysphagia. If the patient had no complaint of dysphagia, EGD was performed 8 weeks after EBD to evaluate any possible stricture. The primary end point in this study was the restenosis rate after EBD. The secondary end point was the number of EBD sessions required to resolve the stricture. A stricture was defined as a difficulty in swallowing solids or an inability to pass an EGD (9.2mm diameter endoscope).

Results: No significant differences were seen among the 3 groups in terms of demographic parameters including age, sex, etiology, stricture location, diameter of the narrowest segment. The restenosis rates of OHA group, EBD alone group were 25.0% (5 of 20 patients), 66.7% (8 of 12 patients), respectively (95% confidence interval, $p = 0.025$). The EBD sessions were less in the OHA group than EBD alone group (median 1, interquartile ranged from 1 to 1.8 vs. median 2, interquartile ranged from 1 to 2.5; $p > 0.05$).

Conclusion: Short period, oral mixture of hydrocortisone sodium succinate and aluminum phosphate gel showed promising results for the prevention of restenosis after EBD for benign esophageal stricture.

Disclosure: Nothing to disclose

P0133 NARROW BAND IMAGING CHARACTERISTICS OF POLYPOID GASTRIC LESIONS: A SINGLE-CENTER PROSPECTIVE STUDY

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Introduction: Gastric polypoid lesions (GPL) are possible endoscopic findings detected during gastroscopies but the histological nature is difficult to determine by white light endoscopy. Hyperplastic polyps (HP), type-1 gastric carcinoids (T1-GC) and adenomas are the most frequent GPL in the stomach and need different management. Narrow-band imaging (NBI) has been associated with high accuracy for the identification of gastric malignant lesions. Few studies tried to assess whether GPL display specific NBI characteristics permitting to endoscopically identify a specific histological type[1,2,3]

Aims and Methods: We aimed to investigate endoscopic NBI appearances of GPL. 40 pts (F 55%; median age 63 (36–85) yrs) presenting at least 1 GPL between March 2016 and March 2018 were prospectively investigated. Gastroscopies were performed by 2 experienced endoscopists. GPL images were recorded during gastroscopies and GPL were removed for histological examinations. Both endoscopists independently reviewed digital images in a blinded manner and registered endoscopic NBI appearances on a specific check-list previously elaborated[4]. 5 variables were taken into consideration: the mucosal and vascular pattern, vascular thickness and density as well as the presence of 'light-blue crest'. Endoscopists could further indicate other features and disagreement was resolved by discussion. GPL were then categorized in 3 different groups (HP, adenomas and T1-GC) using the histological exam as gold standard. Differences of NBI features between groups were analyzed by Fisher's exact test

Results: Overall, 52 GPL were included (29 (55.8%) HP; 18 (34.6%) T1-GC; 5 (9.6%) adenomas). The median size was 7 mm (range 2–35). Agreement between endoscopists was 92.3%. As shown in Table 1, HP had regular circular mucosal pattern in 82.8% while regular tubule-villous pattern was observed in 17.2%. Only one (3.4%) presented light blue crest, while vascular pattern, thickness and density were normal for all HP but one (3.4%) which presented thin vessels. T1-GC presented regular circular mucosal pattern in 94.4% (one presented irregular mucosal pattern), absence of light blue crest in 94.4%, regular vascular pattern in 83.3%, normal vascular thickness in 94.4% and regular vascular density in 83.3% (11.1% presented low density and 5.6% variable vascular density). Both endoscopists observed the presence of a central erosion in 14 (77.8%) T1-GC and 6 (33.3%) had a clear demarcation line in the central part. Adenomas had a

Abstract No: P0133

NBI features	Hyperplastic polyps n = 29 (55.8%)	Adenomas n = 5 (9.6%)	Type-1 gastric carcinoids n = 18 (34.6%)
Mucosal pattern Regular circular Regular tubulo-villous Irregular	24 (82.8%)* 5 (17.2%) 0	1 (20%) 4 (80%)# 0	17 (94.4%)° 0 1 (5.6%)
Light blue crest Present Absent	1 (3.4%) 28 (96.6%)	0 5 (100%)	1 (5.6%) 17 (94.4%)
Vascular pattern Regular Irregular	29 (100%) 0	5 (100%) 0	15 (83.3%) 3 (16.7%)
Vascular thickness Normal or thick Thin or ultrathin	28 (96.6%) 1 (3.4%)	5 (100%) 0	17 (94.4%) 1 (5.6%)
Vascular density High Low Variable	29 (100%) 0 0	5 (100%) 0 0	15 (83.3%) 2 (11.1%) 1 (5.6%)
Other features Central erosion Central erosion + demarcation line	1 (3.4%) 0	0 0	8 (44.4%)^ 6 (33.3%)^

tubule-villous mucosal pattern in 80% ($p = 0.01$ versus other lesions); light blue-crest and regular vascular pattern, thickness and density were absent in all of them. The presence of a regular circular mucosal pattern was more frequently observed in HP and T1-GC compared to adenomas ($p < 0.001$). The presence of a central erosion with or without demarcation line was more frequently observed in T1-GC ($p < 0.001$ vs. HP).

*[Table1. *$p < 0.012$ versus adenoma; °$p = 0.003$ versus adenoma; # versus HP and T1-GC $p = 0.01$; ^ versus HP $p < 0.001$]*

Conclusion: The NBI analysis of the mucosal pattern seems to be effective to endoscopically discriminate between adenomas and HP while the main characteristic of T1-GC is the presence of a central erosion sometimes with a clear demarcation line. Accordingly, NBI could be an important tool to endoscopically distinguish the histological nature of GPL.

Disclosure: Nothing to disclose

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P0134 ELDERLY PATIENTS VS NON-ELDERLY PATIENTS IN CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION; PROPENSITY SCORE MATCHING ANALYSIS

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Introduction: Endoscopic submucosal dissection (ESD) for gastric neoplasms was accepted as a standard treatment even in elderly patients. However, it is difficult to compare directly the clinical outcomes between elderly patients and non-elderly patients because background characteristics are different. Therefore, this study aimed to compare the clinical outcomes between elderly and non-elderly by propensity score matching analysis.

Aims and Methods: Early gastric neoplasms treated by ESD between January 2015 and March 2018 at out hospital were retrospectively reviewed. Elderly patients were defined as those aged 75 years old or more. ESD in elderly (ESD-E, n = 58) and ESD in non-elderly (ESD-N, n = 58) were compared. Multivariate analyses and propensity score matching were used to compensate for the differences in age, gender, ASA-score, underlying disease, Anti-thrombotic agent use, tumor size, tumor location, tumor shape, presence of ulcer, differentiation and operator level, which included factors previously reported to affect the outcomes of ESD. Primary outcome was procedure time. Secondary outcomes were the rates of en-block/complete resection and the rates of complications (aspiration pneumonia/perforation/post-procedure bleeding).

Results: Propensity score matching analysis created 38 matched pairs. Adjusted comparisons between 2 groups showed similar treatment outcomes (median procedure time: 61.5min vs. 77.5min; $p = 0.342$; en-block resection rate: 100% in both groups; complete resection rate: 86.8% vs. 97.4%, $p = 0.200$. However, the rates of complications were higher in ESD-E than those in ESD-N, but not significant. (Aspiration pneumonia: 10.5% vs. 7.9%, $p = 1$, Perforation: 5.3% vs. 0%, $p = 0.493$, post-procedure bleeding: 2.6% vs. 0%, $p = 1$).

Conclusion: ESD for gastric neoplasms in elderly patients achieved favorable outcomes as well as ESD in non-elderly patients. However, we should take care of complications in ESD for elderly patients.

Disclosure: Nothing to disclose

P0135 PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL COMPARING HEMOSTATIC POWDER VERSUS OPTIMAL CLINICAL TREATMENT IN THE MANAGEMENT OF GASTROINTESTINAL BLEEDING FROM MALIGNANCY

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Introduction: Upper gastrointestinal bleeding (UGIB) from malignancy is a clinical emergency associated with high rebleeding and mortality rates (1). Endoscopic treatment with argon plasma coagulation has been shown to provide adequate initial hemostasis but with no impact on rebleeding or mortality rates (2). **Tc-325** (Hemospray™) has been recently introduced into the endoscopic arsenal for the treatment of UGIB.

Aims and Methods: The aim of this study was to compare the efficacy of Hemospray versus optimal clinical treatment in the management of UGIB from malignant lesions. Primary outcomes were 30-day rebleeding and 30-day mortality rates.

A randomized prospective study comparing patients treated with Hemospray versus a control group (optimal clinical treatment). Inclusion criteria were patients with evidence of UGIB from primary or metastatic neoplasia in the last 48 hours. Exclusion criteria included hemoglobinemia drop without evidence of bleeding, bleeding of non-tumor origin, pregnancy and patients under 18 years. To guarantee a study power of 0.8 with 0.05 alpha, a sample size of 100 patients was calculated.

Results: From August 2016 to May 2017, 36 patients (22 males and 14 females, $p = 0.494$) were randomized (Hemostatic Powder = 18; Control group = 18). The mean age was 56.7 years (range: 32–86). Mean hemoglobin at admission was 7.6 (4.3–14.3; $p = 0.183$). ECOG performance status scale was similar between groups ($p = 0.555$). Site of bleeding was: esophagus 6, stomach 20, duodenum 10 ($p = 0.489$). At endoscopy, active bleeding was observed in 13 patients of Hemospray group and 10 patients of the control group ($p = 0.489$). Successful initial hemostasis with Hemospray was achieved in all cases. Additional therapy such as radiotherapy ($p = 1.00$), surgery ($p = 1.00$) or angiography embolization ($p = 0.486$) was similar in both groups. There was no statistical difference in rebleeding rates at 30 days (hemospray 61.4% vs. control 38.9%, $p = 0.502$); nor in 30-day mortality rate (Hemospray 27.8% vs. control 22.2%, $p = 1.00$). Length of hospital stay after bleeding was also similar (Hemospray 16.9 days vs control 13.6 days, $p = 0.149$). There were no complications related to the method.

Conclusion: In this preliminary analysis, treatment with hemostatic powder demonstrated high initial hemostasis rate. However, there was no relevant impact on 30-day rebleeding or 30-day mortality rates. It is still necessary to include more patients to confirm the results.

[Table: Demographic data]

Disclosure: Nothing to disclose

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	Control (N = 18)	Hemospray® (N = 18)	P-value
Age years(mean ± SD)	63.22 ± 2.8	56.5 ± 3.7	0.180
Gender	F = 6 M = 12	F = 8 M = 10	0.494
Setting	Outpatients = 4 Inpatients = 14	Outpatients = 2 Inpatients = 16	0.329
ECOG 0 1 2 3 4	1 2 5 7 0	1 5 6 4 1	0.555
Anticoagulant therapy	3	2	1.00
Hemoglobin	8.43 ± 0.3	7.75 ± 0.6	0.183
Comorbities CVD Liver disease	2 1	1 0	1.00
Active bleeding	10	13	0.489
Bleeding site Esophagus Stomach Duodenum	2 12 4	4 8 6	0.474
Rebleeding	9	11	0.502
Adjuvant therapies Surgery Arteriography radiotherapy	0 2 9	0 0 9	1.00 0.486 1.00
Length of stay (days)	13.67 ± 3.5	16.94 ± 2.7	0.149
30-day Mortality	4	5	1.00

P0136 ENDOSCOPIC MUCOSAL RESECTION OF DUODENAL ADENOMAS: SUCCESS, COMPLICATIONS, RECURRENCE, AND SURGERY-FREE OUTCOMES IN A UK TERTIARY CENTRE

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Introduction: Duodenal adenomas consist of sporadic and familial adenomatous polyposis (FAP) associated adenomas. Endoscopic mucosal resection (EMR) is the recognised technique when considering endoscopic removal of these lesions, but outcomes from large studies are lacking. Leeds Teaching Hospitals (LTHT) is a large tertiary centre that has a local catchment area of more than 800,000 people, and to our knowledge this is the largest UK cohort assessing duodenal EMR outcomes.

Aims and Methods: Retrospective data collection was performed of all patients who underwent duodenal EMR over a 17-year period at LTHT. We collected data on patient demographics, lesion characteristics and outcomes including significant complications, recurrence and surgery-free survival. Procedures were performed by a single advanced therapeutic endoscopist or an endoscopy fellow under supervision.

Results: A total of 98 patients underwent EMR (sporadic n = 23, FAP n = 75). Median adenoma size was 12.5 mm (IQR 9.0–30.0 mm), with 46.9% removed en-bloc. Standard EMR was performed in 87 procedures, and pull-within snare technique in the remaining 11 procedures. Final lesion histology was TA/TVA with LGD (n = 80), TA/TVA with HGD (n = 12), intra-mucosal cancer (n = 3) and in 3 cases data was missing. Patients with FAP were significantly younger with a median age of 49 years ($p < 0.001$).

The overall complication rate was 12.4%. 1 (1.0%) patient had an intra-procedural bleed which could not be managed endoscopically, delayed bleeding occurred in 6 cases (6.2%) and perforation occurred in 5 cases (5.2%), 3 (3.1%) of which could not be managed endoscopically. Following univariate analysis, "pull-within snare" technique ($p = 0.03$), piecemeal resection ($p = 0.002$), and increasing polyp size ($p = 0.003$) were significantly associated with complications. Adenoma recurrence at first follow up was 25.0%.

Surgery was required in 6 patients (6.2%) within 24-months of their EMR, 4 (4.1%) cases for adenomas > 30 mm, 2 (2%) cases for 10–29 mm and no cases for adenomas < 10 mm.

Conclusion: This is the largest cohort in the UK pertaining to duodenal EMR outcomes, with success, recurrence and complications similar to other world-leading endoscopy centres. Adverse outcomes are associated with increasing lesion size, piecemeal resection and EMR technique.

Disclosure: No disclosures

P0137 A META-ANALYSIS OF SCLEROLIGATION VERSUS BAND LIGATION FOR ERADICATION OF ESOPHAGEAL VARICES. A META-ANALYSIS OF SCLEROLIGATION VERSUS BAND LIGATION FOR ERADICATION OF ESOPHAGEAL VARICES

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Introduction: Esophageal band ligation (EBL) for esophageal varices has significantly less rebleeding rates and complications, and needs a lower number of sessions to achieve eradication of the varices than sclerotherapy yet has a higher recurrence rate This is because EBL does not obliterate the deeper varices or perforating veins, whereas the chemical effect of sclerotherapy does Scleroligation (combined sclerotherapy and band ligation) has been used successfully for management of esophageal varices and has been recently evaluated in management of gastroesophageal varices.

Aims and Methods: We aimed to determine therapeutic efficacy and safety of endoscopic scleroligation and endoscopic band-ligation of esophageal varices

A literature search was conducted in the following medical electronic databases: PubMed, CENTRAL, SCOPUS and Web of Science on the 23rd of December 2017 using the following strategy: scleroligation OR (sclerotherapy AND plus AND ligation) AND (Esophageal varices OR varices). 8 randomized controlled trials from 1996 to 2017 were included in the meta-analysis after tight full text screening. The included studies were analyzed by using RevMan 4.2 software to assess the efficacy and safety of Endoscopic Scleroligation (ESL) versus Endoscopic Band ligation (EBL) in management of Varices.

Results: Of 97 citations discovered by initial search, 8 parallel RCTs were finally included in this meta-analysis. We found that there were significantly less bands used in ESL than in EBL ($Chi^2 = 46.80$; 95% CI: −3.13 to −1.30; $df = 6$ ($p < 0000.1$); $I^2 = 87\%$). Compared to EBL, the overall number of sessions to variceal obliteration in ESL was significantly lower [$Chi^2 = 571.90$; 95% CI: −0.54 to 1.12, $I^2 = 99\%$; $p < 0.00001$]. ESL required fewer weeks of treatment than EBL, further confirming its positive therapeutic effect. Variceal recurrence following ESL was significantly lower than with EBL [$Chi^2 = 17.35$; 95% CI: 0.97 to 1.09, $I^2 = 54\%$; $p < 0.03$]. Both procedures had the same adverse effects with no significant difference regarding frequency.

Conclusion: Endoscopic Scleroligation (ESL) shows high efficacy and safety in management of varices with a low incidence of recurrence.

Disclosure: Nothing to disclose

P0138 CAP-ASSISTED REMOVAL OF IMPACTED ESOPHAGEAL FOOD BOLUS: "THE EASY WAY"

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Introduction: The commonest foreign body impacted in the esophagus in adults is a food bolus [1]. The European Society of Gastrointestinal Endoscopy issued clinical guidelines to deal with this problem in 2016 [2]. It recommends either pushing technique or retrieval methods using one of several accessories. However, pushing technique could be associated with adverse events. Also, during retrieval, with the conventional methods, the food bolus tends to fragment into small pieces making extraction both time and effort consuming. Cap-assisted endoscopic extraction of food bolus is an easier method. In this method, a cap is fixed to the tip of the scope and the bolus is removed by applying suction. However, data comparing it to other methods is scarce.

Aims and Methods: We aimed to compare two methods for extraction of an impacted esophageal food bolus; the cap-assisted suction method and the conventional methods. We retrospectively reviewed data from 253 patients who underwent endoscopy for food bolus extraction in the period between 2014 and 2017. We compared the two groups for the rate of en bloc removal, total procedure time, and procedure-related complications.

Results: 253 patients had endoscopy for food bolus extraction. In 76 patients (30%) the push-technique was used. 177 patients (70%) had one of the retrieval methods. The cap-assisted method was used in 84 patients while 93 patients had retrieval with the conventional methods. The application of cap-assisted technique achieved a higher rate of en bloc removal 82.1% compared to 11.8% with the conventional method ($p < 0.001$), a shorter procedure time (6.7 ± 3.2 minutes versus 15.3 ± 4.6 minutes, $p < 0.0001$), and less adverse events (0/84 versus 5/93, $p = 0.01$).

Conclusion: Cap-assisted removal of impacted esophageal food bolus is associated with more en block removal, shorter procedure duration, and less adverse effects compared to conventional methods. We encourage including this method in the options to remove an impacted esophageal food bolus.

Disclosure: Nothing to disclose

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P0139 LONG-TERM OUTCOME OF HYBRID APC FOR ABLATION OF DYSPLASTIC BARRETT'S ESOPHAGUS IN A LOW PREVALENCE COUNTRY

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Introduction: Currently, ablation of confirmed low-grade dysplasia (LGD), high-grade dysplasia (HGD) and residual Barrett's esophagus (BE) after endoscopic mucosa resection (EMR) of early carcinoma is recommended [i-iv]. Radiofrequency ablation is the best study method, but is not readily available in Russia. Moreover, the prevalence of BE and dysplasia is rather low, which may compromise the outcome of other more operator dependent techniques, like Hybrid-APC.

Aims and Methods: The aim of the present study was to evaluate the efficacy and safety of Hybrid APC eradication therapy for BE in a low prevalence setting after a former onsite training. All procedures were performed by a single operator (SK) after a formal onsite training on 3 different occasions by a very experienced endoscopist (HM). Hybrid APC probe was used for marking of the neo-Z-line, then consecutive lifting the Barrett's mucosa with 0.9% saline solution injected by the high-pressure water jet system (ERBEJET 2) and mucosa ablation (PULSED APC, Effect 2, 60 Watt). After that the ablation area was mechanically cleaned with a transparent cap on the tip of the endoscope for further detailed inspection. Detected remained BE was retreated with a second APC application with the lower power (40 Watt). High dose PPI treatment (esomeprazole 80 mg/day) was used after procedures for strong acid suppression that provided an environment for development squamous mucosa on the site of ablation[i]. After complete eradication of BE (histologically and endoscopically confirmed), a control endoscopy was performed at 3 months, 6 months and annually thereafter for taking 4-quadrant biopsies from the whole area of the former BE segment including biopsies of Neo-Z-line. All histological findings were confirmed by an experienced gastrointestinal pathologist.

Results: In our tertiary referral center, we have 120 BE patients registered between July 2014 to September 2017. Of these, 11 patients were diagnosed with LGD and HGD (5 male, 6 female) and were treated with Hybrid APC and included in this long-term follow-up study. At enrollment, the mean age was 46 years (range 25–63). The mean length of Barrett's esophagus was C1 M2. Five EMRs of visible lesions before ablation were performed. In total 18 Hybrid APC sessions have been successfully performed with curative intent. Complete macroscopic and microscopic BE ablation was achieved in all patients after a mean of 1.6 (range 1–3) treatment sessions. No perforations or uncontrollable bleeding occurred. Stricture formation was observed in 1 patient 3 months after Hybrid APC, which was combined with EMR in the same session. This stricture was managed by 1 session of balloon dilatation. The patients were followed for a mean of 2.5 years (range 10–46 months) after complete eradication of BE with a mean number of follow-up endoscopies of 3.0 (range 1–4). Recurrence of intestinal metaplasia was not seen in any patient. Generally, we took 64 biopsy samples, 8 (12.5%) of them contained sufficient subepithelial lamina propria. Buried intestinal metaplasia was not found in any of these biopsies.

Conclusion: We showed that Hybrid APC is a safe and effective method for treatment of dysplastic BE with dysplasia in a tertiary referral center in a country with low prevalence of BE and BE dysplasia. 3-year follow up didn't reveal any recurrence of BE mucosa, buried metaplasia or any major complications. Because Hybrid APC is highly operator dependent our data underscore the importance of a proper training and adherence to a standardized treatment protocol to provide good long term outcomes.

Disclosure: Nothing to disclose

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P0140 THE FOLLOW-UP OF PATIENTS WITH EARLY GASTRIC CANCER AFTER NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION. THE EUROPEAN SINGLE CENTRE STUDY

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Introduction: According to the current guidelines of the European Society of Gastrointestinal Endoscopy (ESGE), the endoscopic resection is the treatment of choice of gastric superficial neoplastic lesions. The most current criteria for the curative treatment include 1 piece (en bloc) resection of mucosal or submucosal membrane ≤500 μm with free lateral and vertical margins and lack of the limfoangioinvasion. In the case of non-curative endoscopic resection, surgical treatment is required. However, the follow-up for patients who did not receive radical surgery was not extensively investigated.

Aims and Methods: We aimed to investigate follow-up of patients with early gastric cancer (EGC) after non-curative endoscopic submucosal dissection (ESD).

The retrospective analysis of prospective assessed database of ESD procedure for EGC, from 2008 to 2018 in Department of Gastroenterology of Pomeranian Medical University Hospital in Szczecin was performed. The follow-up examinations were as follows: endoscopy 3, 12 and 36 months after ESD and CT 24 to 36 months after ESD.

Results: The 81 ESD procedures were performed for 80 EGC patients (M 50, mean age 68.31 +/- 1.71), the en bloc resection rate was n = 73, (91.3%) and curative resection rate (R0) was n = 54, (67.5%). Non-R0 resection was due to: submucosal invasion n = 16, (20.0%), including n = 8, (10.0%) [SM2(+)] and n = 8, (10.0%) [SM3(+)], positive lateral margin n = 9, (11.3%) [LM(+)], including piecemeal resection [PM], positive vertical margin n = 1, (1.3%) [VM(+)]. The median follow-up was 29 months, range 7 - 122.

In the non-R0 group (n = 26; 32.5%; mean age 71.03 +/- 2.08) initially n = 5 patients underwent surgical treatment, n = 17 patients were followed-up without surgery because of lack of consent, poor general condition or comorbidities and n = 4 were lost to follow-up.

In the follow-up group only 1 patient after PM had recurrence of cancer in the +3 months gastroscopy and was sent to surgery. In the initially surgical group, n = 5, (100%) were negative for cancer in the resected specimen. Overall survival was n = 17, (65.4%) patients and cause-specific survival was n = 22, (100%): n = 5, (19.2%) patients died (n = 4 due to comorbidities, n = 1 due to postoperative complications). In the whole non-R0 group only 1 patient (1/22, 4.5%) had recurrence of cancer and was successfully treated with surgery.

Conclusion: Our results confirmed that in group of patients with advanced age or comorbidities who underwent non-curative ESD for EGC, only close observation may be an acceptable option without radical surgical procedure. Further research is required to set up more exact criteria to enrol the follow-up group.

Disclosure: The authors have no competing interests.

P0141 NARROW BAND IMAGING ENDOSCOPY VERSUS LUGOL CHROMOENDOSCOPY IN EARLY DETECTION OF ESOPHAGEAL CANCER IN PATIENTS WITH HEAD AND NECK CANCERS: RANDOMIZED TRIAL

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Introduction: Patients with head and neck cancers have an increased risk for developing an esophageal squamous cell carcinoma (ESCC). Small, superficial, lesions are difficult to detect using only white light endoscopy. To improve detection chromoendoscopy is recommended. The aim of this study was to compare the narrow band imaging (NBI) endoscopy and Lugol chromoendoscopy in the early diagnosis of high-grade dysplasia and esophageal cancer in patients with head and neck cancers.

Aims and Methods: In a randomized trial, patients ≥ 1 year after curative treatment of head and neck cancers were randomly assigned in 2:1 ratio to NBI or Lugol chromoendoscopy. Following white light endoscopy the entire length of the esophagus was examined using 1 of the selected chromoendoscopic method. The primary outcome measure was positive predictive value of finding a lesion requiring biopsy with each method. The secondary endpoints were: number of biopsies/per patient, examination time, endoscopy tolerance (according to visual analogue scale) and characteristics of patients diagnosed with high-grade dysplasia or invasive cancer.

Results: Of the 294 patients included in the study 204 were assigned to NBI group and 90 to the Lugol chromoendoscopy group. In total, 3 ESCC and 2 high-grade dysplasia were detected.The positive predictive value of NBI and Lugol chromoendoscopy were 7.69% (95% CI, 0.94%–25.1%) and 8.11% (95% CI, 1.70%–21.9%), respectively (p = 1).The NBI was significantly superior to Lugol chromoendoscopy in: number of biopsies needed/per patient (26/204 vs. 37/90,

p = 0.003), mean examination time (3.50 min. vs. 5.15 min., p < 0.001) and mean endoscopy tolerance (25mm vs. 36.5 mm, p < 0.002). In all patients diagnosed with high-grade dysplasia or invasive cancer successful endoscopic mucosal resection or endoscopic submucosal dissection were performed.
Conclusion: Diagnostic performance of NBI and Lugol chromoendoscopy seems to be equal but NBI is superior to Lugol chromoendoscopy in terms of number of biopsies/per patient, examination time and procedure tolerance. These results indicate that NBI should be taken into account as a standard examination method for early diagnosis of high-grade dysplasia and esophageal cancer in patients with head and neck cancers and thus replacing cumbersome Lugol staining.
Disclosure: Nothing to disclose

P0142 EFFICACY AND SAFETY OF GASTRIC POEM (G-POEM): RESULTS OF A PILOT SERIES

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Introduction: In contrast to POEM for achalasia, there is only limited data available on the new technique of gastric poem (G-POEM). The question arises whether G-POEM may be a helpful tool for the treatment of gastric emptying disorders (GED) going along with pylorospasm.
Aims and Methods: Patients with clinically, endoscopically and scintigraphically confirmed diagnosis of gastric emptying disorder with pylorospasm and who had undergone repeated endoscopic treatment sessions, e.g. by balloon dilation and/or BoTox injection with short-term relief, were treated by G-POEM. ESD knives with integrated injection function were used (Flush knife, Fujifilm; Dual Knife J, Olympus; Hybrid Knife, Erbe). All procedures were carried out under general anaesthesia using CO^2 insufflation and periinterventional application of i.v. antibiotics. Technical and clinical success, adverse events (AE), as well as the need of repeated endoscopic therapy were evaluated.
Results: From 11/2016 to 04/2018, a total of 9 patients were treated by G-POEM (7 female, 2 male; HSK Wiesbaden n = 7; Frankfurt Höchst n = 2). Pylorospasm was caused by vagal nerve injury after fundoplication surgery (n = 4), thoracal surgery (n = 1), esophageal resection (n = 3), and in 1 case by multiple sclerosis. Mucosal incisions were made at the 5–6 o'clock (n = 8) or the 7 o'clock position (n = 1). Technical success was 100% (complete pyloric incision with collapse of the muscle ring). AE that were judged to be minor complications occured in 3/9 pt (33%; shivering without fever (n = 1), abdominal pain and nausea (n = 1), mucosal ulcerations next to the submucosal tunnel on the next day (n = 1). 6/9 pt underwent at least 1FU examination (mean FU 5.5 ± 4 mo.; range 3–12). Symptom relief was found in 6/6 pt (100%) after 3 months. 2/6 pt (33%) reported symptom deterioration thereafter. 1 patient was referred to gastric pace maker implantation, the other patient underwent endoscopic balloon dilation and BoTox injection with symptom relief thereafter.
Conclusion: G-POEM was shown to be effective and safe in the short term with 100% rates of technical and clinical success. However, relapse of symptoms may occur in the mid term requiring additional treatment strategies.
Disclosure: Nothing to disclose

P0143 RISK FACTORS OF METACHRONOUS GASTRIC NEOPLASM BEYOND 5 YEARS AFTER ENDOSCOPIC RESECTION FOR EARLY GASTRIC CANCER

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Introduction: Endoscopic resection has been standard treatment for selected patients with early gastric cancer (EGC) and the risk factors of metachronous gastric cancer after endoscopic resection discovered throughout previous studies. However, the risk factors over a long period of time has not yet been well demonstrated. To develop an optimal endoscopic surveillance strategy, it is necessary to elucidate the risk factors associated with metachronous tumor development in long-term follow-up.
Aims and Methods: This study aimed to clarify the risk factors of metachronous gastric neoplasm beyond 5 years after endoscopic resection for EGC.
We performed a retrospective analysis of the patients who underwent endoscopic resection for EGC from Jan 2005 to May 2012 in Seoul National University Hospital.
Results: Among 1280 patients with EGC, 663 patients were followed-up for over 5 years, in whom metachronous gastric neoplasm developed in 65 patients beyond 5 years after endoscopic resection for EGC. In multivariate analysis, male (odds ratio, OR 3.242; 95% confidence interval, CI 1.367–7.689; p = 0.008), elevated gross type (OR 5.240; 95% CI 1.872–14.668; p = 0.002), mixed Lauren classification (OR 5.240; 95% CI 2.535–92.054; p = 0.003), intestinal metaplasia (OR 1.456; 95% CI 1.065–1.990; p = 0.019), tumor-positive lateral margin (OR 3.322; 95% CI 1.092–10.104; p = 0.034), synchronous adenoma (OR 2.832; 95% CI 1.261–6.364; p = 0.012) were positive predictive factors for metachronous gastric neoplasm.
Conclusion: Metachronous gastric neoplasm had developed in 9.8% of patients beyond 5 years after endoscopic resection for EGC. Male sex, elevated gross type, mixed Lauren classification, intestinal metaplasia, tumor-positive lateral margin, synchronous adenoma were significantly associated with metachronous tumor development in long-term follow-up.
Disclosure: Nothing to disclose

P0144 EFFICACY OF FULL-SPECTRUM ENDOSCOPY (FUSE) TO VISUALIZE THE AMPULLA OF VATER IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS (FAP): A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Duodenal cancer is one of the extracolonic malignancies which causes death in patients with familial adenomatous polyposis (FAP). However, the visualization of the ampulla of Vater is not always sufficient with standard esophagogastroduodenoscopy (EGD) because of a limited field of view. Full-spectrum endoscopy (FUSE) provides a wider 245-degree field of view with images on the front and left side of the tip of the endoscope. The aim of this prospective study was to evaluate the improvement of visualization of the ampulla of Vater in FAP using FUSE compared to standard EGD.
Aims and Methods: This study included patients with FAP followed-up in our hospital. We excluded individuals with a history of upper gastorointestinal surgery. EGD was performed using FUSE by qualified endoscopists of the Japanese Gastroenterological Endoscopy Society and visibility of the ampulla of Vater was evaluated. All examinations were video-recorded and 2 videos of the duodenum were edited in each patient, 1 of the FUSE group (forward-viewing and left-side viewing) and 1 of the conventional group (forward-viewing alone). 3 qualified endoscopists at an outside institution then reviewed the videos and compared the visibility of the ampulla of Vater between the 2 groups. The visibility of the ampulla of Vater was classified according to Woo et al., as follows: Type 1, the whole area of the papilla; Type 2, the upper part of the papilla including the orifice; Type 3, the upper part of the papilla excluding the orifice; Type 4, the lower part of the papilla including the orifice; or Type 5, no visualization of the papilla. The primary endpoint was the proportion of Type 1 in off-line review of the videos, and the secondary endpoint was that of Type 1 in on-site diagnosis.
Results: 49 FAP patients were enrolled in this study between July 2016 and December 2017. Patients characteristics were as follows: median age of 37 years (range 19–61) and male/female ratio of 38/11. The average observation time of the duodenum was 114 ± 47.9 seconds. Visibility of the ampulla of Vater was determined as follows: for off-line review, reviewers A,B,C for the FUSE group (Type 1/ Type 2-4/ Type 5 = 49, 49,49/ 0, 1, 0/ 0, 0, 0) vs. the conventional group (Type 1/ 2-4/ 5 = 4, 8, 7/ 31, 26, 27/ 14, 15, 15) and for on-site diagnosis, the FUSE group (Type 1/ 2-4/ 5 = 49/ 0/ 0) vs. the conventional group (Type 1/ 2-4/ 5 = 16/ 19/ 14). The visualization of the ampulla of Vater was significantly better in the FUSE group in both on-site diagnosis and off-line review (p < 0.001). Intraclass correlation coefficients were 1.0 (FUSE group) and 0.85 (conventional group).
Conclusion: FUSE EGD is recommended for screening and surveillance endoscopy for patients with FAP.
Disclosure: Nothing to disclose

P0145 ENDOSCOPIC SCORING SYSTEM FOR PREDICTING THE ANASTOMOTIC COMPLICATIONS AFTER ESOPHAGECTOMY: A PROSPECTIVE COHORT STUDY

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Introduction: The postoperative complications relative to gastric conduit reconstruction are still common issues after esophagectomy. We previously reported early diagnosis of ischemic reaction provided the suitable postoperative management and therapeutic intervention to prevent leakage, strictures and necrosis (1). An endoscopic examination is a rapid and highly sensitive procedure to evaluate the gastrointestinal organ. Thus, the novel endoscopic scoring system which enables to predict anastomotic complications after esophagectomy is required.
Aims and Methods: The purpose of this study is the safety and efficacy of an endoscopic evaluation of the anastomotic region in the acute period after esophagectomy.
The patients, who have malignant or end-stage benign esophageal disease, were enrolled. The patients undergo an esophagectomy with reconstruction with a gastric pull-up and a cervical esophagogastrostomy. Anastomotic complications were defined as leakage, strictures, and necrosis.
Endoscopic examinations were performed on the postoperative days (POD) 1, 8, and 15. The investigators prospectively assess the probability of anastomotic complications based on the novel endoscopic scoring system as the following.

Score 1: normal mucosa or erosion, score 2: less than 67% circumferential ischemic mucosa or ulcer formation, score 3: more than 67% circumferential ischemic mucosa or ulcer, or full-circumferential ischemic mucosa or ulcer formation with lesion length less than 20mm, score 4: full-circumferential ischemic mucosa or ulcer formation with lesion length more than 20mm. The highest score was adapted in each patient.
The primary outcome measure was the predicting rate of the anastomotic complications using the scoring system within 2 months after esophagectomy.
Clinical Trials.gov Registry, ID:NCT02937389.
Results: From 2015 April to 2018 April, 49 patients were enrolled in this study. 47 patients underwent esophagectmy to esophageal cancer. 2 patients underwent esophagectomy to benign strictures due to corrosive esophagitis and achalasia. 16 patients (33.3%) developed anastomotic complications after esophagectomy. Anastomotic leakage occurred in 4 patients. A stricture occurred in 13 patients. 1 patient had gastric conduit necrosis.
All patients safely underwent endoscopic examinations without any complications. The incidence rates of each patients score 1, 2, 3, and 4 were 47.9%, 20.8%, 16.7%, and 14.6%. In 72.9% of patients, the maximum value of the endoscopic classification is scored at 1 POD. The incidence rates of anastomotic complications for maximum score 1, 2, 3, and 4 were 4.4%, 20.0%, 75.0%, and 100%, respectively ($p < 0.01$).
Next, the patients with a maximum score 3 or 4 were defined as the high-risk groups of anastomotic complications. The patients with maximum score 1 or 2 was defined as the low-risk groups of anastomotic complications. The sensitivity and the specificity of predicting anastomotic complications in high-risk groups were 62.5% and 100% at 1POD. The sensitivity and the specificity of predicting anastomotic complications in high-risk groups were 81.3% and 93.8% at 8POD. The patients in high risk groups of anastomotic complications had a significantly longer postoperative hospital stay than patients in low-risk groups ($p = 0.02$).
Conclusion: Endoscopic examinations after esophagectomy were safely performed. The application of the endoscopic classification to mucosal ischemia after esophagectomy resulted in suboptimal accuracy to predict the anastomotic complications.
Disclosure: Nothing to disclose

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P0146 A COMPARISON OF THE STRENGTH OF ENDOSCOPIC SUTURE: PARTIAL-THICKNESS SUTURE AND FULL -THICKNESS SUTURE

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Introduction: Conventional surgery requires full-thickness suture in order to ensure the safety from leakage. Full-thickness suture has shown to be more effective than superficial suture, but full-thickness suture has been controversial in endoluminal surgery because it can cause external organs damage or bleeding. Partial-thickness suture has been attempted to ensure the stability, but its effectiveness has been questioned after events of suture tear. The aim of our study was to compare the strength between partial-thickness suture and full-thickness suture to provide information in choosing the adequate suture method.
Aims and Methods: We designed our study in 2 steps. We compared the full thickness suture strength depending on the suture site, and measure the suture strength that needed for the suture to be cut off or to be torn from the sample and their change as the suture width varies. Samples were prepared by cutting the pig stomach into 5 cm diameter circle. Then a loop with a nylon 3-0 suture on the sample was made endoscopically. We defined the depth of the loop as the suture thickness and the distance of the loop as the suture width. The suture thickness was measured and categorized into 2 groups, full-thickness or partial-thickness. The width was measured on the surface of the sample, in the range of 0.6 to 2.2mm, and categorized into 3 groups, narrow, medium and wide. Each sample was placed in the manufactured bite, tightly fastened and the loop was pulled by the tension tester. The maximum suture strength was the force recorded at the tension tester when the loop was detached from the sample.
Results: With the same suture width (1.4cm) and using full-thickness suture method, the antrum had the highest strength considering the thickness of the wall, and the fundus had shown to have the highest elasticity. The mean strength of the partial-thickness suture and the full-thickness suture were 20.18 ± 6.12N ($n = 11$) and 27.79 ± 7.29N ($n = 12$), respectively ($p = 0.0135$), and the strength of the partial-thickness suture was 73% of that of full-thickness suture. As the suture width increased and deepened, the strength of the suture increased with both methods ($p = 0.001$). On average, the width of the partial-thickness suture should be 5 mm longer than the width of the full-thickness suture to reach the same strength as the full-thickness suture.
Conclusion: Partial-thickness suture may be considered as an option for safety in an operative environment if feasible. Because the difference of the intensity between 2 suture methods, it is necessary to consider widening the width when performing the partial-thickness suture to have similar strength. Further studies on endoscopic suture method in gastrointestinal tract are needed.
Disclosure: Nothing to disclose

P0147 AND WHEN NBI DOESN'T SHOW GASTRIC INTESTINAL METAPLASIA: DO WE STILL NEED TO SEPARATE BIOPSY SAMPLES INTO DIFFERENT VIALS?

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Introduction: For the correct staging and classification of chronic atrophic gastritis and gastric intestinal metaplasia (GIM) it is necessary to perform ≥ 4 biopsies (2 from the atrum/incisure and 2 from the body) with the biopsy samples being placed in different vials according to the current recommendations. Virtual Chromoendoscopy with Narrow-Band-Imaging (NBI) assists the diagnosis and vigilance of GIM.
Aims and Methods: We aimed to evaluate if, in the absence of a typical endoscopic pattern of GIM with NBI, biopsy samples can be placed in the same vial without implications in the diagnosis and follow-up of the patient.
Multicentre prospective study of a consecutive series of patient with indication to perform an upper endoscopy with biopsies of both antrum/incisure and body. In every patients, upper endoscopy was performed with NBI. Patients with gastric lesions and/or suggestive areas of GIM were excluded. Patients included were submitted to ≥ 4 biopsies (2 from the antrum/incisure and 2 from the body) with the samples being placed in the same vial for histologic assessment ($n = 182$). Finally, histologic staging systems OLGA and OLGIM were calculated.
Results: OLGA/OLGIM calculation was possible for every patients as it was possible to distinguish samples from antrum/incisure from those of gastric body. In total, 178 (97.8%) presented OLGIM 0 and only 4 (2.2%) presented OLGIM I. 149 (81.9%) presented OLGA 0, 23 (12.6%) presented OLGA I and 10 (5.5%) presented OLGA II. The placement of biopsy samples in the same vial had no implications in the diagnosis and follow-up in none of the patients since no one was diagnosed with severe gastric atrophy/intestinal metaplasia (negative predictive value of 100%).
Conclusion: In the absence of a typical endoscopic pattern of GIM with NBI, biopsy samples can be placed in the same vial if it is desired to determine the presence of *Helicobacter pylori* or even to abstain from biopsies if this is not the case. This change in clinical practice can have a significant financial impact on endoscopy costs.
Disclosure: Nothing to disclose

P0148 ENDOSCOPIC DIAGNOSIS OF *HELICOBACTER PYLORI* ERADICATION HISTORY USING LINKED COLOR IMAGING AND DEEP LEARNING: A SINGLE-CENTER PROSPECTIVE STUDY

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Introduction: *Helicobacter pylori* (HP) eradication is a critical therapeutic approach to reduce gastric cancer mortality. In Japan, 1.5 million people annually undergo HP eradication; meanwhile, it has been revealed that despite successful eradication, the risk of gastric cancer persists for patients who already show progressed mucosal atrophy and intestinal metaplasia[1]. Post-eradication patients demonstrate a negative reaction for the majority of noninvasive HP infection tests. As a consequence esophagogastroduodenoscopy (EGD) represents the only examination that enables distinction between HP uninfected patients at extremely low risk for gastric cancer and patients who have a history of HP eradication therapy. With the present study we planned to create a novel computer aided endoscopic diagnosis (CAED) system for HP eradication history using linked color imaging (LCI) and deep learning (DL). LCI is a new image-enhanced endoscopy (IEE) that enhances slight differences in mucosal color, while DL is a type of machine learning technology that imitates neural network in the brain.
Aims and Methods: The aim of this prospective study was to create a CAED system to distinguish between HP uninfected people and patients who have history of HP eradication therapy, using LCI and DL. In this study, we included patients who underwent EGD and were tested for serum HP antibodies (HPab) or urea breath test (UBT) at our medical clinic. Patients with active HP infection, in the absence of eradication history, were excluded from the study. As a gold standard for HP infection status, we used HPab titer for uninfected subjects (< 3 U/ml, $n = 148$), and UBT value for eradicated patients ($< 2.5\%$, $n = 81$). Patients underwent HP eradication out at our hospital. In total, 229 subjects were enrolled in this study. In order to evaluate the diagnostic accuracy of the CAED system patients were subdivided in 2 groups: a training group ($n = 189$, HP uninfected $= 128$, eradicated $= 61$); and a test group ($n = 40$, HP uninfected $= 20$, eradicated $= 20$). Comparing the output data from the test group with the actual data on HP infection status allowed us to assess the accuracy of the CAED system. During the course of the EGD an endoscopist took 3 LCI pictures of the lesser curvature, greater curvature, and antrum of the stomach using EG-L580NW (Fujifilm Co., Japan). The LCI images were subsequently augmented by rotation and right-left flip. We generated 2,508 training images and 480 testing images. An original DL model was designed, which has 18 deep convolutional layers for the CAED system. R (version 3.3.2.) was used for statistical analyses.

Results: Area under the curve (AUC) of the receiver operating characteristics (ROC) for the lesser curvature, greater curvature, and antrum were 0.95 (95% CI 0.914–0.981), 0.93 (95%CI 0.882–0.969), and 0.89 (95%CI 0.843–0.944), respectively.
Conclusion: Patients with an HP infection are easy to diagnose without using EGD because noninvasive infection reaction is positive. In contrast, EGD is the only examination capable of distinguishing between HP uninfected patients with low gastric cancer risk and patients with a history of eradication. The CAED system demonstrated excellent accuracy in distinguishing between the 2 groups using LCI. Our next goal is to apply our findings to clinical practice.
Disclosure: Nothing to disclose

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P0149 ENDOSCOPIC INTERVENTION FOR PANCREATIC FLUID COLLECTIONS HAS BETTER OUTCOMES THAN PERCUTANEOUS OR SURGICAL DRAINAGE- A META-ANALYSIS

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Introduction: Inflammatory pancreatic fluid collections are common complications of both acute and chronic pancreatitis. They may be drained endoscopically (ED), percutaneously (PD) or surgically (SD) with diverse efficiacy. Several retrospective and case control studies but only a limited number of randomized trials compared the outcomes of these treatment modalities.
Aims and Methods: A meta-analysis was performed using the preferred reporting items for systematic review and meta-analysis protocol. A comprehensive literature search was conducted until November 2017 to identify studies comparing at least 2 of the treatment options regarding mortality, clinical success, recurrence, complications and length of hospitalisation (LoH). Initially, 1248 and 2539 articles were identified in Embase and PubMed, respectively, but only 25 studies were suitable for the meta-analysis. The meta-analysis is registered at PROSPERO under CRD42018079200.
Results: ED provided a higher rate of clinical success (OR = 4.10; 95%CI 1.76, 9.54; p = 0.001) and lower postoperative LoH (weighted mean difference (WMD) = −21.23; 95% CI −37.09, −5.37; p = 0.009) compared to PD based on 6 studies (including 650 and 166 patients, respectively). The postoperative LoH (WMD = −4.42; 95% CI −6.05, −2.80; $p < 0.001$) was shorter after ED than after SD based on 14 studies (including 789 and 750 patients, respectively). The recurrence and complication rates were higher (OR = 10.30; 95% CI 2.78, 38.18; $p < 0.001$ and OR = 3.29 95% CI 1.39, 7.77; p = 0.007, respectively), while the clinical success rate was lower (OR = 0.12; 95% CI 0.07, 0.21, $p < 0.001$) in PD compared to SD based on 11 studies (including 8404 and 7161 patients, respectively).
Conclusion: ED and SD are equally effective in the treatment of inflammatory pancreatic fluid collections, but ED is associated with shorter LoH. PD has lower success rate compared to the other modalities.
Disclosure: Nothing to disclose

P0150 COMPARISON BETWEEN ENDOSCOPIC SUBMUCOSAL DISSECTION AND SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION FOR ESOPHAGEAL SUBMUCOSAL TUMORS ORIGINATING FROM THE MUSCULARIS PROPRIA LAYER

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Introduction: Endoscopic submucosal dissection (ESD) or submucosal tunneling endoscopic resection (STER) is widely acknowledged as an important treatment option for esophageal submucosal tumor from the muscularis propria layer. However, the clinical outcomes of ESD or STER for esophageal submucosal tumor have not been completely evaluated.
Aims and Methods: The aim of this study is to compare the 2 different treatments. We retrospectively collected the data of 876 patients who had undergone ESD or STER for esophageal submucosal tumors from January 2011 to September 2015 in the Endoscopy Center of Zhongshan Hospital. Gender, age, tumor size, depth and shape, procedure time, complications, postoperative length of stay, and follow-up were compared between ESD and STER groups.
Results: 424 patients received ESD, while 452 patients received STER. There was no significant differences in age, gender, tumor size, depth and shape, en bloc resection rate, complications, postoperative hospital stay ($p > 0.05$). The patients receiving STER had apparently a longer procedure time due to closing the tunnel entrance (ESD vs STER, 23.2 ± 16.5 min vs. 44.0 ± 25.8 min, $p < 0.001$). No recurrence and death was occurred in the STER and ESD groups during a mean follow-up of 50.0 and 51.8 months, respectively.
Conclusion: Both ESD and STER would likely be effective and safe alternatives for resecting SMTs ≤ 10mm. Accounting for safety and preventing perforation, we are inclined to STER for SMTs > 10mm. Additionally, the choice between the 2 procedures will also depend on the depth and shape of submucosal tumors.
Disclosure: Nothing to disclose

P0151 THE CLINICAL IMPACT OF CLOSURE OF THE MUCOSAL DEFECT AFTER DUODENAL ESD

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Introduction: Delayed complications (bleeding or perforation) are major concerns of duodenal ESD. Recently, we conducted a retrospective study including about 170 cases of duodenal ESD and found both perforation and bleeding was much lower than those reported by previous reported (presented at DDW 2018). We have routinely closed the post-ESD mucosal defect as far as possible, and we hypothesized the discrepancy of the outcomes between ours and previous studies was come from the difference in the proportion of complete closure of post ESD mucosal defect.
Aims and Methods: The aim of this study was to assess the efficacy of prophylactic closure of mucosal defect after duodenal ESD. This is a retrospective study from a university hospital. We collected the outcomes of duodenal ESD in 169 patients with duodenal epithelial neoplasia (174 lesions) treated by ESD at our department between July 2010 and June 2017. Study subjects were divided into 3 subgroups according to the degree of closure of post-ESD mucosal defect; complete group, incomplete group, and not attempted group. The proportion of delayed complications (including delayed bleeding and delayed perforation), the maximum serum level of C-reactive protein (CRP), and the total hospital stay were compared among these subgroups. Moreover, a multivariate logistic regression model to find risk factors for delayed complications.
Results: The proportion of delayed complications of patients in complete group, incomplete group, and not attempted group were 1.7%, 25%, and 15.6%, respectively. The difference between complete group and the others was significant ($p < 0.01$). Maximum serum CRP level was much lower in complete group (1.51 ± 2.18 vs. 6.28 ± 10.0mg/dl. $p < 0.01$) and hospital stay was significantly shorter in complete group than in incomplete/none group (median [range] 4 [4–13] vs. 7 [3–58] days, $p < 0.01$). Multivariate analysis revealed complete closure was an only independent predictor to reduce delayed complications and it revealed about 95% significant decrease of delayed complications.
Conclusion: The present study revealed that complete closure of the mucosal defect after duodenal ESD significantly decreased delayed complications and improved other outcomes such as inflammatory reaction or duration of hospital stay.
Disclosure: Nothing to disclose

P0152 GASTRIC DYSPLASIA IN FAMILIAL ADENOMATOUS POLYPOSIS - WHAT IS THE RELEVANCE?

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Introduction: Familial adenomatous polyposis (FAP) is an inherited autosomal-dominant disease characterized by the development of neoplasms in both upper and lower gastrointestinal tract. With the implementation of prophylactic colectomy, the incidence of colorectal cancer has declined and extracolonic manifestations have become more relevant.
In what gastric lesions are concerned, FAP patients are known to have an increased risk for gastric dysplasia, although it is unclear if these lesions confer an increased risk of gastric cancer.
Aims and Methods: The aim of our study was to characterize gastric dysplastic lesions in patients with FAP. We enrolled 144 patients with germline mutation in the APC gene from 63 FAP families and we retrospectively reviewed 366 Upper Gastrointestinal Endoscopies (UGE) performed during regular surveillance at the Familial Cancer Clinic.
Statistic tests: Chi-square, Fisher's Exact Test, Student T test, Mann-Whitney U test, Cox Regression Model
Results: From the 144 patients included in the study, 94 (Men: 49/Women: 45, mean age 48.3 ± 14,8 years) underwent UGE at least once during a median follow up period of 12.7 ± 8.9 years.
81.9% of patients had classical FAP and 18.1% presented the attenuated phenotype. 14.9% of patients did not have family history of FAP and only 6.4% had family history of gastric cancer.
Gastric dysplastic lesions were detected in 16 patients (17%): 37 endoscopically visible lesions (Paris classification: 0-Ip: 10, 0-IIa: 26, 0-IIa+IIc: 1) and 1 case of dysplasia in random biopsies. Regarding their location, the majority of dysplastic lesions were at the antrum (70.3%) and 18.9% were found within fundic gland polyps (FGP)
Mean age was significantly higher in patients with gastric dysplastic lesions compared with those without dysplasia (59.3 ± 15.7 vs. 46.0 ± 13.7 years, p = 0.001).

Histopathologic findings revealed 28 lesions with low-grade dysplasia (LGD), 8 with high-grade dysplasia (HGD) and 2 adenocarcinomas, both diagnosed in the first UGE performed.
In regard to the evolution of dysplasia, 7 patients maintained LGD in the subsequent EGDs; only one patient had progression from LGD to HGD, in a 1 year period. This case involved multifocal dysplasia of the antrum and the patient underwent subtotal gastrectomy.
The majority (70.3%) of gastric dysplastic lesions were treated endoscopically (endoscopic mucosal resection: 16; polypectomy: 9; endoscopic submucosal dissection: 1) and surgery was conducted in 2 cases.
Gastric dysplasia was positively associated with the presence of gastric polyps and flat lesions ($p = 0.014$ and $p < 0{,}001$, respectively) and with atrophic gastritis and/or intestinal metaplasia ($p = 0.001$). Gastric dysplasia was not associated with FAP phenotype, *Helicobacter pylori* infection or the presence/number of FGP.
Conclusion: Despite the high prevalence of gastric dysplasia in FAP patients, its course is indolent. This may allow endoscopic surveillance and validate a conservative treatment strategy in the majority of cases.
Disclosure: Nothing to disclose

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P0153 CLINICAL SCORE TO PREDICT THE CHANCE OF SUCCESSFUL ENDOSCOPIC APPROACH OF ESOPHAGEAL LEAKS: CAN IT GUIDE OUR CLINICAL PRACTICE?

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Introduction: The endoscopic approach of esophageal perforations poses a therapeutic challenge. Recently, a predictive score has been proposed to predict the chance of successful endoscopic stenting in benign esophageal leaks. This score consists of 4 clinical variables that proved to be effective in discriminating the probability of success, especially when the probability of success is $\geq 70\%$ or $\leq 50\%$, with lower discriminatory power in case of intermediate probabilities (50–70%).
Aims and Methods: We aimed to evaluate the applicability of the clinical score in a cohort of patients with anastomotic leaks managed with fully /partially covered self-expanding metal esophageal stents.
Multicenter retrospective cohort study including patients submitted to endoscopic stenting due to anastomotic leak. Demographic data, score variables (etiology, leak size and location and C-reactive protein), clinical success, and need for additional therapies were assessed. The score and consequent probability of success of the therapy ($\leq 50\%$, 50–70%, $\geq 70\%$) were calculated and its agreement with clinical success was assessed.
Results: 39 patients included; 59% men, mean age 65 ± 10.7 years old, submitted to esophageal stenting after cancer surgery - esophagectomy ($n = 10$), gastrectomy ($n = 26$) - and bariatric surgery ($n = 3$), with an average of 2 stents /patient. Clinical success achieved in 59% of patients, with mean resolution time of 67.91 ± 41 days.
Application of the score:
Predicted probability of success $\geq 70\%$ ($n = 11$): Clinical success in 8/11 (72.8%); Clinical failure in 3/11: combination therapy with stenting, OTSC and fibrin glue-1; death -2.
Predicted probability of success 50–70% ($n = 17$): Clinical success in 11/17 (64.7%); Clinical failure in 6 /17: surgery-1; therapy with OTSC and fibrin glue-1; death-4.
Predicted probability of success $\leq 50\%$ ($n = 11$): Clinical success in 4/11 (36.4%); Clinical failure in 7/11: combined therapy with stenting and endosponge-1; surgery-4; death-2.
Conclusion: The application of this predictive model proves to be useful in clinical practice, favoring management with endoscopic stenting in patients with probability of success $\geq 50\%$. It is cautious to consider other therapeutic options in patients with a lower probability of success.
Disclosure: Nothing to disclose

Reference

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P0154 CLINICAL MANAGEMENT OF ENDOSCOPICALLY RESECTED PT1 COLORECTAL CANCER

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Introduction: Implementation of colorectal cancer (CRC) screening programs and the improvement of endoscopic techniques increases the endoscopic resection of polyps with early invasive CRC (pT1 Nx M0). The risk of lymph-node metastasis often leads to additional surgery, but despite guidelines, correct management remains unclear
Aims and Methods: Aim of this study was to assess factors affecting the decision-making process in endoscopically resected pT1-CRCs in an academic centre.
We retrospectively reviewed patients undergoing endoscopic resection of pT1 CRC from 2006 to 2016. Clinical, endoscopic, surgical treatment and follow up data were collected and analysed. Such lesions were categorized according to endoscopic/histological risk-factors in low- and high-risk groups. In detail, low-medium grade of differentiation, no lymphovascular invasion, no tumour budding, Haggit 1–3 and Kikuchi sm1, and en bloc resection was considered as low-risk pT1-CRC. Comorbidities were classified according to Charlson index (CCI). Surgical referral for each group was computed, and dissociation from current European CRC screening guidelines recorded. Multivariate analysis for factors affecting the post-endoscopic surgery referral was performed.
Results: 72 patients with endoscopically resected pT1-CRC were included. Overall, 20 (27.7%) and 52 (72.3%) were classified as low- and high-risk, respectively. In the low-risk group, 11 (55%) were referred to surgery, representing an over-treatment as compared with current guidelines. In the high-risk group, a non-surgical endoscopic surveillance was performed in 20 (38.5%) cases, representing a potential under-treatment). After median follow up of 30 (6–130) months, no patients developed tumour recurrence. At multivariate analysis, age (OR 1.21, 95% CI 1.02–1.42; $p = 0.02$) and comorbidities (CCI) (OR 1.67, 95% CI 1.12–3.14; $p = 0.04$) were independent predictors for subsequent surgery.
Conclusion: A substantial rate of inappropriate post-endoscopic treatment of pT1-CRC was observed, when compared with current guidelines. This was apparently related with an over-estimation of patient-related factors rather than endoscopically or histological-related factors.
Disclosure: Nothing to disclose

P0155 PINE-CONE AND VILLI PATTERNS ARE ENDOSCOPIC SIGNS SUGGESTIVE OF ULCERATIVE COLITIS-ASSOCIATED COLORECTAL CANCER AND DYSPLASIA

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Introduction: Patients with ulcerative colitis (UC) are at high risk for the development of colorectal neoplasia: colitis-associated cancer or dysplasia. We recently performed a randomized controlled trial comparing targeted vs. random biopsy and demonstrated that targeted biopsies were almost comparable to random biopsies in terms of the neoplasia detection rate when performed by specialists; however, the appropriate site for targeted biopsy is still unclear. Therefor suggestive endoscopic findings of neoplastic lesions for targeted biopsy are necessary for the further effective surveillance colonoscopy.
Aims and Methods: We aimed to elucidate key endoscopic findings suggestive of neoplastic lesions for targeted biopsy in UC. We created 769 stereomicroscopic pictures (509 neoplastic, 260 non-neoplastic) mimicking magnifying colonoscopic images from surgically resected specimens stained with undiluted Carrazzi's hematoxylin solution, including areas of 25 lesions in 15 preoperatively diagnosed patients with UC-associated neoplasia. Surgical procedures were performed between April 2016 and October 2017 at a single referral center (Department of Surgical Oncology, the University of Tokyo, Japan). Two gastrointestinal (GI) surgeons/endoscopists, who were blinded to the pathological diagnosis, independently assessed the images and classified them according to Kudo's pit pattern and surface morphology, such as pine-cone/villi patterns. GI pathologists independently made pathological findings. The correlation between stereomicroscopic and pathological findings (neoplastic vs. non-neoplastic) for each image was investigated. The interobserver agreement was assessed using *kappa* statistics.
Results: Kudo's neoplastic pit patterns (type III-V) were significantly correlated with the presence of neoplasia (sensitivity 77.4%, specificity 89.5%, positive

predictive value 92.8%), with a substantial concordance rate (*kappa* value 0.677). A hundred regions presented with pine-cone/villi patterns, which showed high specificity (96.8%) and positive predictive value (92.0%) for neoplasia, although sensitivity was low (21.4%). Concordance rate was also substantial (*kappa* value 0.625). A revision of the endoscopic findings of flat dysplasia with non-neoplastic pit patterns (9 lesions in 6 patients) revealed that 7 of 9 lesions had a reddish area with a demarcation line in each neoplastic lesion.
Conclusion: Targeted biopsies in surveillance colonoscopy for patients with UC must focus on lesions showing pine-cone/villi patterns in addition to Kudo's neoplastic pit patterns such as type III, IV or V. For some flat neoplastic lesions with non-neoplastic pit patterns such as type I or II, a reddish area with a demarcation line may be one of the effective clues for targeted biopsy.
Disclosure: Nothing to disclose

P0156 IMPACT OF ACTIVE MONITORING ON QUALITY INDICATORS OF COLONOSCOPY

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Introduction: In the last decade, colonoscopy has proven to be the most efficient screening tool for colorectal cancer (CCR). It still carries many limitations, and the application of certain quality indicators can improve its performance. A minimum withdrawal time (WT) of 6 minutes is recommended and adenoma detection rate (ADR) increases with WT. ADR is a reliable index of careful inspection of the mucosa, and is inversely correlated to the development of interval cancers. Goal of our work: to evaluate the impact of active monitoring of WT known by the endoscopist on quality of colonoscopy, measured by the ADR.
Aims and Methods: Withdrawal time and adenoma detection rate are the quality indicators measured in our department. 8 gastroenterologists from the Bellevue Medical Center department of endoscopy have prospectively performed 373 colonoscopies over a period of 15 months, from February 2016 to April 2017. Quality indicators were measured in the first phase (Phase I) without the operator's knowledge (n = 252 colonoscopies) and in the second phase (Phase II) with the operator being aware of the monitoring (n = 121 colonoscopies). Other quality indicators (bowel preparation, cecal intubation) were also measured in the 2 phases.
Results: The study gathered 373 colonoscopies (206 men and 167 women), of which 252 in phase I and 121 in phase II. The mean Boston Bowel Preparation Scale was 7.71/9 with a slight improvement between the 2 phases: 7.696 in phase I vs. 7.74 in phase II. The mean cecal intubation rate was 96.1% without significant difference between the 2 phases. The mean WT was 9.21 ± 6.38 minutes [2–53], with improvement from 9.16 to 9.62 minutes between phases I and II (p = 0.539). The adjusted WT, after substracting polypectomy time, rises from 7.47 to 8.18 minutes (p = 0.141). There was no difference in ADR between the two phases: 26.7% (H: 29.1%, F: 24.1%) vs. 25.6% (H: 22.9%, F: 29.4%) (p = 0.815, IC 95% [0.5866; 1.6874]). However ADR seemed to be affected by WT in both phases: OR 23.41, p < 0.001 and OR 5.899, p = 0.015 in phases I and II respectively, with a tendency towards improvement of ADR in phase II.
Conclusion: Colonoscopy with an active monitoring system known to the endoscopist shows an improvement in WT, and seems to sharpen the inspection of the mucosa, demonstrated by the tendency to improvement in ADR and quality of bowel preparation. The implementation of a mandatory monitoring system with measurement of ADR and WT for each endoscopist could contribute in improving ADR and the overall quality of colonoscopy.
Disclosure: Nothing to disclose

P0157 LOWER GASTROINTESTINAL SYMPTOMS AND SYMPTOM-BASED TRIAGING SYSTEMS ARE POOR PREDICTORS OF CLINICAL SIGNIFICANT DISEASE ON COLONOSCOPY

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Introduction: Previous studies have shown lower gastrointestinal symptoms alone are a poor marker of clinically significant disease (CSD) on colonoscopy. At-risk triaging systems, such as the NICE guidelines, are recommended to help clinicians stratify patient referrals in order to prioritise those with potential CSD, in particular colorectal cancer (CRC) and inflammatory bowel disease (IBD) for early investigation.
Aims and Methods: We aimed to determine the prevalence of CSD and the diagnostic yield of symptoms in an Irish cohort and to determine the impact of applying at risk triaging protocols on patient selection and outcome.
Retrospective cohort study of sequential patients who underwent a colonoscopy for investigation of lower gastrointestinal symptoms as the primary indication over a 2-year period at our institution. Patients were identified from an endoscopy database, those with known IBD, previous CRC, a hereditary cancer syndrome or had a colonoscopy within the last 5 years, or without a clear indication were excluded. Basic demographics, symptoms, colonoscopy findings and subsequent histology were documented. CSD was defined as colorectal cancer, high-risk adenoma or inflammatory bowel disease including microscopic colitis. CSD rates were analysed by symptom and by NICE criteria, positive or negative. Odds ratios (OR) and p values were determined as appropriate and one-way anova used to compare groups.
Results: 1116 patients were identified, 493 (44%) males, mean age 54.3 (16–91), in all 287 (25%) were excluded. Colonoscopy indications were; chronic diarrhoea n = 188 (22%), PR bleeding n = 148 (18%), symptomatic anaemia n = 212 (26%), abdominal pain n = 108 (13%), alternating diarrhoea and constipation n = 79 (10%), chronic constipation n = 57 (7%), weight loss n = 37 (4%).
Overall prevalence of CSD was low 17%, (n = 141); colorectal cancer 20 (2.4%), high-risk adenoma 40 (5%), inflammation 75 (9%) [IBD 66 (8%), microscopic colitis 9 (1%)]. As expected, PR bleeding was positively associated with a diagnosis of CRC, OR 2.87 (95% CI 1.08 - 7.61) and HRA, OR 2.31 (95% CI 1.10-4.83), while chronic diarrhoea was associated with IBD, OR 2.5 (95% CI 1.50–4.20). The diagnostic yield of PR bleeding 18% (n = 27), and chronic diarrhoea 17% (n = 32), for CSD, were significantly higher than for other symptoms, symptomatic anaemia 11%, (n = 23), alternating diarrhoea and constipation 11% (n = 9), chronic constipation 7% (n = 4), weight loss 5% (n = 2) and abdominal pain 5% (n = 6), p = 0.016. In all 439 (53%) patients were NICE criteria (+) ive for CRC and 381 (46%) for IBD, 671 (81%) were positive for either criteria, while 217 (19%) fitted neither. Positive NICE criteria improved diagnostic yield for CRC and IBD, but overall detection rates remained low; 3% versus 0.9%, OR 7.7 (95% CI 1.77 to 33.56, p = 0.0064) for CRC and 9% versus 2.8% (OR 3.5, 95% CI [1.99–6.17] p < 0.0001) for IBD. The diagnostic yield for CSD overall for NICE positive patients was 18%, similar to the unselected cohort.
Conclusion: The prevalence of CSD in symptomatic patients is low (17%) and application of symptom-based triaging systems did not improve diagnostic yield. Our data suggests the routine addition of biomarkers into diagnostic algorithms for patients presenting with lower GI symptoms may be beneficial and warrants further investigation.
References: none
Disclosure: No conflict of interest

P0158 WARFARIN OR DIRECT ORAL ANTICOAGULANT; WHICH IS RISKY FOR POST-POLYPECTOMY BLEEDING?

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Introduction: Patients who undergo endoscopic resection of colorectal polyps under medication with anticoagulants, warfarin and direct oral anticoagulant (DOAC) for theirs cardiovascular/neurovascular conditions are increasing.
Aims and Methods: In this study, we investigated which has higher risk for post-polypectomy bleeding.

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		Univariate Odds ratio	p-value	Multivariate Odds ratio	p-value
Anticoagulant agents	DOAC	ref			
	Warfarin	2.4 (0.76–9.73)	0.17		
Heparin bridging	No	ref		ref	
	Yes	3.0 (1.15–8.87)	0.02	3.1 (1.14–8.28)	0.03
NSAIDs/Corticosteroid	No	ref		ref	
	Yes	5.0 (1.26–17.3)	0.01	8.6 (2.27–32.7)	0.002
Number of removed polyps	<3	ref		ref	
	≥3	2.7 (1.08–7.22)	0.03	2.9 (1.18–7.34)	0.02

286 patients receiving anticoagulant therapy underwent hot-snare polypectomy of colonic polyps at Kurashiki Central hospital between January 2012 and December 2017. 6 patients under treatment for concurrent gastrointestinal bleeding were excluded. In total, medical records of 280 patients (705 colorectal polyps) were retrospectively reviewed. DOAC (rivaroxaban, apixaban, edoxaban or dabigatran) was used in 83 patients and warfarin in 197 patients. Anticoagulants were discontinued according to the guideline of Japan Gastroenterological Endoscopy Society in 2012 when the cessation of anticoagulants was required. Delayed bleeding was defined as hematochezia requiring emergent colonoscopy within 4 weeks after polypectomy. Analyzed factors were; anticoagulants, antiplatelet agents, heparin bridging, comorbidities (diabetes mellitus, hypertension, hemodialysis, hyperlipidemia, liver cirrhosis), age, sex, number of removed polyps, and maximal size of polyps in each patient.

Results: Delayed bleeding occurred in 25 (8.9%) patients, who were all completely managed with endoscopic hemostasis. The incidence rate of post-polypectomy bleeding was 10.7% in patients with warfarin and 4.8% with DOAC; the difference did not reach statistical significance ($p = 0.17$). Patients with warfarin had more chance of heparin bridging than those with DOAC (62.4% vs. 14.5%). In 145 patients without heparin bridging, the bleeding rates were similar between the patients with warfarin (4.1% (3/74) and those with DOAC 5.6% (4/71). Multivariate analysis identified heparin bridging (odds ratio = 3.1; 95% confidential interval (CI), 1.1–8.3), non-steroidal anti-inflammatory drug or corticosteroid user (odds ratio = 8.6; 95% CI, 2.3–32.7), and resection of more than 3 polyps (odds ratio = 2.9; 95% CI, 1.2–7.3) as significant and independent risk factors associated with post-polypectomy bleeding. Thromboembolism occurred in 1 patient (0.4%) with heparin bridging. *[Risk factors associated with post-polypectomy bleeding]*

Conclusion: Warfarin and DOAC had similar risk for post-polypectomy bleeding, and heparin bridging was associated with an increased risk of post-polypectomy bleeding. Given that heparin bridging was more frequently performed in patients with warfarin, DOAC may be preferable in terms of post-polypectomy bleeding.

Disclosure: Nothing to disclose

P0159 SUPERIOR HIGH-QUALITY COLON CLEANSING WITH 1L NER1006 VERSUS SODIUM PICOSULFATE + MAGNESIUM CITRATE, 2L POLYETHYLENE GLYCOL + ASCORBATE, OR ORAL SULFATE SOLUTION: POST HOC POOLED ANALYSIS OF THREE RANDOMISED PHASE 3 CLINICAL TRIALS

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Introduction: High-quality colon cleansing is associated with improved lesion detection during colonoscopy (1-3). The cleansing efficacy and safety of NER1006, a novel 1L polyethylene glycol (PEG)-based bowel preparation, was evaluated in 3 randomised phase 3 trials DAYB[4], MORA[5], and NOCT[6].

Aims and Methods: For each trial, this post hoc analysis compared the level of high-quality segmental cleansing attained by NER1006 versus its comparator: Sodium Picosulfate + Mg Citrate (SPMC; DAYB), 2L PEG + Ascorbate (2LPEG; MORA) and Oral Sulfate Solution (OSS; NOCT). Dosing regimens varied by trial. All trials had treatment-blinded central reader-assessed cleansing scores and similar recruitment criteria. Alternative primary endpoints were overall and right colon cleansing using the validated Harefield Cleansing Scale (HCS)[7]. The number and share of high-quality segments (HCS score 3-4) attained by NER1006 versus its comparator were analysed in 3 primary analysis populations: The full analysis set (FAS; all randomised patients), the modified FAS (mFAS; FAS excluding any patient who failed lab screening after randomisation and who also did not take their study treatment), and the Per-protocol set (PP; FAS with fulfilled entry criteria, who took ≥75% of both study preparation doses, had data for at least 1 of the primary endpoints, and no major protocol deviations).

Results: A total of 1,985 patients were included in this analysis (Table 1). In each of the 3 primary analysis populations (FAS, mFAS, PP), day before dosing with NER1006 attained significantly more high-quality segments than with SPMC (16.9% vs. 10.4%; $p < 0.001$, 17.4% vs. 10.7%; $p < 0.001$, 18.4% vs. 10.7%; $p < 0.001$). Overnight split dosing with NER1006 showed more high-quality segments than with 2LPEG (46.1% vs. 29.0%; $p < 0.001$, 47.5% vs. 30.2%; $p < 0.001$, 48.7% vs. 32.5%; $p < 0.001$). Morning only dosing with NER1006 AM/AM also achieved more high-quality segments than overnight split dosing with 2LPEG PM/AM (46.8% vs. 29.0%; $p < 0.001$, 48.1% vs. 30.2%; $p < 0.001$, 50.6% vs. 32.5%; $p < 0.001$). Finally, overnight split dosing with NER1006 PM/AM delivered more high-quality segments than with OSS (40.1% vs. 36.2%; $p = 0.013$, 45.0% vs. 40.2%; $p = 0.005$, 48.8% vs. 44.0%; $p = 0.011$). No serious adverse events were reported in the entire population in this post hoc pooled analysis.

[Table 1. Colon segments with Harefield Cleansing Scale score 3-4 (high-quality), per treatment, in three central reader-assessed phase 3 trials]

Conclusion: NER1006 delivered more colon segments with high-quality cleansing scores than SP+MC, 2LPEG+Asc, or OSS. NER1006 is the first bowel preparation to demonstrate a superior high-quality colon segment cleansing efficacy versus these 3 current alternatives through adequately powered randomized controlled trials. The encouraging high cleansing efficacy of NER1006 AM/AM may help patients reduce their total bowel preparation time.

Disclosure: AR: NER1006 phase 3 trial investigator. No other conflicts of interest. BA: Employee of Norgine, PU: NER1006 phase 3 trial investigator. No other conflicts of interest. SS: NER1006 phase 3 trial investigator. No other conflicts of interest.

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P0160 R0 RESECTION MARGIN, A NEW QUALITY MEASURE IN ERA OF NATIONAL BOWEL SCREENING?

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Introduction: Colorectal cancer is the second most commonly diagnosed cancer in Ireland. (1) Incomplete polypectomy is common among Endoscopists.(2) NCCS (National Colon Cancer Screening) colonoscopies are offered to bowel cancer screening patients after a positive Faecal Immunochemical Testing (FIT). These anecdotally have larger polyps.The goal of polypectomy is to achieve an R0 margin meaning that the margin is free from abnormal tissue.

Aims and Methods: To determine whether there is an association of R0 resection margin with Endoscopist, histopathologist, size, location and technique of polypectomy in an NCCS cohort. It was a retrospective observational study on NCCS colonoscopies between October 2013 and June 2017. All these procedures were conducted in a single centre at Louth county hospital (LCH). SPSS software was used for statistical analysis. Statistical significance was set a priori at $p < 0.05$.

Results: In this ongoing study a total 542 colonoscopies were performed with no polyps in 19%. Here we present a subanalysis of 186 colonoscopies on which 707 polyps were identified. The average age was 66 years (SD 2.8) with 190 (27%) females. The polyp distribution was 255 (36%), 85(12%) and 365 (52%) in right, transverse and left colon respectively. Most of the polyps were less than 5 mm (59%) with 11.5% more than a cm in size. 152 (27%) had an R0 margin histologically, and 30 (5%) had involvement of the margin. In 373 (67%) polyps pathologist were unable to assess the margin and (3%) polyps were not retrieved. Polypectomy technique in the form of hot snare had a direct relation with R0

Abstract No: P0159

	DAYB		MORA			NOCT	
Phase 3 trial	**NER1006**	**Sodium Picosulfate+ Mg Citrate**	**NER1006**	**NER1006**	**2L PEG+ Ascorbate**	**NER1006**	**Oral Sulfate Solution**
Split dosing regimen	PM/PM	AM/PM	PM/AM	AM/AM	PM/PM	PM/AM	PM/AM
FAS: Patients, N	258	257	283	283	283	310	311
FAS: High-quality segments, n (%) [P vs. comparator]	218/1290 (16.9) [p < 0.001]	134/1285 (10.4)	653/1415 (46.1) [p < 0.001]	662/1415 (46.8) [p < 0.001]	411/1415 (29.0)	621/1550 (40.1) [p = 0.013]	563/1555 (36.2)
mFAS: patients, N	250	251	275	275	272	276	280
mFAS: High-quality segments, n (%) [P vs. comparator]	218/1250 (17.4) [p < 0.001]	134/1255 (10.7)	653/1375 (47.5) [p < 0.001]	662/1375 (48.1) [p < 0.001]	411/1360 (30.2)	621/1380 (45.0) [p = 0.005]	563/1400 (40.2)
Per-Protocol: Patients, N	172	207	220	218	232	233	239
Per-Protocol: High-quality segments, n (%) [P vs. comparator]	158/860 (18.4) [p < 0.001]	111/1035 (10.7)	536/1100 (48.7) [p < 0.001]	552/1090 (50.6) [p < 0.001]	377/1160 (32.5)	568/1165 (48.8) [p = 0.011]	526/1195 (44.0)

FAS, Full Analysis Set. mFAS, modified Full Analysis Set (FAS excluding patients who failed lab screening after randomisation and who also failed to take their study treatment). Per-Protocol (FAS with fulfilled entry criteria, who took ≥75% of both study preparation doses, had data for at least one of the primary endpoints, and no major protocol deviations).

margin ($p<0.003$) with an inverse relation of Endoscopic mucosal resection (EMR, $p<0.004$). Accessibility of margins also had a linear relation with the size of the polyp, resection technique, statistically significant difference between hot snare and biopsy to cold biopsy and snare ($p<0.02$) and the reporting pathologist. Achieving an R0 margin was not statistically significant with endoscopist (our experienced endoscopist on average do more than 300 colonoscopies per year), size and location of the polyp.

Conclusion: Only 25% of the polyps retrieved achieved an R0 margin while in 71% cases pathologist were unable to assess the margin. A multidisciplinary approach has to be developed between the endoscopist and pathologist for achieving R0 margin. Polypectomy requires significant focused training and experience to maximize success. In future, this could be included as a key performance indicator for polypectomy.We also recommend more studies on margin analysis.

Disclosure: Nothing to disclose

Reference

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P0161 COMPARING THE EFFICACY AND SAFETY BETWEEN UNDERWATER ENDOSCOPIC MUCOSAL RESECTION AND CONVENTIONAL ENDOSCOPIC MUCOSAL RESECTION IN RESECTING SESSILE COLORECTAL NEOPLASMS: A PROPENSITY SCORE-MATCHED COHORT STUDY

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Introduction: Endoscopic resection of colorectal polyps has been shown to reduce colorectal cancer related death1. For sessile colorectal polyps, endoscopic mucosal resection (EMR) is an established method for the removal2. However, recurrence after EMR is a major limitation. Piecemeal resection and intraprocedural bleeding are reported to be risk factors of recurrence after EMR3,4. Underwater EMR (UEMR) was proposed as an alternative method for removal of colorectal polyps5. There is no large-scale dataset directly comparing the efficacy and safety of UEMR with conventional EMR in resecting average sized lesions.

Aims and Methods: The aim of our study is to compare efficacy and safety of UEMR with conventional EMR in average sized colorectal sessile polyps using a large retrospective cohort with propensity score matched design.

A retrospective observational study was conducted on all adult patients referred to us for endoscopic resection of sessile colorectal polyps between August 2012 and November 2017. During this period, conventional EMR was performed until August 2015, when UEMR was introduced to our hospital, and UEMR was performed for all lesions after August 2015. Follow-up of the patients was by a clinic visit around 7–14 days after the procedure to monitor adverse events. Surveillance colonoscopy was scheduled according to MSTF guidelines. The outcome measurements included en bloc resection rate, procedure time, bleeding, and muscle layer injury. We match and compensate the baseline differences in both groups in a 1:1 ratio by calculating propensity scores using a multivariable regression model.

Results: 462 lesions in 407 consecutive patients were treated. In the first study period between August 2012 and August 2015, all of the 256 lesions in 224 patients were resected by conventional EMR. In the second study period between August 2015 and November 2017, all of the 206 lesions in 183 patients were resected by underwater EMR.

The propensity score matching created 170 matched pairs (totally 340 patients). The mean age is 64 years old. The mean tumor size is 14.6mm, 73% of the resected lesions are less than 20mm. 28% of the lesions has been biopsied or resected before.

There is no difference between the en bloc resection rate of UEMR (89%) and conventional EMR (87%). The mean resection time in UEMR group (8mins) is significantly shorter than conventional EMR (10mins).

The risk of intraprocedural bleeding is lower in UEMR (4.1% versus 18.2%) while the risk of delayed bleeding is low in both groups (0.6%–1.2%). The risk of muscle layer injury is also low in both groups (1.2%).

Conclusion: Our study is the largest study comparing UEMR with conventional EMR. We confirmed that UEMR could be an alternative to conventional EMR in resecting sessile colorectal polyps. It has similar en bloc resection rate, shorter procedure time, and causes less intraprocedural bleeding than conventional EMR. The risk of muscle layer injury is similar to conventional EMR and cannot be ignored. Further investigations are required to compare the long-term outcome between both procedures.

Disclosure: Nothing to disclose

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P0162 INCREASED WITHDRAWAL TIME ALONE MAY NOT IMPROVE ADENOMA DETECTION RATE: A MULTI-CENTRE STUDY ON IMPACT OF INDIVIDUAL QUALITY SCORECARDS

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Introduction: Adenoma detection rate (ADR) is a key indicator of colonoscopy quality. Previous studies have shown that performance feedback can improve ADR, but these were mostly based in the West and lack examination of factors associated with response.

Aims and Methods: The aim of this study is to compare individual ADR before and after implementation of scorecard, and determine patient and procedure factors associated with response in a multi-centre study in Singapore.

We documented patient factors (age, gender), procedure factors (bowel preparation, withdrawal time, indication) and histology findings for all colonoscopies performed in March 2014-August 2017 at Gastroenterology and Surgical units of 2 hospitals. After 1 year of baseline data collection, endoscopists were informed of colonoscopy quality tracking at unit briefings. After an adjustment period, we issued 6-monthly scorecards confidentially (intervention). They reported individual withdrawal time (WT), completion rate, complication rate, polyp/adenoma detection rate, average Boston Bowel Preparation Score (BBPS), adenoma count per colonoscopy (APC), as well as unit averages and percentiles. Endoscopists with >25 scopes in each 6-monthly period were included in analysis. Regression models were used to derive patient age, sex and indication adjusted ADR, proximal ADR, APC and largest polyp size in all complete colonoscopies with at least fair bowel preparation (BBPS>4). A benchmark for overall ADR of 25% was adopted. Those below this benchmark at baseline but showed significant increase in ADR after intervention were identified as responders. t test and chi-square test were used to compare patient and procedure factors between responders and non-responders.

Results: 33 endoscopists who performed 21760 scopes met the inclusion criteria. Overall adjusted baseline ADR was 27.3%($\pm$1.3%) and increased to 31.8%($\pm$0.9%) after intervention ($p<0.01$). At baseline, 12 endoscopists had ADR$<$ 25%. Their ADR increased from 17.0%($\pm$2.0%) to 27.3%($\pm$1.3%) after intervention ($p<0.01$), with highest ADR in the 6 months immediately after intervention. APC, proximal ADR, proportion of cases with largest polyp<5mm also increased after intervention (0.25 to 0.50, 8.8% to 16.3%, 14.7% to 22.8% respectively, all $p>0.01$). 6 responders and 6 non-responders were identified. Responders had higher mean patient age (60.0 vs. 56.9 years, $p<0.01$), performed more scopes with BBPS$\geq$5 (94.9% vs. 92.0%, $p<0.01$) and more screening scopes (33.4% vs. 25.3%, $p<0.01$) than non-responders. Non-responders had shorter WT, but this difference was not significant after intervention (8.35min vs. 8.39min, $p=0.83$).

Conclusion: Quality scorecards were successful in improving ADR in a multi-centre study in Asia. Response to feedback is multi-factorial. Increased WT alone without improving other modifiable factors may not result in improved ADR after feedback.

Disclosure: Nothing to disclose

P0163 USEFULNESS OF JNET CLASSIFICATION WITH DUAL-FOCUS MAGNIFICATION FOR DIAGNOSIS OF COLORECTAL TUMORS: SINGLE CENTER RETROSPECTIVE STUDY

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Introduction: Narrow-band imaging (NBI) magnifying endoscopy has been reported to be useful for qualitative and quantitative diagnosis of colorectal lesions. Recently, Japan NBI Expert Team (JNET) classification was advocated which is the first universal narrow-band imaging magnifying endoscopic classification of colorectal tumors. However, magnifying endoscopy requires high experience and skill. On the other hand, dual-focus NBI with electronic zoom (DF-NBI) can easily provide almost the same image of optical zoom magnifying images only by button push.

Aims and Methods: The aim of study is to clarify the usefulness of JNET classification with DF-NBI for colorectal tumors. We analyzed consecutive 290 colorectal lesions, which were diagnosed by JNET classification with DF-NBI observation before endoscopic treatment or surgery between April 2017 and

March 2018. The instrument used in this study was a dual focus endoscope (CF-HQ290L/I; Olympus Medical Systems). The resected lesions were pathologically diagnosed in accordance with the criteria of the World Health Organization. Using these cases, we examined the relationship between each type of the JNET classification with DF-NBI and histopathologic findings. We calculated sensitivity, specificity, positive and negative predictive value (PPV and NPV), and accuracy for each category of the classification.
The JNET classification; the colorectal NBI magnifying classification consists of 4 types that are classified based on vessel pattern and surface pattern. The characteristics of Type 1 are invisible vessel pattern and having regular dark or white spots as surface pattern. The characteristics of Type 2A are regular vessel pattern, such as regular caliber or distribution, and regular surface pattern. The characteristics of Type 2B are irregular vessel pattern, such as variable caliber, irregular distribution, and irregular or obscure surface pattern. The characteristics of Type 3 are loose vessel areas or interruption of thick vessels and amorphous surface pattern. Indicators of types; Type 1 as hyperplastic polyp (HP) or sessile serrated polyp (SSP), Type 2A as low-grade dysplasia (LGD), Type 2B as high-grade dysplasia (HGD) or superficial submucosal invasive cancer (SM-s), and Type 3 as deep submucosal invasive cancer (SM-d).
Results: I. Final diagnosis: 38 Type 1 (26 HPs, 8 SSPs and 4 LGD), 229 Type 2A (8 HPs, 216 LGD, 4 HGD and 1 SM-d), 8 Type 2B (2 LGD, 5 HGD and 1 SM-s), and 2 Type 3 (2 SM-d).
II. Diagnostic ability: The respective sensitivities, specificities, PPV, NPV, and accuracies were as follows: Type 1, 81.0%, 98.3%, 89.5%, 96.7%, and 95.7%; Type 2A, 95.2%, 80.4%, 96.1%, 77.1%, and 92.8%; Type 2B, 60.0%, 99.3%, 75.0%, 98.5%, and 97.8%; and Type 3, 66.7%, 100%, 100%, 99.3%, and 99.6%.
Conclusion: Our results suggest that JNET classification with DF-NBI is not only convenience but also have sufficient diagnostic ability. However, the sensitivities of JNET Type 2B and Type 3 were lower than that of Type 1 and Type 2A. Therefore, JNET Type 2B and Type 3 need to be examined by increasing the number of cases. Further investigation comparing DF-NBI and conventional magnifying NBI is needed in the near future.
Disclosure: Nothing to disclose

P0164 EFFECTIVENESS OF SUBMUCOSAL EPINEPHRINE INJECTION FOR LARGE COLON POLYP EMR

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Introduction: Currently, the use of endoscopic submucosal dissection is more widespread than Endoscopic Mucosal Resection (EMR) as a treatment for large colon polyps in Japan. However, the effectiveness and simplicity of EMR has never changed and it is still a key treatment for type 0-Ip and 0-Isp polyps. Although the intra-procedural bleeding rate is not high, reaching hemostasis once bleeding occurs requires time. A detachable snare, often used for type 0-Ip polyps, is effective in reducing intra-procedural bleeding. For short pedicle or large 0-Isp polyps, an effective prevention for intra-procedural bleeding after large colon EMR is desired. A 1:20000 epinephrine submucosal injection has been used for colonic diverticular bleeding, and is effective and safe for even massive diverticular bleeding.
Aims and Methods: The aim of this study was to reveal the risk factor of intra-procedural bleeding and to evaluate the effectiveness of submucosal 1:20000 epinephrine injection in large colon polyp EMR.
Between January 2015 and February 2018, patients with 0-Is, 0-Isp, or 0-Ip polyps over 2 cm treated by EMR or polypectomy were enrolled. Age, sex, polyp size, location, Paris classification,use of anti-thrombotic agents, intra-procedural bleeding, post polypectomy bleeding were evaluated retrospectively. Intra-procedural bleeding was defined as spurting bleeding or arterial pumping occurring during the procedure. Bleeding within 14 days after the procedure was defined as post-polypectomy bleeding.
Results: A total of 117 patients of over 2cm colon polyp were treated by EMR or polypectomy.
1:20000 epinephrine submucosal injection was used in 11 patients. Mean size of polyp was 22mm ± 3mm (range: 20–40mm), over 25mm polyp were 20% 24/117). Pathological diagnosis of polyp was adenoma, 46 (39%): mucosal cancer, 41 (35%): submucosal cancer, 7 (6%): others, 21 (18%). Paris classification was 0-Is, 6 (5%): 0-Isp, 33 (28%): 0-Ip, 60 (51%): 0-IIcnt;) were treated by polypectomy with detachable snare, 86 cases (73%) were treated by EMR, 15 cases (12%) were treated by EMR with detachable snare. Only 3 (3%) post polypectomy bleeding occurred in EMR cases.
Intra-procedural bleeding was occurred in 10 cases. Despite no intra-procedural bleeding occuring in the sub mucosal epinephrine injection group, there was no significant different compared conventional serum saline injection with epinephrine injection ($p = 0.286$). Detachable snare was effective to prevent intra-procedural bleeding ($p = 0.047$).Polyp size over 25mm was a risk factor of intra-procedural bleeding ($p = 0.015$).
Conclusion: 1:20000 epinephrine injection should be performed for over 25mm colon polyp to prevent intra-procedural bleeding after EMR without detachable snare.
[Comparison non-bleeding group with intra-procedural bleeding]
Disclosure: Nothing to disclose

P0165 THE EFFECT OF PROPHYLACTIC CLIP PLACEMENT ON DELAYED BLEEDING FOLLOWING ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL LESIONS: A META-ANALYSIS

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Introduction: The main aim of this study was to conduct a meta-analysis on the effect of clipping on DPB following endoscopic mucosal resection (EMR) of colorectal lesions ≥ 20 mm.
Aims and Methods: The main aim of this study was to conduct a meta-analysis on the effect of clipping on DPB following endoscopic mucosal resection (EMR) of colorectal lesions ≥ 20 mm. We performed a search of PubMed and the Cochrane library for studies comparing the effect of clipping vs. no clipping on DPB following endoscopic resection. The Cochran Q test and I^2 were used to test for heterogeneity. Pooling was conducted using a random-effects model.
Results: 13 studies with a total of 7794 polyps were included. Overall, when lesions of all sizes and types of endoscopic resection (conventional polypectomy, EMR or endoscopic submucosal dissection [ESD]) were included, DPB was observed less frequently with clipping (1.3%) as compared to no clipping (2.7%) (pooled OR 0.50, 95% CI: 0.25–0.91, $p = 0.02$). In the subgroup analyses, clipping was also associated with a decrease in the rate of DPB after (1) resection of lesions ≥20 mm (pooled OR: 0.33; 95% CI: 0.18–0.62; $p < 0.001$) and for lesions ≥20 mm removed by EMR (pooled OR 0.24, 95% CI: 0.12–0.50, $p < 0.001$).
Conclusion: Prophylactic clipping may reduce DPB following EMR of large colorectal lesions. Future trials are needed to further identify risk factors and stratify high risk cases in order to implement a cost-effective preventive strategy.
Disclosure: Nothing to disclose

P0166 PROPER INTERVAL TO SECOND COLONOSCOPY AFTER PREPARATION FAILURE IN THE FIRST PROCEDURE - PROSPECTIVE RANDOMIZED TRIAL

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Introduction: We investigated the outcome of a second colonoscopy after preparation-associated failure of the first colonoscopy and determine the proper timing of a second colonoscopy.
Aims and Methods: Patients who failed in their first colonoscopy due to poor bowel preparation were randomly allocated to 2 groups: next day repeated colonoscopy with sodium phosphate (NaP) 45mL group (Next day group) vs after 7 days repeated colonoscopy with polyethylene glycol (PEG) 4L (After 7 days group). Age, sex, past medical history, current medication, bowel habit, reason for colonoscopy were compared between the 2 groups. The quality of bowel preparation was assessed using Ottawa scale. Bowel preparation scale, colonoscopic findings and polyp detection rate were compared between the 2 groups.
Results: A total of 101 patients with unacceptable colonic preparation were enrolled. 51 patients were included in Next day group and 50 patients in After 7 days group. Next day group showed the better quality of bowel preparation than After 7 days group (4.75 ± 2.45 vs. 5.52 ± 2.24, $p = 0.003$). There was no

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	Non-Bleeding group (n = 107)	Intra-procedural group (n = 10)	P-value
Anti-thrombotic agents, n(%)	11 (10%)	2 (20%)	0.34
Location (C/A/T/D/S/R)	7/22/6/6/53/13	1/3/2/1/3/0	*
0-Is/0-Isp/0-Ip/0-IIa/others	5/30/56/15/1	1/3/4/2/0	*
EMR without detachable snare, n(%)	76 (71%)	10 (10%)	0.047
Epinephrine injection, n(%)	11 (10%)	0 (0%)	0.286
Polyp size over 25mm, n(%)	19 (17%)	5 (50%)	0.015

significant difference in age, sex, current medication, reason for colonoscopy, colonoscopic findings and polyp detection rate between the 2 groups. Constipation and past history of abdominal surgery was found to be predictive of a failed repeated preparation (Odd ratio = 1.54, 95% CI (1.14–2.07), p = 0.004).
Conclusion: Second colonoscopy on next day with NaP 45 mL was more effective than after 7 days with PEG 4L in colonic preparation failure.
Constipation and past history of abdominal surgery were significant risk factors of repeated preparation failure.
Disclosure: Nothing to disclose

P0167 1L NER1006 ACHIEVES HIGH-QUALITY BOWEL CLEANSING WITH LOWER TOTAL FLUID VOLUME INTAKE THAN STANDARD 2L POLYETHYLENE GLYCOL + ASCORBATE: A POST-HOC ANALYSIS

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Introduction: Successful bowel cleansing is required for effective colonoscopy. Polyethylene glycol (PEG)-based bowel preparations are widely used for this, despite many still requiring high fluid volume intake. To enhance the patient experience, the phase 2 study OPT[1] assessed the clinical proof of concept of NER1006, a novel 1L PEG-based bowel preparation, versus standard 2L PEG + ascorbate (2LPEG). Here we report the cumulative segmental cleansing score versus total fluid intake for NER1006 and the Control.
Aims and Methods: The OPT study had 2 parts and evaluated 5 different low volume PEGs vs the control. This post-hoc analysis assessed the lead phase 3 candidate, NER1006, from Part 2 of the study vs the Control. Treatment-blinded colonoscopists assessed the bowel cleansing quality using the Harefield Cleansing Scale (HCS). For each patient, the sum of observed segmental cleansing scores (0–4) for each of the 5 segments (cumulative maximum total = 20), and the total fluid volume intake (i.e. preparation volume + mandatory additional clear fluid volume + voluntary ad libitum clear fluid volume) were assessed. The number and share of patients who attained high-quality cleansing (segmental HCS scores 3 or 4) in all segments (cumulative HCS score of 15 or higher) were calculated.
Results: 60 patients underwent screening colonoscopy (Table 1). They were either 40 to 70 years old with a known personal or familial risk of contracting colorectal cancer, or 55 to 70 years old. 30 patients per group had their bowels prepared with overnight split dosing regimens of either NER1006 or 2L PEG. Among patients on NER1006, 29/30 (97%) achieved cumulative segmental scores of 15 or higher versus 11/30 (37%) on the 2L PEG. Beyond the total required minimum of 2L, total fluid volume intake seemed independent of the cleansing quality. 2L PEG showed larger cleansing variability. At an average of 3004 ± 718 mL (SD) for the NER1006 group the total fluid volume intake was significantly lower than for the 2LPEG group (3667 ± 530 mL; p < 0.001). Half of the patients (15/30) taking NER1006 chose to drink under 3L in total but still achieved a very high level of cleansing.

	NER1006		2LPEG	
Sample Size, n	30		30	
Dose intake start time	5–6pm	7–8am	5–6pm	7–8am
Preparation	500	500	1000	1000
Required additional fluid	500	500	500	500
Required fluid Total	2000		3000	
Total fluid volume intake ml, mean [SD]	3004 [718]		3667 [530]	
P-value	[p < 0.001]			
Patients with a cumulative segmental HCS score ≥15, n (%)	29/30 (96.7)		11/30 (36.7)	

[Table 1. Split dosing regimens, mean total volume intake and cumulative HCS scores]

Conclusion: Overnight split dosing with NER1006 can achieve a clinically useful bowel cleansing with a low total volume intake. NER1006 achieved its cleansing success mostly at the high quality level and at a significantly lower total fluid intake than standard 2L PEG + ascorbate.

Disclosure: Lucy Clayton and Bharat Amlani, employees of Norgine Ltd. Cesare Hassan was an investigator in the DAYB study and received honoraria from Norgine Ltd or investigator advisory board attendance.

P0168 ENDOSCOPIC FEATURE OF DEPRESSED TYPE COLORECTAL NEOPLASMS IN MAGNIFYING ENDOSCOPY AND ENDOCYTOSCOPY-

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Introduction: Colorectal cancers are generally recognized to develop from polyps. This adenoma-carcinoma sequence theory has been in the mainstream of development of colorectal cancers. However, recently the existence of many depressed-type cancers has been revealed, which are considered to emerge directly from normal epithelium, not through the adenomatous stage. This theory is called de novo pathway.
Now, it is possible to presume the histology of colorectal lesions using magnifying endoscopy (pit pattern classification) and endocytoscopy (EC classification). We can observe not only the structural atypia but also the cellular atypia *in vivo*.
Aims and Methods: The aim is to clarify the endoscopic characteristics of depressed-type colorectal neoplasms, demonstrating the validity of pit pattern and EC classification.
A total of 30021 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our unit from April 2001 to May 2017. Of these, 22958 lesions were low-grade dysplasia, 5913 were high-grade dysplasia and 1150 were submucosally invasive (T1) carcinomas. According to the developmental morphology classification, they were divided into 3 types: depressed, flat and protruded-type. We investigated the rate of T1 carcinomas and the characteristics of depressed-type neoplasms concerning pit pattern and EC classification.
Results: The rate of T1 carcinomas in depressed-type lesions reached to 62.1%, meanwhile that in flat-type and protruded-type lesions was 3.4% and 2.9%, respectively. Within less than 5mm in diameter, that was 10.4%, 0% and 0%, respectively. Most of the flat-type (91.9%) and protruded-type (94.3%) lesions showed type IIIL or IV pit pattern corresponding to adenomas, whereas 91.7% of the depressed-type lesions were characterized by type IIIS, VI or VN pit patterns corresponding to carcinomas. As for endocytoscopy, most of the flat- and protruded-type lesions showed EC2 corresponding to adenomas. In contrast, the depressed-type lesions were observed as EC3a (39.0%) and EC3b (53.5%) corresponding to invasive carcinomas.
Conclusion: This study revealed the diagnostic characteristics of depressed-type lesions. They show typically typeIIIS,VI or VN pit patterns in magnifying endoscopy and type EC3a or EC3b in endocytoscopy. These lesions tend to invade the submucosal layer even when they are small. I-t is important to diagnose colorectal neoplasms according to their morphology.
Disclosure: Nothing to disclose

P0169 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (CR-ESD): THE PATHOLOGICAL POINT OF VIEW. DOES THE RISK OUTWEIGH THE BENEFITS? A SPANISH PROSPECTIVE MULTICENTRE STUDY

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Introduction: One of the main benefits associated with CR-ESD is to achieve an oncological curative resection in tumours with superficial submucosal invasive carcinoma (SSIC) and no other risk factors for lymph node metastasis. However, ESD has a higher complication rate than EMR. In addition, at least theoretically, the oncological outcomes for non-invasive CR lesions (Vienna classification ≤ 4) removed by EMR should not be worse than those achieved with ESD.

Aims and Methods: To assess the prevalence of SSIC on colorectal lesions removed by ESD, and to evaluate the complication rate for these procedures. We recorded prospectively, in an intention-to-treat basis, the lesions selected for ESD and performed by members of the ESD interest group (a division of the SEED Endoscopic Resection Working Group) of the Spanish Society of Digestive Endoscopy (SEED). Delayed bleeding, immediate and delayed perforation were defined as complications.

Results: We prospectively included 393 lesions in 392 consecutive patients with CR neoplasms scheduled for ESD from January 2016 to January 2018 in 15 centres. Case volume was over 40 ESDs in 4 hospitals. Median size of the tumours was 35 mm (range 5 - 20). Median duration of the procedures was 104 min (range: 10 - 375). The duration of the procedures was significantly correlated with size ($R^2 = 0.17$; $p < 0.0001$). The morphology of the polyps was 64 LST-G homogeneous type (16%), 120 LST-G mixed type (31%), 127 LST-NG FE type (32%), 31 LST-NG PD type (8%) and other morphologies for the remaining (13%). The location of the tumours was as follows: rectum n = 111 (28.2%); sigmoid n = 37 (9.4%); descending colon n = 28 (7.1%); splenic flexure n = 9 (2.3%); transverse colon n = 38 (9.7%); hepatic flexure n = 33 (8.4%); ascending colon n = 75 (19.1%) and cecum n = 62 (15.8%). 25 cases had received previous endoscopic treatment (6.3%). The *en bloc* resection rate was 80.4% (n = 316). There were 17 (4.3%) aborted procedures. Most of them as a result of technical difficulty although in 2 cases an intraprocedural perforation occurred (only 1 of them requiring surgery). The R0 resection rate was 72%. The final pathological report showed: Vienna 1; n = 14 (4%); Vienna 2; n = 2 (1%); Vienna 3; n = 196 (50%); Vienna 4; n = 130 (33%) and Vienna 5; n = 16 (4%). 1 of the lesions was a neuroendocrine tumor (1%) and the pathology for another 17 (4%) are pending. Regarding the Vienna 5 cases, a curative resection (R0, SSIC, G1/G2, ly -, v-) was achieved in 8 tumours (2%). Deep submucosal invasion was observed in 5 cases (1.3%). Additionally, 2 cases showed G3 (0.7%) and the invasion depth could not be assessed in another 1 case (0.2%). Regarding complications, a delayed bleeding occurred in 19 patients (5%). There were 54 intraprocedural perforations (13.7%), 8 delayed perforations (2%) and 1 case developed both (0.2%). Surgery was needed in 10 cases: 8 perforations (2%) and 2 hemorrhages (0.7%).

Conclusion: The frequency of SSIC without risk factors for lymph node metastasis is low (2%) in our Western multicentre ESD series. Most of the procedures were performed for lesions not capable to develop metastatic disease. 1 every 2 ESDs was performed for mucosal low-grade neoplasms. The complication rate was 21%. The clinical benefit of ESD, in terms of avoiding surgery, might be controversial when only the pathological results are considered.

Disclosure: Nothing to disclose

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P0170 IMPACT OF A LOW FIBER DIET ON BOWEL CLEANSING QUALITY BEFORE COLONOSCOPY: PRELIMINARY DATA FROM A RANDOMIZED STUDY COMPARING 1 DAY VERSUS 3 DAYS

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Introduction: Inadequate bowel cleansing is a major burden for endoscopy units. Although, a low fiber diet (LFD) is usually recommended before colonoscopy, there is no evidence regarding the number of days required to achieve a proper bowel cleansing.

Aims and Methods: The purpose of the study was to assess the quality of bowel cleansing comparing a 3-day LFD-based regimen with 1-day LFD-based regimen. Consecutive patients scheduled for outpatient colonoscopy in a tertiary care Hospital were included between December 2017 and February 2018. Patients with past poor bowel preparation and not willing to participate in the study were excluded. Patients were randomized to: 1-day LFD (Group 1) or 3-day LFD (Group 2). All patients received 2-L split-dose polyethylene-glycol (PEG) plus ascorbic acid before colonoscopy. A structure LFD was designed by an endocrinologist. Compliance was assessed using a validated questionnaire and a personal food intake record. Cleansing was considered to be adequate if the Boston Bowel Preparation Scale (BBPS) scored ≥ 2 points at each colonic segment. The analysis was carried out by intention-to-treat (ITT) and *per*-protocol (PP). A superiority analysis was performed to demonstrate that colon cleansing after a 3-day LFD regimen was superior to 1-day LFD with a margin of 10%. Assuming a type I error of 5%, a power of 80% and considering a dropout rate of 15%, a total of 202 participants *per* group were required.

Results: 287 patients (60 ± 14.5 years, 51% males) were included from December 2017 to February 2018, 143 in group 1 and 144 in group 2. No differences were found between the 2 groups with respect to demographic variables, comorbidity, received treatments, change in bowel habits, indication for colonoscopy, compliance with the diet or cleansing solution and polyp/adenoma detection rates. Cleansing quality (BBPS scale ≥ 2 points at each colonic segment) was not significantly different between groups in ITT analysis (82.6% vs. 88.2%, $p = 0.17$; Odds Ratio (OR) 1.6, 95% confidence interval (CI) [0.81–3.08]) or in PP analysis (83.8% vs. 90.4%, $p = 0.10$; OR 1.8, 95% CI [0.88–3.79)]. However, there was a significant difference in favour of the 3-day LFD either in ITT analysis (86.7% vs. 93.8%; $p = 0.04$) or PP analysis (86.8% vs. 94.1%; $p = 0.04$) in the quality of the left colon.

Conclusion: Preliminary analysis suggests that the number of days following a LFD before colonoscopy does not significantly affect the total quality of bowel cleansing but the 3-day LFD regimen may improve cleansing quality in the left colon. (NCT03247452)

Disclosure: Nothing to disclose

P0171 PERIOPERATIVE HEPARIN BRIDGING FOR ENDOSCOPIC RESECTION OF THE COLORECTAL TUMOR FOR PATIENTS RECEIVING ANTICOAGULATION RESULTED IN A HIGHER INCIDENCE OF BLEEDING COMPLICATION THAN OTHER HIGH-RISK ENDOSCOPIC PROCEDURES

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Introduction: In the ESGE and Japanese guidelines, perioperative heparin bridging is recommended for high thrombotic risk patients who are receiving anticoagulation and require high-risk endoscopic procedures.

Aims and Methods: We retrospectively investigated clinical outcomes of patients with atrial fibrillation who had been applied perioperative bridging anticoagulation by intravenous unfractionated heparin for high-risk endoscopic procedures from April 2006 to June 2015. The heparin bridging method was as follows. (1) Warfarin was discontinued 5 days before the procedure and intravenous unfractionated heparin was started with 5000 unit bolus followed by 500 unit per kilogram of body weight per day continuous intravenous injection. (2) Activated partial thromboplastin time (APTT) was evaluated to adjust the dose of heparin to raise APTT 45 to 70 seconds. (3) Heparin was discontinued 4–6 hours before the endoscopic procedure and resumed from the next morning. (4) Warfarin was also resumed along with heparin with a loading dose of 5mg for 3 days followed by a preoperative dose of the patient. (5) Heparin was discontinued when INR reached 1.6 or higher. The primary outcomes were arterial thromboembolic events within 30 days of the endoscopic procedures, and postoperative bleeding events that needed endoscopic hemostasis or blood transfusion.

Results: During the study period, 76 cases received high-risk endoscopic procedures. Among them, 2 cases refused heparin bridging, thus we assessed 74 (19 females) cases with a mean age of 73.8 years old in the study. The endoscopic procedures were colorectal EMR or ESD (29 cases), gastric ESD (23 cases), endoscopic sphincterotomy (15 cases), esophageal ESD (5 cases), and duodenal EMR (2 cases). There was no arterial thromboembolic event within 30 days of the procedures, however, 19 cases (25.7%) experienced postoperative bleeding complications. The bleeding incidence was very high with colorectal EMR/ESD, 15 out of 29 cases (51.7%). It was significantly higher than any of other high-risk procedures. Between the bleeding group and non-bleeding group, there was no significant difference in the maximum size of the colorectal tumor resected, numbers of the tumor resected, type of the procedures (EMR vs ESD), and concomitant use of low dose aspirin. Accordingly, we could not find any risk factors for postoperative bleeding of colorectal EMR/ESD.

Conclusion: Our study indicated that warfarin interruption and perioperative intravenous heparin bridging warranted the very low risk of arterial thromboembolism for patients with atrial fibrillation with high-risk endoscopic procedures. On the other hand, the incidence of postoperative bleeding was high, especially with colorectal EMR/ESD. Perioperative heparin bridging should be applied only for high thrombotic risk patients provided with a sufficient information of postoperative bleeding.

Disclosure: Nothing to disclose

P0172 1L NER1006 EVENING/MORNING DOSING SUSTAINS SUCCESSFUL COLON CLEANSING IN 7 OUT OF 8 PATIENTS EVEN 7+ HOURS AFTER THE SECOND DOSE: POST HOC ANALYSIS OF OVERNIGHT SPLIT-DOSING REGIMENS OF 1L NER1006 VERSUS 2L POLYETHYLENE GLYCOL + ASCORBATE OR ORAL SULFATE SOLUTION

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Abstract No: P0172

Overall HCS cleansing success, per hour after dose 2	NER1006 PM/AM	2L PEG + ascorbate PM/AM	NER1006 PM/AM	Oral sulfate solution PM/AM
Phase 3 trial	MORA	MORA	NOCT	NOCT
Patients (mFAS2), N	262	260	255	260
≤3 h, n/sample (%)	30/32 (93.8%)	55/61 (90.2%)	18/19 (94.7%)	20/20 (100%)
>3–4 h, n/sample (%)	44/46 (95.7)	42/46 (91.3%)	58/65 (89.2%)	46/48 (95.8%)
>4–5 h, n/sample (%)	53/53 (100%)	55/56 (98.2%)	63/64 (98.4%)	64/69 (92.8%)
>5–6 h, n/sample (%)	37/37 (100%)	32/34 (94.1%)	49/54 (90.7%)	56/60 (93.3%)
>6–7 h, n/sample (%)	38/41 (92.7)	25/28 (89.3%)	22/25 (88.0%)	28/32 (87.5%)
>7 h, n/sample (%)	49/51 (96.1%)	26/32 (81.3%)	25/28 (89.3%)	24/31 (77.4%)
Missing, n/sample (%)	2/2 (100%)	3/3 (100%)	0	0

[Table 1. Hourly overall HCS cleansing success after dose 2 of a bowel preparation using the split-dosing regimen]

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Introduction: High-quality bowel cleansing facilitates effective colonoscopy[1–3]. Split dosing is the preferred treatment regimen. A waiting time of 7 or more hours to the start of colonoscopy after dose 2 may reduce the chances of cleansing success, so treatments with sustained high efficacy would be valuable[4]. Afternoon procedures may also reduce the colonoscopy yield[5]. NER1006 is a novel 1L polyethylene glycol (PEG)-based bowel preparation. It was evaluated in the 2 phase 3, randomized, treatment-blinded assessor trials MORA[6] and NOCT[7]. This post hoc analysis assessed the duration of the cleansing efficacy after the second dose, of NER1006 evening/morning dosing versus 2L PEG + ascorbate (2LPEG) or oral sulfate solution (OSS).

Aims and Methods: Patients aged 18–85 years were randomized to receive a split-dosing regimen of either evening/morning (PM/AM) NER1006, or 2LPEG or OSS. Overnight split dosing started at ~6:00 pm (±2 h) with dose 2 at ~6:00 am (±2 h). The percentage of patients with overall bowel cleansing success (Harefield Cleansing Scale grades A and B) was analysed by duration between the end of the second dose of the bowel prep plus mandatory fluids and the start of colonoscopy (1-h intervals: ≤3, >3-4, >4-5, >5-6, >6-7, or >7 h). Data were analysed in the modified full analysis set 2 (mFAS2) population, which comprised all patients who received at least 1 dose of study drug and who had documented primary colonoscopy data from a central reader. Patients included in the analysis of variance (ANOVA) between time intervals and colon cleansing success also needed calculable time intervals after dose 2.

Results: Data from 1037 patients were included in the analysis (Table 1). In time intervals from up to 3 h to over 7 h after dose 2, successful bowel cleansing was attained in at least 88% (7 out of 8) patients with NER1006 PM/AM dosing regimen. At >7 hours NER1006 PM/AM attained at least 89.3% HCS cleansing success whereas this level of cleansing efficacy was not attained by either 2LPEG or by OSS which both showed reduced success rates after 7 hours (81.3% and 77.4%, respectively). The ANOVA revealed a significant decline in efficacy over time for OSS ($p=0.033$). No such differences were observed for NER1006 PM/AM ($p=0.32$; MORA, $p=0.36$; NOCT) or 2LPEG ($p=0.15$).

Conclusion: Split dosing with NER1006 evening/morning dosing can, in a reproducible fashion, deliver overall cleansing success in 7 out of 8 patients even after 7 or more hours post dose 2. This sustained efficacy may become particularly useful for afternoon or delayed colonoscopies.

Disclosure: Bharat Amlani and Lucy Clayton, employees of Norgine Ltd. Cesare Hassan was an investigator in the DAYB study and received honoraria from Norgine Ltd or investigator advisory board attendance

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P0173 COMPARISON OF COLONOSCOPY WITH VIRTUAL CHROMOENDOSCOPY USING THIRD GENERATION NARROW BAND IMAGING SYSTEM TO CHROMOENDOSCOPY WITH INDIGO CARMINE IN LYNCH PATIENTS

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Introduction: Colonoscopic screening with indigo carmine chromoendoscopy (ICC) in Lynch Syndrome (LS) patients improves adenoma detection rate and is widely used nowadays. Nevertheless, it is a time- and-money-consuming technique which requires a dedicated training. Narrow band imaging (NBI) is a well-known virtual chromoendoscopy technique that highlights superficial mucosal vessels and improves contrast for adenomas. We conducted a prospective multicenter study in a back-to-back fashion to compare 3rd generation NBI to ICC for detecting colonic adenomas in LS patients.

Aims and Methods: 138 patients underwent a double colonoscopy, first with NBI, followed by ICC, in a back-to-back fashion. All polyps detected in either pass were removed for histopathological analysis. The primary outcome measure was the number of patients with at least 1 adenoma after NBI compared with the number of patients with at least 1 adenoma after NBI and ICC. Proportions were compared with the paired exact test (McNemar's test). Continuous variables were compared with the Wilcoxon signed-rank test.

Results: All of the 138 patients were proven MMR mutation carriers (MLH1 = 33%, MSH2 = 47%, MSH6 = 15%, PMS2 = 4%, EPCAM = 1%). Mean age (SD) was 40.5 (14.7) years, 64 (46.4%) were male. The median time for an NBI procedure was 8 minutes (interquartile range [IQR] 6-11) compared to 13 minutes (IQR 8-17) for ICC. At least 1 adenoma was detected during the initial NBI pass in 36 (26.1%) of 138 patients. ICC detected additional adenomas in 35 (25.4%) of 138 patients. 56 patients (40.6%) had at least 1 adenoma detected after both NBI and ICC; this represents an increase of 55.6% of the adenoma detection rate (ADR) ($p<0.0001$). The total number of adenomas increased from 53 after NBI pass to 101 after ICC pass with a mean number of adenomas detected per patient of 0.4 (0.7) after NBI pass vs 0.7 (1.2) after both NBI and ICC passes ($p<0.0001$). The ADR for flat adenomas was 15.2% after NBI vs 31.9% after ICC ($p<0.0001$). The ADR increased for right sides adenomas (14.5% after NBI vs 23.2% after ICC, $p=0.0005$) as well as for diminutive adenomas ≤5mm (21.7% after NBI vs 37.7% after ICC, $p<0.0001$). Detection of both sessile adenomas (13.0% NBI vs 15.9% ICC, $p=0.125$) and adenomas > 5mm (8.0% NBI vs 10.9% ICC, $p=0.125$) did not differ significantly between the 2 techniques. After adding white light detected adenomas, the total ADR of the study was 43.5%.

Conclusion: Colonoscopy with indigo carmine chromoendoscopy detects significantly more adenomas than 3rd generation NBI in LS patients, whereas sessile and > 5mm adenomas are equally detected. Although less time consuming, NBI colonoscopy cannot be recommended to replace indigo carming chromoendoscopy in LS patients.

Disclosure: Nothing to disclose

P0174 OPTICAL BIOPSY OF DIMINUTIVE COLORECTAL POLYPS WITH REAL-TIME USE OF "ARTIFICIAL INTELLIGENCE"-ASSISTED ENDOSCOPY

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Introduction: Computer-aided diagnosis (CAD) for colonoscopy is drawing attention as an attractive tool to identify neoplastic polyps requiring resection from non-neoplastic polyps that can be left *in situ* [1]. However, its role has not been established because of the lack of high-quality clinical trials.
Aims and Methods: We aimed to clarify the efficacy of "real-time" use of CAD with endocytoscopes (520-fold ultra-magnifying endoscopes [2]) with a single arm, open-label, prospective trial. This trial included 821 patients undergoing colonoscopy with use of CAD in a tertiary university hospital between June and December 2017. CAD predicted pathology (neoplastic or non-neoplastic) of the detected diminutive polyps (≤5 mm) based on real-time outputs. CAD performance was evaluated, with the actual pathology of the resected specimen as the gold standard. The CAD system had been trained with 61925 endocytoscopic images acquired from a total of 5 university hospitals and cancer center hospitals in advance. Primary endpoint was the assessment of whether CAD demonstrated a ≥90% negative predictive value (NPV) for identifying diminutive, rectosigmoid adenomas, which is the threshold required to perform the "diagnose-and-leave" strategy for non-neoplastic polyps. Secondary outcome measures included the diagnostic accuracy in the whole colon.
Results: Overall, 466 diminutive polyps (including 250 in the rectosigmoid colon) from 325 patients were assessed by CAD using both the narrow-band imaging (NBI) mode and the methylene blue-stained mode. CAD was able to analyze 98.1% (457/466) of the polyps. Intention-to-treat analysis, in which non-analyzable polyps were treated as misdiagnosed ones, revealed mean NPVs for CAD regarding diminutive, rectosigmoid adenomas of 95.2% (95% confidence interval, 90.3–98.0) with the NBI mode and 93.7% (88.3–97.1) with the stained mode. For the total diminutive polyps, CAD demonstrated accuracy of 91.6% (88.7–94.0) with the NBI mode and 90.3% (87.3–92.9) with the stained mode.
Conclusion: Real-time use of CAD offered the performance that allowed the "diagnose-and-leave" strategy for diminutive, rectosigmoid non-neoplastic polyps. (This trial is registered with UMIN Clinical Trial Registry, No. UMIN000027360)
Disclosure: YM, SK, and MM are inventors of the patented "Image-processing instrument and method" (No. 6059271 in Japan) with inventors' premiums paid by Showa University. YM, SK, MM, and HI have received speaking honoraria from Olympus Corp. KM received research funding from Cybernet Corp. All the other authors have no conflict of interests relating to the present paper.

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P0175 FULLY AUTOMATED DIAGNOSIS SYSTEM WITH ARTIFICIAL INTELLIGENCE USING ENDOCYTOSCOPY TO IDENTIFY HISTOLOGICAL INFLAMMATION ASSOCIATED WITH ULCERATIVE COLITIS

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Introduction: In treatment goal of ulcerative colitis (UC), the incremental benefit of achieving histological healing beyond that of endoscopic mucosal healing has been suggested; persistent histological inflammation increases the risk of exacerbation and dysplasia. However, it is extremely difficult for conventional endoscopy to distinguish histological active/healing.
Aims and Methods: The aims of this study were to develop and evaluate a computer-aided diagnosis (CAD) system to predict the presence of histological activity using endocytoscopy (520-fold ultra-magnifying endoscope).
We retrospectively collected 9095 endocytoscopy images from 107 patients with UC. Among them, 4562 images from 57 patients were used for machine learning. The other 4533 images from 50 patients were used to validate CAD. Endocytoscopy images and biopsy samples of each patient were collected from 6 colorectal segments: cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. All endocytoscopy images were tagged according to the Geboes index. The outcome measure was the diagnostic ability of CAD to differentiate histological active/healing based on patients. The secondary outcome measures were the diagnostic ability of CAD based on all segments of all patients.
Results: CAD provided diagnosis outputs for 100% (4533/4533) of the validation images with a diagnosis time of 0.2 s/image. The diagnostic sensitivity, specificity, and accuracy of CAD were as follows; 83% (95% confidence interval, 64%–94%), 95% (76%–100%), and 88% (76%–96%) in the patient-based analysis, 77% (64%–87%), 97% (94%–99%), and 93% (89%–96%) in the segment-based analysis.
Conclusion: Our CAD system allows fully automated identification of persist histological inflammation associated with UC.
Disclosure: Nothing to disclose

P0176 WHAT IS THE COST OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN FRANCE? A PROSPECTIVE MEDICO-ECONOMIC STUDY

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Introduction: There is no economic assessment existing in Europe today about submucosal dissection.
As yet, the CCAM (Health Insurance System) has not delivered a listing of price quotation concerning this new medical procedure. It is an expensive technique in terms of time and material. The primary aim of this study is to assess the costs and benefits of endoscopic submucosal dissection. The secondary aims of the study are to assess the part of sterile medical devices (SMD) in the overall cost of the procedure, to determine predictive factors for a positive cost/benefit balance and to do a medico-economic comparative with surgery for superficial colonic neoplasms.
Aims and Methods: A monocentric prospective study including all hospitalized ESD patients was conducted from January 2015 to December 2017. The global cost of hospital stays was measured by summing up the actual cost of SMD used for ESD using a bottom-up approach (micro-costing) and the hospitalization day cost was extrapolated from the results of the National Cost Study for these patients. The revenue is based on DRGs (Diagnosis Related Goups).
The difference between the overall cost and the revenue provide the medico-economic study with core information. We have selected in the same center patients who had surgery from 2009 to 2017 for superficial colonic tumors with anatomopathology data. Univariate comparisons employ the Fisher exact test for qualitative variables and the Wilcoxon rank test for quantitative variables. All the statistical tests carried out provided significant values for $p < 0.05$.
Results: We had 193 patients having ESD in 2015-2016-2017. 80% of the lesions were colorectal lesions and 20% oesogastric. The average age was 68.8 years. The average duration of the procedure was 133 minutes. The rate of monobloc resections was 93%, with 78% R0 and 71.4% curative. 20 perforations (10.4%) were to be deplored. The rate of hemorrhages was 6.7%. The hospitalization day cost €463.18 with an average length of 3.6 days. The medical devices cost €970.77 the procedure cost € 1,604.96 which gave a global cost of €3,464 subtracted from a €2,727 gain. Consequently, we had a negative budgetary balance of €- 737 per patient with a global extracharge of €142,232 for the 193 patients. The medical devices represented 60.4% of the procedure cost. We identified only 1 predictive factor for a positive budgetary balance which was a severity level of DRG higher than 1 (OR 49.21; IC95% 11.3–214.25; $p < 0.0001$). We compared colonic surgery and ESD for superficial lesions in the same center/hospital. 69 patients were in surgery and 71 in ESD. There is no significant difference between the 2 groups in terms of age, localization, anatomopathology or ASA score. The size of lesions was twice higher in ESD than in surgery (50 mm vs. 25 mm; $p < 0.0001$). The average length of hospitalization was superior in surgery (11 days vs. 2 days in ESD; $p < 0.0001$). Morbidity at 30 days was not significantly superior in surgery (28 vs. 14% in ESD; 0.061). At country level, the cost of surgery was 5 times higher if we consider revenue related to the stay (€8,960 vs. €1,770; $p < 0.0001$). But at the hospital scale, the budgetary balance was positive for surgery patients €+542 whereas it was negative €-1,300 in the dissection group.
Conclusion: As of today, the ESD benefit/deficit balance is negative in 80% of cases.
This overcharge is due to a lack of act ranking. Specific dissection equipment accounts for the largest share of expenditures. It is clearly less morbid and expensive than classic surgery
Disclosure: Nothing to disclose

P0177 REAL TIME DIAGNOSTIC SYSTEM FOR COLORECTAL CANCER USING ARTIFICIAL INTELLIGENCE

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Introduction: Endocytoscopy (EC) enables *in vivo* observation of nuclei at about 500-fold magnification during gastrointestinal endoscopy. We have developed a system using artificial intelligence that provide a predictive pathological diagnosis for colorectal lesion in real time based on EC image during examination [1]. Our computer aided diagnosis (CAD) system for EC (EC-CAD) analyzes 312 image features of EC obtained as a result of texture analysis. We used a support vector machine to help classify these many features and output 4 predictive

pathological diagnoses (non-neoplastic, adenoma, SSA/P, invasive cancer). The high diagnostic ability of EC-CAD to distinguish between adenoma and invasive cancer has already revealed in previous report [2]. As a next step, we conducted a prospective study to evaluate the real-time use of the current system.
Aims and Methods: The primary endpoint of this study was to verify the positive predictive value (PPV) in distinguishing invasive cancer from other lesions was 90% or higher when EC-CAD was applied for examination. This prospective study was conducted at Showa University Northern Yokohama Hospital from June 2017 to December 2017. In this study, we used the software constructed based on EC images obtained by staining cell nuclei with 1.0% methylene blue. At the start of the study, we used software that let the system learn 16800 images. During the study period, we made an update 3 times (the number of learning images for the system: 1st 18966 images, 2nd 32265 images, 3rd 36586). The subjects were colorectal lesions of 20mm or more in diameter which histological evaluation was performed after EC observation. Regarding the diagnostic results given by the EC-CAD, since a plurality of endoscopic images were acquired from one lesion, the majority decision method adopting the most frequent diagnosis results was used as a final diagnosis of the system. As a sub analysis, the endoscopists were divided into experts and trainee based on the difference in experience, and it was examined whether procedure time and diagnostic accuracy using EC-CAD were affected by the expertise.
Results: A total of 106 colorectal lesions (4 non-neoplasms, 34 adenomas, 68 invasive cancers (10 T1 cancers, 58 T2-T4 cancers)) from 99 patients were included. 77% (6434/8313) of the acquired EC images were able to be diagnosed by EC-CAD. Regarding the diagnostic performance of EC-CAD to distinguish invasive cancers from other lesions, sensitivity, specificity, accuracy, PPV and negative predictive value (NPV) were 93%, 97%, 94%, 98% and 88%, respectively. Considering experts and trainees separately, the sensitivity, specificity, accuracy, PPV, NPV were 93% vs. 93%, 97% vs. 100%, 94% vs. 94%, 98% vs. 100% and 89% vs. 67%, respectively. The time taken for EC image acquisition was 5.6 seconds on average. There was no significant difference in image acquisition time between experts (5.5 sec) and trainees (6.3 sec).
Conclusion: This study suggested that EC-CAD will provide a reliable diagnosis with PPV 90% or higher in distinguishing invasive cancer from other lesions, regardless of the experience of endoscopists.
Disclosure: Nothing to disclose

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P0178 TRAINEES' INFLUENCE ON ADENOMA DETECTION AND FOLLOW-UP RECOMMENDATIONS AT SCREENING AND SURVEILLANCE COLONOSCOPIES

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Introduction: Colonoscopy has emerged as the main diagnostic and therapeutic tool in the detection of colonic adenomas. Training future endoscopists is essential to meet future demands.
Aims and Methods: Studies have shown somewhat conflicting results regarding the influence of trainee-participation on adenoma detection rates (ADR), mostly showing positive or indifferent effects of trainee participation. A previous prospective study by our group showed no adverse effect of trainee participation on ADR. However, this study did not include first-year trainees or subsequent surveillance exams. The aim of the current investigation was to see, whether the inclusion of first year trainees magnifies the noted difference and whether trainee participation affects ADRs or the timing of subsequent surveillance exams.
A retrospective analysis of average-risk screening colonoscopies over a 3-year interval was performed. Patients with poor preparation were excluded. The final analysis included 4922 screening colonoscopies between the years 2004–2006, as well as 2184 subsequent surveillance exams. Data were collected from pathologic and endoscopic electronic data bases. The primary outcome was the ADR at colonoscopies with and without trainee participation.
Results: Trainees participated in 1131 (23%) screening exams and in 232 (11%) surveillance exams. ADR did not significantly differ ($p = 0.19$) for screening exams with trainee participation (19.5%) or those without (21.4%). ADRs were generally higher at surveillance exams, both with (22.4%) and without (27.5%) trainee participation. The noted difference of ADRs at surveillance colonoscopies with or without trainee participation did not reach statistical significance ($p = 0.1$). Multivariate analysis showed no influence of first year fellow participation on the outcome. When surveillance recommendations differed from guidelines, shorter surveillance intervals were given more frequently if trainees participated during the initial screening procedure ($p = 0.0001$).
Limitations: Single-center, retrospective study.
Conclusions: ADR did not significantly differ at screening or surveillance colonoscopies with or without trainee participation. There was a trend towards higher ADR at surveillance exams in both groups. The inclusion of first year trainees had no adverse effect on the outcome. However, trainee participation may result in shortened surveillance recommendations after initial screening exams.
Disclosure: Nothing to disclose

P0179 DEVELOPMENT OF A REAL-TIME ENDOSCOPIC IMAGE DIAGNOSIS SUPPORT SYSTEM USING DEEP LEARNING TECHNOLOGY IN COLONOSCOPY

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Introduction: The development of a real-time robust detection system for colorectal neoplasms will significantly reduce the risk of missed lesions during colonoscopy. However, gaps in colonoscopy skills among endoscopists, primarily due to experience, have been identified, and solutions are critically needed.
Aims and Methods: To overcome this experience gap, we aimed to develop an artificial intelligence (AI) system that automatically detects early signs of colorectal cancer during colonoscopy.
Patients with and without colonic polyps and those with colorectal cancer were included. A training data set of colonoscopic still and video images consisting of 5,000 images of 2,116 early-staged colorectal cancers or precursor lesions and 134,983 images of noncancerous tissue were provided. Using this training set, Deep Learning algorithms were provided to learn the colonoscopic features of the disease. The diagnostic accuracies and area under the receiver-operating characteristic curve of this algorithm as well as the processing speed of this AI system were measured by using validation set of 4,840 images (705 images with 752 lesions and 4135 images without lesions) from consecutive patients with and without early-staged colorectal cancers or precursor lesions.
Results: The sensitivity and specificity of the system were 97.3% (95% confidence interval [CI] = 95.9%–98.3%) and 99.0% (95% CI = 98.6%–99.2%), respectively, and the area under the curve was 0.975 (95% CI = 0.964–0.986) in the validation set. The sensitivities were 98.0% (95% CI = 96.6%–98.8%) in the polypoid subgroup and 93.7% (95% CI = 87.6%–96.9%) in the nonpolypoid subgroup. A supplementary human observational study demonstrated that the AI system had a superior diagnostic yield as endoscopists, including experienced, fellows, and beginners (Figure 1). The system analyzed all 4,840 images in 106.0 s (average, 21.9 ms/image), whereas endoscopists required median 725.2 s (IQR = 655–914) to analyzed the 309 images. In addition, this system achieved in real-time detecting and displaying results of each video frame within 33 milliseconds (30 frames per second).
Conclusion: We have developed a real-time endoscopic image diagnosis support system using deep learning technology that automatically detects early signs of colorectal cancer during colonoscopy. This AI system can alert endoscopists in real time to avoid missing abnormalities such as polyps during colonoscopy, improving the early detection of this disease.
[Table 1. Diagnostic performance of AI system for detecting and displaying early stage colorectal early-staged cancers and precursor lesions]
Disclosure: Nothing to disclose

Abstract No: P0179

	Sensitivity* (n) (95% CIs)	Specificity** (n) (95% CIs)	
		Without lesions	With lesions
All lesions (752 lesions)	97.3% (732/752) (95.9–98.3)	99.0% (4092/4135) (98.6–99.2)	90.2% (636/705) (87.8–92.2)
Polypoid lesions (641 lesions)	98.0% (628/641) (96.6–98.8)	99.0% (4092/4135) (98.6–99.2)	89.1% (529/594) (86.3–91.3)
Flat and depressed lesions (111 lesions)	93.7% (104/111) (87.6–96.9)	99.0% (4092/4135) (98.6–99.2)	96.4% (107/111) (91.1–98.6)

*Sensitivity was defined as AI correctly detected lesion number/number of all lesions; **Specificity was defined as AI negative image number/ true lesion negative image number (images without lesions); Correct answer was defined when AI detect and display loci of lesion by flag.

P0180 GRADING OF DYSPLASIA FOR DIAGNOSING COLORECTAL ADENOMAS USING ENDOCYTOSCOPY (EC)

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Introduction: Recent opinions have expressed that if an endoscopic diagnosis of adenomas can be made with high accuracy, then the omission of a pathological diagnosis following endoscopic resection is acceptable. Currently, there is no clear consensus regarding whether endoscopic treatment is required for all adenomas. Colonoscopy-based grading of dysplasia can be clinically effective for diagnosing adenomas, if such a diagnosis of adenomas, particularly of low-grade adenomas, can be made with high accuracy.
Aims and Methods: In this study, we focused on the existence of mixed-pit pattern type I lesions in slit-like lumens, which is an endocytoscopy (EC) finding characteristic of adenomas, and investigated pathological findings that were correlated with this observation. We retrospectively examined 700 lesions among the neoplastic lesions that could be observed by EC between May 2005 and May 2017 and that were classified as EC2 according to the EC classification system and could be pathologically examined via endoscopic resection. Lesions characterized by mixed-pit pattern type I in slit-like lumens were classified as EC2 normal pit (NP) sign (+), while those characterized by slit-like lumens only were classified as EC2 NP sign (−). We investigated the final pathological diagnosis results. In addition, we investigated the concordance rate of surveillance interval recommendation in EC diagnosis and pathological diagnosis based on USA guideline, and also examined the location, diameter, and morphological type of NP (+) lesions to elucidate their clinical traits. In order to evaluate the concordance rate of EC 2 NP sign, 3 experts (T.K., Y.M. and M.M) and 3 trainees (T.W.,T.K and K.M) reviewed digitally recorded EC images of the lesions.
Results: A total of 466 lesions were classified as EC2 NP sign (+). Of these, low-grade adenomas accounted for 450 lesions and advanced lesions (high-grade dysplasia, tubulovillous adenoma, invasive cancer) accounted for 16. NP sign (+) as an indicator of low-grade adenomas had a sensitivity of 85.4%, specificity of 90.8%, positive predictive value of 96.6%, negative predictive value of 67.1%, accuracy of 86.7%, and positive likelihood ratio of 9.23. It was 95.5% that the concordance rate of surveillance interval recommendation based on USA Guideline compared with EC and pathological diagnosis. Furthermore, an examination of the EC2 NP (+) rate by location, diameter, and morphological type of the lesions revealed that 75.7% were located in the proximal colon ($p < 0.001$), 81.4% of the lesions were ≤10 mm in diameter ($p < 0.001$). Further, 79.8% were of the flat/depressed type ($p < 0.001$). The interobserver agreement for the EC2 diagnosis using EC2 NP sign among the 3 experts were 0.82, 0.90, and 0.94 and among the 3 trainees were 0.84 (T.K., Y.M.), 0.78 (T.K.-M.M.), and 0.82 (Y.M.-M.M.), respectively. The intraobserver agreement of the 3 experts were 0.84 (T.W.-T.K.), 0.86 (T.W.-K.M.) and 0.98 (T.K.-K.M.), and the 3 trainees were 0.80, 0.80 and 0.86, respectively.
Conclusion: These results suggest that when using EC for diagnosing colorectal neoplastic lesions, NP sign is a good indicator of low-grade adenomas with the EC2 classification. It was suggested that EC diagnosis could make the Resect and Discard strategy practicable regardless of polyp size. Furthermore, the NP (+) rate tended to be high in lesions located in the proximal colon, that were ≤10 mm in diameter, and that were of the flat/depressed type.
Disclosure: Nothing to disclose

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P0181 DEVELOPMENT OF A MODIFIED SMSA SCORING SYSTEM WITH IMPROVED ACCURACY IN THE PREDICTION OF COMPLICATIONS OF ENDOSCOPIC MUCOSAL RESECTION IN THE COLON

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Introduction: The SMSA (*size, morphology, site, access*) scoring system allows stratification of the complexity of endoscopic mucosal resections (EMR). However, the influence of other lesion characteristics in EMR outcomes is widely recognized.
Aims and Methods: The aim of this study was to develop a modified SMSA scoring system with complementary lesion characteristics and determine its accuracy in the prediction of complications of EMR. Consecutive colorectal, non-pedunculated lesions, ≥20mm, referred to EMR between January 2015 and December 2016 were included. Lesions with previous resection attempts were excluded. The relation between SMSA and total complication rate (intra-procedure and post-EMR bleeding, intestinal perforation and post-polypectomy syndrome) was evaluated. Additional predictive characteristics of complications were determined and their incorporation into the SMSA evaluated.
Results: A total of 225 lesions were selected, mean size 29.5 ± 13.0 mm, most of type 0-IIa (37.3%) or 0-Is (28.0%) of the Paris Classification, with granular surface (72.9%). Technical success of EMR was 94.2% (n = 212), with *piecemeal* (68.9%) or *en bloc* (31.1%) resection, and was related to the SMSA ($p < 0.001$). Total complication rate was 22.6%: intra-procedure bleeding = 15.1%; post-EMR bleeding = 6.1%; intestinal perforation = 0.9%; post-polypectomy syndrome = 0.9%. The area under the ROC curve of the SMSA for prediction of complications was 0.70 (95%CI 0.61–0.79, $p < 0.001$). On multivariate analysis, lesion component 0-IIb or 0-IIc (OR = 2.4, 95%CI 1.1–6.5, $p = 0.041$) and non-granular/mixed surface type (OR = 2.6, 95%CI 1.2–5.9, $p = 0.020$) were associated with complications independently of the SMSA. The incorporation of the 2 characteristics into the SMSA (component 0-IIb/IIc = 2 points, non-granular/mixed surface = 3 points) had a significantly increased association with the total complication rate (area under the ROC curve = 0.79), by a difference of 0.087; $p = 0.032$ (*DeLong et al. method*).
Conclusion: The incorporation of the Paris Classification (component 0-IIb or IIc) and lesion surface type (granular or non-granular) into the SMSA scoring system increased its accuracy in the prediction of complications of EMR.
Disclosure: Nothing to disclose

P0182 MAP SIGNIFICANTLY CORRELATES WITH ADR BUT NOT WITH PDR FOR BOTH SCREENING AND ALL COLONOSCOPIES

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Introduction: ADR (adenoma detection rate) is generally accepted quality indicator. For possible gaming with ADR other indicators are needed. MAP (mean adenoma per colonoscopy) reflects the quality of examination of entire colon and is considered to be the most objective quality indicator.
Aims and Methods: The aim of our study was to compare MAP with ADR and PDR (polyp detection rate) of all colonoscopists in our department. We retrospectively assessed the quality indicators of all colonoscopies performed in non-university hospital Frydek-Mistek from January 2013 to December 2017. We counted ADR, PDR and MAP for all colonoscopies in patients over 50 years of age excluding therapeutic, IBD, management of complications and sigmoideoscopies (screening, surveillance, diagnostic) and separately only for screening colonoscopies. Correlations between MAP/ADR and MAP/PDR were performed using Pearson's correlation coeficient, $p < 0.05$ was considered significant.
Results: The group for statistics comprised 6925 patients (3620 men, 3305 women, mean age 66.2 years). There were positive correlations between ADR and PDR both for all and for screening colonoscopies ($p = 0.044$, $p = 0.025$) wchich was also proven in previous studies. There were positive correlations between MAP and ADR for all and screening colonoscopies ($p = 0.009$, $p < 0.005$) but not for MAP and PDR ($p = 0.176$, $p = 0.055$), see the table.

Endoscopist	PDR screening	ADR screening	MAP screening	PDR all	ADR all	MAP all
1	64.7	41.3	0.727	60.7	39.1	0.641
2	82.9	49.3	0.876	79.2	47.0	0.833
3	55.3	40.0	0.770	55.2	37.7	0.610
4	65.6	49.3	0.916	58.2	41.7	0.719
5	66.9	48.3	1.029	61.3	45.0	0.827
6	83.7	57.0	1.209	77.1	48.6	0.906

Conclusion: In our study there were significant positive correlations between MAP and ADR but not between MAP and PDR for both all and screening colonoscopies. Considering MAP to be the most objective quality indicator, the quality of colonoscopy is better reflected by ADR than PDR.
[ADR, PDR and MAP of all and screening colonoscopies]
Disclosure: Nothing to disclose

P0183 CORRELATION BETWEEN ADR OF SCREENING AND ALL COLONOSCOPIES - IS IT POSSIBLE TO CALCULATE ADR FOR ALL COLONOSCOPIES IN PRACTICE?

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Introduction: ADR (adenoma detection rate) is generally accepted quality indicator and is calculated from screening colonoscopies in patients over 50 years of age. For possible gaming with ADR for screening colonoscopies, monitorig of ADR for all colonoscopies is discussed nowadays.
Aims and Methods: The aim of our study was to compare ADR for colonoscopies from various indications and to find correlation between ADR of screening and all examinations. We retrospectively assessed the quality indicators of all

colonoscopies performed in non-university hospital Frydek-Mistek from January 2013 to December 2017. We counted ADR for all colonoscopies in patients over 50 years of age excluding therapeutic, IBD, management of complications and sigmoideoscopies (screening, surveillance, diagnostic) and separately only for screening colonoscopies. Correlation analysis was performed using Pearson's correlation coeficient, multiple chi square test was used to compare patients' age and one way ANOVA was used to compare proportion of men and women among endoscopists, $p<0.05$ was considered significant.
Results: In study period, 10472 colonoscopies and sigmoideoscopies were done in total. The group for statistics comprised 6925 patients over 50 years of age (3620 men, 3305 women, mean age 66.2 years). Among six endoscopists, there were differenciens in proportion of men and women ($p=0.048$) and age of patients ($p=0.002$). This should be taken into consideration when comparing various endoscopists but it does not affect the correlation analysis of ADR from all and screening colonoscopies. ADR for screenig and surveillance were higher than for diagnostic colonoscopies in all endoscopists, ADR for all colonoscopies were lower than for screening but sufficiently over 25 %, see the table. There was positive correlation between ADR of screening and all colonoscopies ($r=0.906$, $p<0.005$).

Endoscopist	N all	ADR all	N screening	ADR screening	N surveillance	ADR surveillance	N diagnostic	ADR diagnostic
1	1467	39.1	567	41.3	380	45.3	520	32.1
2	419	47.0	146	49.3	186	52.7	87	31.0
3	815	37.7	170	40.0	226	48.7	419	30.3
4	1394	41.7	430	49.3	379	44.6	585	39.4
5	2406	45.0	700	48.3	589	52.8	1117	38.9
6	424	48.6	86	57.0	115	47.0	223	46.2

Conclusion: Calculation of ADR for all colonoscopies was possible in our department and there was positive correlation with ADR for screening colonoscopies. Because of inclusion of diagnostic examinations, ADR for all colonoscopies was lower than for screening but still over recommended values.
[ADR for screening surveillance, diagnostic colonoscopies and all together]
Disclosure: Nothing to disclose

P0185 RATIO OF RIGHT-SIDED TO LEFT-SIDED DYSPLASTIC COLONIC POLYPS IS A VALID KEY PERFORMANCE INDICATOR

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Introduction: Quality improvement in performance of colonoscopy, with special attention to the detection of proximally located precursors, have the potential to prevent postcolonoscopy colorectal cancer [1].
Aims and Methods: A prospective analysis of consecutive diagnostic or surveillance colonoscopies for various indications performed from 2013 - 2017 by an endoscopist with high lesion detection rate. The primary outcome was a detection of dysplastic polyp (DP); secondary outcome - a detection of non-dysplastic polyps (nDP) but with inflammatory and postinflammatory polyps exclusion. Findings from colonoscopies were evaluated with regard to number, size, distribution, prevalence, and incidence of polyps with and without dysplasia. Differences in numbers of the polyps were calculated using between subject and within subject ANOVA and Pearson's $\chi 2$-test. For the multivariate analysis, a logistic regression test was used. All statistical analyses were performed using SPS STATISTICS 24 and a p-value of less than 0.05 was considered statistically significant.
Results: A total of 3811 colonoscopies were analysed. Adenomas detection rate was 26.03% (regardless of the patients' age and an indication for colonoscopy). The crude caecal intubation rate was 93.55%. After exclusion of patients with hemicolectomy, 1480 patients were included in the study; their mean age: 64.43 ± 12.92 years. In those 1480, 65.54% ($n=970$) of patients with average age at 66.89 ± 11.69, had at least one polyp with dysplasia; 623 individuals had only DP and 347 had DP and nDP. The remaining 34.46% ($n=510$) of patients had only nDP.
There were 499 patients with DP located only in the right colon (RC) (caecum, ascending and transverse colon), 273 patients only in the left colon (LC) (descending, sigmoid and rectum) and 198 patients in both sides of the colon.
Although, there was no difference in the proportion between patients with DP $\geq$ 1 cm in the right and the LC (2.4% vs. 2.2%, $p=0.48$), respectively, but significant differences were noted ($p<0.001$) when patients with smaller than 1 cm DP were compared ($\chi 2=117.52$; 18.3% vs. 10.3%) or regardless their size in both colonic parts (10.3% vs. 6.2%) - in group of patients in age $\geq$ 50 ($\chi 2=112.59$ $p<0.001$) or in all patients regardless their age ($\chi 2=94.39$ $p<0.001$).
In total, 3892 polyps were removed: 1549 from the RC and 2343 from the LC (39.80% vs. 60.20%). 1254 DP were located in the RC and 678 DP in the LC (64.9% vs. 35.1%); 295 nDP and 1665 nDP were found respectively in the RC and the LC (15.05% vs. 84.95%). The proportion of DP amount was significantly greater on the right colon when compared with the left colon ($M=0{,}85$; $SD=1.33$ vs. $M=0.46$; $SD=0.91$) ($F=25.86$ $p<0.001$). The same rule was even noticeable when DP in more proximal colon (caecum, ascending colon) were compared with more distal colon (sigmoid, rectum) ($F=9.67$ $p<0.01$). This correlation disappears when we compare polyps in the right and the left colon without differentiation between polyps; then ratio of polyps (nDP and DP) in the right colon to polyps in the left colon becomes < 1 ($F=39.82$ $p<0.001$).
Conclusion: Right-sided colon polyps more likely to have dysplasia compared with left-sided polyps. Therefore, missing a polyp in the right colon is likely more significant than missing one in the left colon and guidelines should focus attention on the proximal colon and provide feedback to endoscopists regarding their proximal adenoma detection rates.
Ratio of dysplastic polyps located in the right colon to dysplastic polyps in the left colon is a valid key performance indicator.
Disclosure: Nothing to disclose

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P0186 LAPAROSCOPY ENDOSCOPY COOPERATIVE SURGERY (LECS) TO OVERCOME THE LIMITATIONS OF ENDOSCOPIC RESECTION FOR COLORECTAL TUMORS

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Introduction: We established a new procedure, laparoscopy endoscopy cooperative surgery (LECS) procedure to overcome the limitations of endoscopic resection (ER) for colorectal tumors. This procedure involves local full-thickness resection using a combination of laparoscopy assisted colectomy (LAC) and endoscopic submucosal dissection (ESD), which is quite different from the conventional method. In this report, we clarify the feasibility of performing a safe full-thickness resection with an adequate surgical margin by LECS with ESD.
Aims and Methods: The aim of this study is to clarify the feasibility of performing a safe full-thickness resection with an adequate surgical margin by LECS with ESD. We performed full-thickness resection for 17 colorectal tumors in 17 patients (male: female 10:7; mean age, 66.5 years) by LECS. The clinicopathological outcomes of these 17 cases and the feasibility of full-thickness resection were evaluated retrospectively.
The indications for LECS in patients with colorectal tumors were as follows: 1) intra-mucosal carcinoma (Tis) and adenoma with high-grade atypia (Vienna Classification, Category 3, 4) accompanied by wide and severe fibrosis in the submucosal layer (tumor recurrence after endoscopic or surgical resection), 2) intra-mucosal carcinoma (Tis) and adenoma with high-grade atypia involving the diverticulum or appendix, and 3) involving intraluminal or intramural growth-type submucosal tumors.
Results: We successfully performed full-thickness resection using LECS in 17 cases (Tis cancer [n = 6], adenoma [n = 9], schwannoma [n = 1], and gastro-intestinal stromal tumor [GIST] [n = 1]. The average tumor diameter was 22.4mm (range, 8–41mm). LECS was successfully performed in 17 all cases without conversion to open surgery; the R0 rate was 100%. The indications for LECS were as follows: involvement of the mucosa of the appendix (n = 6), tumor accompanied by severe fibrosis (n = 5), involvement of a diverticulum (n = 3), submucosal tumor (n = 2), and poor endoscopic operability (n = 1). We experienced no complications (*e.g.*, leakage or anastomotic stricture), and the median hospital stay was 6.4 (range, 4 to 12) days. All 17 patients who were followed for $\geq$3 months (average, 30.8 months; range, 3–72 months) showed no residual or local recurrence. Thus, the use of the ESD technique in LECS, can achieve a safe oncological margin in cases involving colorectal tumors. Furthermore, a high complete resection rate, with an adequate surgical margin and a lower local recurrence rate can be expected.
Conclusion: We developed a LECS procedure to overcome the limitations of colorectal ESD, and completed the full-thickness resection of tumors that were considered to have a high risk of perforation. LECS was a safe, feasible, minimally-invasive procedure that achieved the full-thickness resection of colorectal tumors and which showed excellent clinical outcomes.
Disclosure: Nothing to disclose

P0187 FEASIBILITY AND SAFETY OF WATCH AND WAIT STRATEGY OF DELAYED BLEEDING AFTER COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION: IS EMERGENCY COLONOSCOPY REALLY NEEDED?

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Introduction: Colorectal cancer (CRC) is one of the most common causes of cancer-related death worldwide, colorectal endoscopic submucosal dissection (ESD) has spread rapidly as an effective treatment strategy for early-stage CRC. However, there is major concern about bleeding as a complication of this procedure. While some reports have been published on the management of delayed bleeding after colorectal ESD, there is no consensus on the optimal treatment protocol for which situations we should perform emergency colonoscopy for delayed bleeding after ESD. The criteria of judgement for emergency

colonoscopy remains unclear. In this study, we attempted to extract the risk factors for delayed bleeding after colorectal ESD and to evaluate whether emergency colonoscopy is really needed. The aim of this study is to investigate the feasibility and safety of this "watch and wait strategy" of delayed bleeding.
Aims and Methods: The data of 454 consecutive patients who underwent ESD at Omori Red Cross Hospital between April 2012 and February 2018 were reviewed in this study. The watch and wait strategy is a protocol of delayed bleeding after colorectal ESD: We assess these following conditions after delayed bleeding; shock index≥1, and/or moderate amount of hematochezia more than 5 times. If these conditions are not satisfied, we carefully observed the clinical courses without emergency colonoscopy. All subjects were divided into 2 groups (bleeding group and no-bleeding group) to investigate the potential risk factors for delayed bleeding and assessed the necessitation of emergency colonoscopy based on watch and wait strategy. We investigated the age, sex, comorbidities, antithrombotic agents, location, macroscopic appearance, lesion size, sample size, fibrosis, hemostatic forceps use, prophylactic clip closure, peak blood pressure, nicardipine use, en-bloc resection rate, pathology, and operation time.
Results: We excluded 15 neoplasms from the analysis, with the final analysis performed on the remaining 439 lesions. All subjects were divided into 2 groups: bleeding group (27 neoplasms), and no-bleeding group (377 neoplasms). In bleeding group, there are no cases which require emergency colonoscopy for hemostasis after delayed bleeding under this "watch and wait strategy". The location of rectum, and lesion size ≥40mm were identified by multivariate analysis as being significantly and independently associated with bleeding after ESD (OR: 5.547, and 3.967, 95% CI = 1.456 - 21.130, and 1.003 - 15.696, respectively; $p \leq 0.05$ for all).
Conclusion: Our results suggest that the location of rectum, and lesion size ≥40mm are an independent factors of delayed bleeding after colorectal ESD, but there were no cases which require emergency colonoscopy, blood transfusion, or serious condition caused by delayed bleeding under our "watch and wait strategy".
Disclosure: Nothing to disclose

P0188 COMPUTER-AIDED DETECTION FOR COLONOSCOPY USING DEEP LEARNING

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Introduction: Colonoscopy and endoscopic eradication of neoplastic lesions are effective for the reduction of colorectal cancer incidence. However, 26% of colorectal diminutive neoplasms were reported to be missed in one colonoscopy (1). To reduce the number of missed cases, we developed a prototype computer-aided detection (CADe) system for colonoscopy (2).
Aims and Methods: The aim of this study was to evaluate the performance of the developed CADe system for colorectal polyps by using recorded video data. To develop the CADe system, we collected 84 full high-definition colonoscopy videos from study participants who underwent total colonoscopy from April 2015 to October 2015 at Showa University Northern Yokohama Hospital. Each colonoscopy video recorded from cecal intubation to withdrawal of the scope across the anus. Therefore, these videos included polyp-positive and polyp-negative frames. Regarding the machine learning process, 2 expert endoscopists annotated all the frames regarding the presence or absence of a polyp. These videos included 166 polyps. The video data of 105 polyps were randomly selected, and 80-min polyp-negative videos were used for machine learning. If the system detects a polyp in the frame, it outputs an alert. To evaluate the performance of the system, we extracted 61 polyp-positive videos and 20-min polyp-negative videos from the study materials as validation sample. The percentage of correctly detected polyps and false-positive detection rate for the negative frames were calculated using the validation sample. Correct detection by the system was defined as a system output of an alert for more than half the length of each polyp-positive video.
Results: The system correctly detected 92% (56/61) of the polyps. Regarding morphological assessment, 92% (36/39) of flat lesions and 91% (20/22) of protruded lesions were correctly detected. With regard to the negative videos, the false-positive detection rate was 59% (19,680/33,088 frames).
Conclusion: The results showed that artificial intelligence has the potential of automated detection of colorectal lesions. Further machine learning is required to reduce false-positive detections. We have already begun to use the system in real-time practice to collect more learning materials.
Disclosure: Nothing to disclose

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P0189 AUTOMATIC ANATOMICAL CLASSIFICATION OF COLONOSCOPIC IMAGES USING DEEP CONVOLUTIONAL NEURAL NETWORKS

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Introduction: Total colonoscopy is commonly used for screening examinations in many countries. However, specialized skill training is required until one can handle a colonoscope freely and diagnose an abnormal region accurately. One of the reasons that it takes a long period to acquire such skills is the difficulty in recognizing anatomical locations during colonoscopy. Recently, various computer-aided diagnosis (CAD) systems with deep convolutional neural networks (CNN) have achieved remarkable performance in many medical fields including the diagnosis of colorectal diseases. A CNN system that can recognize anatomical locations during colonoscopy may assist undertrained practitioners efficiently.
Aims and Methods: We constructed a CAD system with CNN based on GoogLeNet architecture to categorize colonoscopic images according to anatomical locations. 7 anatomical categories were used; terminal ileum, cecum, ascending colon to transverse colon, descending colon to sigmoid colon, rectum, anus and indistinguishable image. We retrospectively obtained images that were taken during total colonoscopy performed from January, 2017, to November, 2017, at single center in Japan. We used 9995 images of 409 cases for training the CNN system, and independent 5121 images of 118 cases for validating its performance. For each validation process of an image, the CNN system provided a probability score ranging from 0 to 100%, which indicates the probability for which category an image would belong to. We drew receiver operating characteristic (ROC) curve and calculated the area under the curves (AUCs) by each category.
Results: In the validation process, the CNN system correctly recognized 66.6% of images (3410/5121). The rates of correct recognition by each anatomical category were 69% (145/209) for terminal ileum, 50% (211/423) for cecum, 51% (891/1742) for ascending to transverse colon, 90%(1872/2081) for descending to sigmoid colon, 23% (109/467) for rectum, and 91%(182/199) for anus, respectively. The specificity for each category were 99.3% for terminal ileum, 98.2% for cecum, 93.8% for ascending to transverse colon, 60.9% for descending to sigmoid colon, 98.1% for rectum, and 97.8% for anus. The calculated AUCs by the ROC curves were more than 0.8 for each anatomical category; 0.979 for terminal ileum, 0.940 for cecum, 0.875 for ascending to transverse colon, 0.846 for descending to sigmoid colon, 0.835 for rectum, and 0.992 for anus. The CNN system provided 507 images with a probability score of more than 99% that showed 91.7% accuracy in total.
Conclusion: We constructed the new CNN system with clinically relevant performance for recognizing anatomical locations of colonoscopic images, which may reduce the burden and time of acquiring the colonoscopic technique for beginners.
Disclosure: Nothing to disclose

P0190 VALIDITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LARGE COLORECTAL TUMORS ACCORDING TO PIT PATTERN ANALYSES BY MAGNIFICATION ENDOSCOPY

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Introduction: Endoscopic submucosal dissection (ESD) has enabled en-bloc resection of an early-stage gastrointestinal tumor, which has many advantages of histological assessment, irrespective of the lesion's size. Although the use of ESD for colorectal tumors has been studied, a definite indication for ESD among them is controversial.
Aims and Methods: The present study aimed to assess the validity of colorectal ESD. We analyzed clinicopathological findings for 376 early-stage colorectal sessile polypoid and superficial tumors greater than 20mm resected endoscopically or surgically (296 low/high-grade intraepithelial neoplasias and 80 submucosal invasive carcinomas) after observation by magnification chromoendoscopy. They were classified into 3 subtypes according to their morphology: 25 cases of sessile polypoid-type, 329 cases of laterally spreading tumor (LST) and 22 cases of the depressed-type. Moreover, LSTs are divided into 193 cases of granular types (LST-G) with aggregates of even or uneven nodules on the surface and 136 cases of non-granular types (LST-NG) with a smooth surface. Submucosal invasive carcinomas were classified into 23 minute (SM-minute Ca) and 57 deep cases (SM-deep Ca; over 1mm from the muscularis mucosae to the deepest of invasion).
Results: All 22 depressed-types were SM-deep Ca cases. The rates of SM-deep Ca cases in LSTs were significantly lower than those in the polypoid and depressed-types, respectively (LST 22 cases, 7% vs polypoid 15 cases, 60%; $p < 0.01$, LST vs depressed 100%; $p < 0.01$). In 338 cases with a type non VN pit pattern, the rates of intraepithelial neoplasias and SM-minute Ca cases were 94%, while all 38 lesions with a type VN pit pattern were SM-deep Ca cases. There was significant

relationship between histology and pit pattern ($p<0.01$). According to LSTs, all 182 LST-Gs with a non VN pit pattern were intraepithelial neoplasias and SM-minute Ca cases. In 22 SM-deep Ca cases of LSTs, all 11 LST-Gs showed a type VN pit pattern, while only 2 cases in 11 LST-NGs showed a type VN pit pattern. There was significant relationship between subtypes and pit pattern in submucosal deep invasion of LSTs ($p<0.01$).

Conclusion: We suggest that the treatment for early-stage colorectal tumors greater than 20mm should be determined on the basis of the morphology and pit pattern by magnification colonoscopy. It is necessary to consider surgical resection for most of depressed and sessile polypoid-types because of the high rates of submucosal deep invasion. According to LSTs, LST-Gs with a type non VN pit pattern are possible to allow of endoscopic piecemeal mucosal resection because of absence of SM-deep Ca cases, while LST-NGs should be considered a definite indication for ESD and it is necessary to obtain en-bloc specimens for precise histological assessment, because a few SM-deep Ca cases with a type non VN pit pattern cannot be correctly diagnosed despite of using magnification endoscopy.

Disclosure: Nothing to disclose

P0191 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION FOR NOVICE ENDOSCOPISTS: THE UTILITY OF SUBMUCOSAL POCKET CREATION USING A TRACTION DEVICE

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Introduction: Endoscopic submucosal dissection (ESD) evolved as a method for en bloc resection of large early-stage gastrointestinal tumours for accurate histopathological evaluation in Japan. Colorectal endoscopic submucosal dissection (ESD) can be technically difficult for various reasons, such as submucosal fibrosis. A thin muscular layer can lead to increased perforation rates and longer procedure times. Novel strategies, such as the submucosal pocket creation method, have been reported to overcome these difficulties. Additionally, we recently introduced a new technique, submucosal pocket creation using a traction device (TD). This device is designed to be fixed with clips on the free edges of a mucosal overlay to deflect the diseased mucosa away from the dissection plane during submucosal dissection. When colorectal ESDs are initially performed, we use this technique to facilitate a safe and efficient procedure.

Aims and Methods: We aimed to evaluate the utility of submucosal pocket creation using the TD during colorectal ESD as required by trainee endoscopists. At the Cancer Institute Hospital of Japanese Foundation for Cancer Research from January to March 2018, we retrospectively investigated outcomes of 82 colorectal ESDs performed by 2 groups of endoscopists (A and B). Group A comprised 5 endoscopists with less than 50 cases of colorectal ESD experience and group B comprised 5 endoscopists with more than 500 cases of ESD experience.

Results: There were few practical differences in terms of therapeutic outcomes between the 2 groups. In contrast, the rate of using the TD in group A was significantly higher than that in group B. The details are presented in the table.

	Group A (n = 63)	Group B (n = 19)
Rate of using the TD (%)	41.2 (26/ 63)	21.1 (4/ 19)
Size of specimen (mm)	33 (15–70)	35 (25–70)
Rate of en bloc resection (%)	100 (63/ 63)	100 (19/ 19)
Median time of the procedure (min)	51.0 (18–165)	40.0 (5–190)
Perforation (%)	1.6 (1/63)	0 (0/ 19)
Clinically significant bleeding (%)	1.6 (1/63)	0 (0/ 19)

Conclusion: The technique of submucosal pocket creation using TD for colorectal ESD enabled trainees to perform colorectal ESD effectively and safely even in the initial period when they were under the supervision of ESD experts.
[therapeutic outcomes]

Disclosure: Nothing to disclose

P0192 CLASSIFICATION OF NUCLEAR MORPHOLOGY OF EC FINDINGS IN COLORECTAL ENDOCYTOSCOPY

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Introduction: Endocytoscopy (EC) is a next-generation endoscopy that allows diagnostic imaging at 520× magnification. In the EC classifications, lesions diagnosed as EC3a vary extensively from adenoma to SM-m, including some lesions that are unsuitable for endoscopic treatment. Therefore, to improve the accuracy of assessing the depth of invasion based on the EC classification, we investigated the presence or absence of 2 factors; high degree of nuclear enlargement (HNE) and multilayered nuclei (MNs), that are indicators of SM-m.

Aims and Methods: Between May 2005 and March 2018, we retrospectively examined 721 lesions diagnosed as EC2 or EC3, according to the EC classification. We subclassified EC 3a into 2 grades (low grade and high grade) and defined low grade as not recognizing both HNE and MNs, and high grade as for any of the 2 factors. We examined the diagnostic accuracy of SM-m based on this EC3a subclassification. In addition, we compared the diagnostic ability of EC for SM-m with that of other modalities; narrow-band imaging (NBI) and pit pattern.

Results: The sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and positive likelihood ratio for the diagnostic accuracy of the EC3a subclassification were 90.4%, 91.5%, 81.0%, 96.0%, 91.2%, and 10.7 ($p<0.001$). Diagnostic performance for predicting SM-m or worse among EC, NBI and pit pattern is as follows: The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy about EC were 96.8%, 92.4%, 96.6%, 92.8%, 95.4% respectively. On the other hand, Those of NBI were 98.6%, 52.2%, 83.7%, 93.9%, and 84.6%, and pit pattern were 96.1%, 83.3%, 93.4%, 89.7%, 92.4%, respectively.

Conclusion: From the EC findings, the presence of HNE, and MNs are important risk factors for SM-m or worse outcomes. Furthermore, the EC3a subclassification taking account of these findings could be effective for the diagnosis of SM-m or worse.

Disclosure: Nothing to disclose

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P0193 EARLY-STAGE COLORECTAL PROTRUDED TUMOR WITH DEPRESSION MAY ORIGINATE FROM "DE NOVO" CANCER

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Introduction: It is widely accepted that the majority of colorectal cancers develop through polypoid growth. However, recent studies have shown that depressed tumors also contribute to the development of colorectal cancers. According to careful observation during colonoscopy, a protruded tumor with depressed morphology at the top of the lesion is sometimes detected and it is difficult to diagnose and treat it precisely. The present study aimed to evaluate the importance of early-stage colorectal protruded tumors with depression.

Aims and Methods: We analyzed clinicopathological findings for 2108 early-stage colorectal protruded sessile tumors excluding pedunculated types, resected endoscopically or surgically (2013 low/high-grade intraepithelial neoplasias and 95 submucosal invasive carcinomas) after observation by magnification chromoendoscopy. They were classified into 2 subtypes according to depression at the top of a lesion: 14 cases with depression and 2094 cases without depression.

Results: All 14 protruded tumors with depression were submucosal invasive carcinoma (SM-Ca) cases, and the rates of SM-Ca cases in them were significantly higher than those in protruded tumors without depression (81/2094, 4%; $p<0.01$). In SM-Ca cases, the tumors with depression (11.3 ± 2.9mm in diameter) were significantly smaller than those without depression (18.8 ± 9.2mm; $p<0.01$). According to adenomatous glands in the tumors, all 14 SM-Ca tumors with depression had no adenomatous glands, and the rates of cases containing adenomatous glands in them was significant lower than those in tumors without depression (44/81, 54%; $p<0.01$). According to the bases of SM-Cas, all 14 tumors with depression showed a type I pit pattern surrounding depression, which suggests that the bases are covered with normal mucosa. On the other hand, all 81 tumors without depression showed type III, IV or V pit patterns, which suggests that the bases are composed of neoplastic glands. There was significant relationship between the presence of depression and histology of the bases of protruded SM-Cas ($p<0.01$).

Conclusion: Our findings suggest that the treatment for early-stage colorectal protruded sessile tumors should be determined on the basis of the detection of depressed morphology and pit pattern diagnosis by magnification colonoscopy. It is necessary to consider surgical resection for the protruded tumors with depression, because they are all submucosal invasive carcinoma cases. Also, they may originate from what we call de novo cancers, depressed-type tumors, because all their cases are submucosal invasive carcinomas regardless of their small size and have no adenomatous glands and moreover their bases are covered with normal mucosa. Therefore, we should always pay attention to protruded tumors with depression during colonoscopy.

Disclosure: Nothing to disclose

P0194 CLINICOPATHOLOGICAL FEATURES OF LOCAL RECURRENCE CASES RESECTED BY JUMBO FORCEPS BIOPSY USING NARROW BAND IMAGING ENDOSCOPY IN PATIENTS WITH DIMINUTIVE POLYPS

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Introduction: Cold forceps polypectomy (CFP) is often used to remove diminutive colorectal polyps. It does not induce thermal damage to tissue, and therefore has few complications such as postoperative bleeding and perforation. Other advantages are that it can be implemented using routine biopsy techniques, and the resected tissue can be recovered easily and reliably after resection. In addition, jumbo biopsy forceps are considered superior to standard forceps for removing colorectal polyps. The observation to check the margin of resected regions using narrow band imaging (NBI)-enhanced endoscopy can also improve complete resection rate. However, in such cases, we sometimes experience local recurrence cases, the issue of features of them have not been clarified in detail.
Aims and Methods: In this study, we examined the clinicopathological features of locally recurrent lesions after jumbo forceps biopsy assisted by NBI endoscopy for patients with diminutive polyps. This multicentre, prospective, single-arm observational study was conducted at 11 institutes of the National Hospital Organization in Japan between January 2015 and September 2016. Patients aged 20–75 years with diminutive polyps ≤5 mm were enrolled. A total of 503 patients were prospectively assessed, and 1015 polyps were resected. In addition, a total of 955 lesions were resected in the 471 patients who were followed up 1 year after CFP to examine the polypectomy sites for local recurrence (follow-up rate; 94.1%). We analysed the local recurrence rate, clinicopathological characteristics of primary polyps and local recurrent polyps, as well as resection rates and adverse events.
Results: Local recurrence occurred in 20 (2.1%) cases of the 955 lesions subjected to 1-year follow-up. The patients consisted of 14 (70%) men and 6 (40%) women with a median age of 67.5 years. The primary polyp morphologies were: 0-Is lesions in 17 (85%) cases, 0-IIa lesions in 2 (10%), and a 0-Isp lesion in 1 (5%) case. The mean size of the primary polyps was 3.9 ± 0.9 mm. The number of resected primary polyps in the right and left colon were 12 (60%) and 8 (40%) cases, respectively. The histological diagnoses of the primary resected polyps were adenomas in all cases. The complete resection rate was 100% (20/20). The rate of one-bite polypectomy was 55% (11/20). Immediate bleeding occurred in 1 (5%) case; delayed bleeding and perforation were not observed. The mean size of local recurrent polyps was 1.5 ± 0.6 mm and all were less than 3 mm in size. Re-CFP successfully managed local recurrent polyps in all cases, and the rate of one-bite polypectomy for local recurrent polyps was 95% (19/20). No adverse events occurred in any of the cases. The histological diagnoses of local recurrent polyps were adenomas in all cases.
Conclusion: The local recurrence rate after CFP using jumbo biopsy forceps assisted by NBI endoscopy for diminutive polyps was acceptable (2.1%). Even if local recurrence occurred, the size would be small and it could be treated using re-CFP.
Disclosure: Nothing to disclose

P0195 LONG-TERM OUTCOMES AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION WITH THE STAG BEETLE KNIFE JR FOR EARLY COLORECTAL NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for treating early colorectal neoplasms, and an insulation-tipped knife, hook knife, flush knife, or dual knife is conventionally used to perform ESD. However, because these devices are used without fixation to the target tissue, there is the potential risk of adverse events due to an unexpected incision or perforation. To reduce the risk of adverse events associated with a conventional knife when performing ESD, we used a scissors-type stag beetle (SB) knife Jr, which maintains an adequate dissection layer and prevents unexpected muscular layer injury. We previously reported that performing colorectal ESD with the SB knife Jr is easy, safe, and technically efficient. However, there is a need for more long-term clinical data to establish the full advantages of colorectal ESD with the SB knife Jr, with respect to favorable survival rates and very low recurrence rates.
Aims and Methods: The aim was to evaluate the long-term outcomes of ESD performed with the SB knife Jr for early colorectal neoplasms. ESD was performed for 163 lesions in 151 patients (male:female ratio = 78:73; mean age = 69 years) between October 2010 and March 2015. Data for 137 lesions in 126 patients (84.1%) who were confirmed dead or had follow-up for more than 3 years were identified and analyzed. The en bloc resection rate, complete resection rate, curative resection rate, resected tumor size, procedural time, complications, and long-term outcomes, including local and distant recurrence rates, and survival rates (3/5-year overall survival [OS] and 3/5-year disease-specific survival [DSS]) were evaluated. The survival rates were analyzed for the entire study cohort, and the local and distant recurrence rates were analyzed for the cohort that underwent curative resection or those who were observationally managed with non-curative resection.
Results: The patients' mean age was 68 ± 10 years, and the male:female ratio was 67:59. On histopathology, the prevalence rate for tubular adenoma was 29.9% (41/137), with Tis in 46.7% (64/137), T1a in 10.2% (14/137), and T1b in 13.1% (18/137). The mean resected tumor size was 32.5 ± 16.5 mm, and the median procedure time was 80 (range, 15 - 420) min. The en bloc resection rate, complete resection rate, and curative resection rate were 97.8% (134/137), 94.2% (129/137), and 83.9% (115/137), respectively. No perforations occurred during the procedure. The delayed bleeding rate was 3.6% (5/137); rectal stricture occurred in one patient (0.7%) and was treated conservatively.
For long-term outcomes, the local recurrence rate was 1.6% (2/123), and no distant recurrence was observed in the recurrence analysis cohort. On survival analysis (median follow-up period: 52.8 [range, 5.5–89.3] months), the 3/5-year OS and DSS rates were 94.2%/92.1% and 99.0%/99.0%, respectively. 1 patient (0.7%, 1/137) died of colorectal cancer, and 9 (6.6%, 9/137) died of other diseases.
Conclusion: ESD provides good long-term outcomes for patients with early colorectal neoplasms. Even though the local recurrence rate is very low, patients should be monitored after ESD.
Disclosure: Nothing to disclose

P0196 MUCOSAL FLATTENING-ASSISTED COLONOSCOPY (FAC) FOR IMPROVING ADENOMA DETECTION RATE: A SYSTEMATIC REVIEW WITH PAIRWISE AND NETWORK META-ANALYSIS

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Introduction: The adenoma detection rate (ADR) has emerged as the most important quality measure in colonoscopy, as it predicts the risk of interval cancer after colonoscopy. Improving ADR is the central focus of the current quality movement in colonoscopy. The fold flattening devices could ameliorate the ADR.
Aims and Methods: The aim of the study was to compare the efficacy of mucosal flattening assisted colonoscopy vs standard colonoscopy to improve the adenoma detection rate in patients undergoing colonoscopy. Secondary outcomes evaluated were intubation rate, time of endoscopy, number of polyps found, number of advanced adenomas, number of cancer, safety of procedures. We searched, from inception to April 7 2018. Search terms included "adenoma detection rate AND improving colonoscopy"; "Adenoma detection rate AND (Endo Cuff OR Endo Vision OR Endo Rings)"; "adenoma detection rate AND improving device". All references from the reviewed articles were searched for any other articles that may have been missed. Randomized Clinical Trials (RCT) comparing flattening assisted colonoscopy to standard colonoscopy, for any indication, were included in the analysis. Data were analyzed by Intention To Treat and Per Protocol. Pooling methods was initially pairwise; potential effect modifiers were evaluated and than network meta analysis, was conducted by STATA software using the mvmeta command; relative ranking was evaluated by surface under the cumulative ranking curves (SUCRA) routine.
Results: Starting from 138 abstracts initially evaluated, a total of 10 articles were included. The ADR of a total of 6407 patients (Endocuff 2986, EndoRing 354 and Standard 3067) were evaluated. Overall, using Endocuff, ADR improved with an OR of 1.36 (c.l.95% 1.12 to 1.60) p = 0.001. A significant Heterogeneity was present: Overall I-square 60.0% p = 0.01. Sub grouping studies in 3 level of ADR in the SC, (< = 25%; >25% and <=40%, >40%) the OR between the 2 treatment arms are significantly different.In the studies with higher ADR no difference was present between Endocuff and SC: OR 1.07 (c.l95% 0.85 to 1.34) p = 0.184, in lower ADR, OR = 1.85 (c.l95% 1.35 to 2.53) p = 0.000; intermediate ADR, OR = 1.43 (c.l.95% 1.13 to1.77) p = 0.014. These results are similar for both PP and ITT analysis. In the network meta analysis ADR Log odd ratio comparing SC vs Endocuff was 0.29 [c.l.95%.11 to.47] p = 0.001; Log odd ratio standard colonoscopy vs Endo Ring was -0.018 [c.l.95% -.42 to.38] p = 0.929. Endocuff vs EndoRing in direct (log OR = −0.33 [c.l.95% -.88 to.22] p = 0.24 and Indirect comparison (log OR = −0.29 [c.l.95% -.98 to.41] p = 0.42 provide not significant difference probably due a beta error (Figure). Testing for inconsistency was not signicant: $chi^2(2) = 0.01$; Prob > $chi^2 = 0.9966$. Endocuff device reach the higher (SUCRA) percentage of effectiveness: 92.3 and the higher probability to be the best 84.8%. The probability to be the first or second best was 99.9%
Conclusion: Endocuff devices improve ADR overall by 1.33 - 1.34 both on per protocol and by intention to treat analysis. The improvement was not significant

when the ADR was greater than 40% using standard colonoscopy. Endocuff was clinically and statistically relevant when ADR with standard colonoscopy is lower than 25%. (O.R. 1.87 ITT analysis). About Endoring no definitive conclusion could be drawn due to the scarce literature available, although the preliminary analysis did not shown an advantage when was compared to standard colonoscopy. Direct and indirect comparison between Endoring vs Endocuff did not provide definitive conclusions
Disclosure: Nothing to disclose

P0197 FORWARD-VIEWING ENDOSCOPE FOR ERCP IN PATIENTS WITH BILLROTH II GASTRECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: The forward-viewing endoscope has been increasingly used to perform endoscopic retrograde cholangiopancreatography (ERCP) in patients who underwent Billroth II gastrectomy.
Aims and Methods: This study intended to assess efficacy and safety of the forward-viewing endoscope for ERCP in Billroth II gastrectomy patients compared with conventional side-viewing endoscope using a systematic review and meta-analysis. A systematic review was conducted for studies that evaluated the outcomes of ERCP for patients with Billroth II gastrectomy. Random-effect model meta-analyses with subgroup analyses were conducted. The methodological quality of the included publications was evaluated using the risk of bias assessment tool for non-randomized studies. The publication bias was assessed.
Results: In total, 25 studies (1 randomized, 18 retrospective, 1 prospective, and 5 case series studies) with 2446 patients (499 forward-viewing and 1947 side-viewing endoscopes) were analyzed. The pooled afferent loop intubation rate was higher with the forward-viewing endoscope (90.3%, 95% confidence interval (CI):85.6–93.6% vs. 86.8%, 95% CI:82.8–89.9%). The pooled selective cannulation rate was higher with the side-viewing endoscope (92.3%, 95% CI:88.0–95.2% vs. 91.1%, 95% CI:87.2–93.9%). The pooled bowel perforation rate was higher with the side-viewing endoscope (3.6%, 95% CI:2.3–5.7% vs. 3.0%, 95% CI:1.7–5.3%). The pooled pancreatitis rate was higher with the forward-viewing endoscope (5.4%, 95% CI:3.6–8.0% vs. 2.5%, 95% CI:2.3–5.7%). The pooled bleeding rate was higher with the forward-viewing endoscope (3.0%, 95% CI:1.6–5.5% vs. 2.0%, 95% CI:1.4–3.0%). The heterogeneity among the studies was not significant. The publication bias was minimal.
Conclusion: This meta-analysis indicates that the forward-viewing endoscope is as safe and effective as conventional side-viewing endoscope for ERCP in patients with Billroth II gastrectomy.
Disclosure: Nothing to disclose

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P0198 LIVER HYDATID CYST - WHEN DO WE NEED BILIARY STENTING IN MANAGEMENT PROTOCOL. A STUDY OF 56 CASES FROM A TERTIARY REFERRAL CENTRE IN INDIA

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Introduction: Hydatidosis, a zoonotic infection, is due to the larval stage of the tapeworm Echinococcus (E.). The outmost layer of a cyst, the ectocyst or pericyst, is formed by compressed and fibrotic host tissue and may become calcified, whereas inner layers are of parasitic origin and act as a germinal centre. A cyst may or may not contain daughter cyst(s). Secondary echinococcosis can develop in the same or other organs. Most patients will have a single organ involvement in primary echinococcosis. In adults the liver represents the prevalent site (50–70%) and lungs are the second commonest site (10–30%). Rupture into the biliary tree is the commonest complication (up to 25% of cases) and can be associated with biliary obstruction by daughter cysts.
Aims and Methods: We aimed to identify the subset of patients suffering from liver hydatid cysts who will require ERCP with biliary stenting in the management protocol.
We analyzed our data in tertiary care urban centre from October 2010 to March 2017 for liver cysts. Total 56 patients were identified with liver cysts that were operated, out of which 43 had liver hydatid cyst. Who were operated for the same. As a part of protocol all our patients underwent Cystectomy - *non-radical* alternative. It comprises cyst de-roofing and cyst content evacuation without removal of the pericyst, plus or minus omentoplasty and whenever required they were subjected to ERC (Endoscopic retrograde cholangiography) and stenting of biliary system. We have opted for surgery after routine protocol of Albendazole pre operatively except the patients who presented with cholangitis due to cyst internal rupture. None of the patients in our series was of type CE 1 (WHO Classification).
Results: Out of 43 patients we found biliary communication (on imaging, preoperatively) in 18 patients, out of which we required ERC in 11 (25.6%) patients postoperatively. 2 patients were presented with cholangitis and jaundice preoperatively so they were subjected to ERC preoperatively. Total 9 patients had demonstrable biliary communication on table (20.9% of total). A factor which was found significant in our series was distance from hilum. ERC group patient had average distance of 1.66 cm vs. 4.35 cm in non-ERC group. Size of cyst (10.79cm vs. 9cm), Serum alkaline phosphatise level (103.88 vs. 62.13, normal range up to 80), and Bilirubin levels (1.54 vs. 0.75) were statistically insignificant. ERC group patient had average hospital stay of 9.22 vs. 3.2 days for non ERC group. 1 patient had combined liver spleen hydatid cyst. We have 1 mortality in our series (elderly patient presented to us with severe cholangitis and sepsis with internal rupture of cyst) he was operated upon after ERC but did not survive due to multiorgan failure. None of the patients had recurrence in our present series, in average follow up of 3 months to 7 yrs. 1 patient had fluid collection which was treated with percutaneous drainage.
Conclusion: Cystectomy - a non radical alternative of hydatid disease is practical and feasible approach.
ERC is needed in patents with biliary communication and patients with cholangitis due to rupture in the biliary tree.
Majority should be subjected to ERC post operatively when we identify bile in the cyst.
Preoperative ERC only of patients with cholangitis.
Cyst which is near to hilum has more chances of biliary communication rather than large peripheral cysts.
However larger studies are needed to reciprocate the same findings. Morbidities are higher in internal rupture cases.
Disclosure: Nothing to disclose

P0199 COMPARISON OF DEXMEDETOMIDINE WITH MIDAZOLAM VERSUS MIDAZOLAM ALONE FOR SEDATION DURING ERCP: A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Dexmedetomidine (DEX) is a highly selective α2-adrenoceptor agonist that elicits sedative and analgesic effects in humans. Recently, DEX has been used for endoscopic sedation. However, the usefulness and safety of DEX for sedation during endoscopic procedure has not been fully evaluated.
Aims and Methods: The aim of this study was to compare the efficacy and safety of standard sedation using midazolam (midazolam group) with combination sedation using DEX and midazolam (midazolam+DEXgroup). A prospective, observational study was conducted in 89 patients who underwent ERCP. Written informed concents were obtained from all patients before enrollment. Satisfaction score among patients were evaluated with Visual Analogue Scale. Body motion during sedation (1–5; 5 represents discontinuance of procedure), vital signs and the recovery time were assessed.
Results: 46 patients were administrated with midazolam alone (midazolam group) and 43 patients were administrated with DEX and midazolam (midazolam+DEX group). The baseline characteristics and procedure time were similar between the 2 groups. Body motion was significantly lower in midazolam+DEX group than in midazolam group (1.50 vs. 2.58, $p<0.0001$), Satisfaction score, recovery time, respiratory depression, hypotension and bradycardia were not significantly different between the 2 groups.
Conclusion: The present study suggests that a combination of DEX and midazolam is as safe as midazolam alone for sedation during ERCP. This combination provides less body motion than midazolam alone without extending recovery time.
Disclosure: Nothing to disclose

P0200 UTILITY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR THE MANAGEMENT OF SYMPTOMATIC PANCREAS DIVISUM IN CHILDREN: EXPERIENCE FROM A SINGLE CENTER IN CHINA

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Introduction: Pancreas divisum (PD) is the most common congenital anomaly of the pancreas. Most PD individuals are asymptomatic, but a few may present symptoms in the form of recurrent acute pancreatitis (RAP), chronic pancreatitis (CP) or pancreatic-type pain. Currently, most PD-related studies published in the literature have been limited to adults. Clinical data in pediatric PD are relatively insufficient. However, it is important to early diagnose and timely treat symptomatic PD, especially in children for the better clinical outcomes.

Aims and Methods: To estimate the safety and efficacy of endoscopic retrograde cholangiopancreatography (ERCP) for the treatment of symptomatic PD in children. We retrospectively analyzed patients of symptomatic PD(s-PD) who were younger than 18 years old from January 2011 to December 2017 in our institute. The s-PD included PD with RAP (RAP group) and PD with CP (CP group). All children were treated with ERCP as a main therapy. During an ERCP, minor endoscopic sphincterotomy combined with dorsal duct stenting(Mi-ESCS) was performed for complete PD (CPD) patients, and Bi-papilla ESCS (Bi-ESCS) was performed for incomplete PD (IPD) patients. ERCP-related data, complications, clinical outcomes, and follow-up data were collected and analyzed. Long-term follow up was carried out to observe occurrence of developing CP in RAP group, children's recovery, as well as their weight, growth and intelligence.
Results: A total of 312 pediatric ERCPs were performed for 157 children during this period. Of which 34 were PD cases, among which 30 were s-PD. The endoscopic detection rate of PD was 21.7%. Of the 30 s-PD patients, 19 were PD with RAP, among which 17 were CPD and 2 were IPD. The other 11 were PD with CP, among which CPD and IPD were 7 and 4 respectively. A total of 84 therapeutic ERCPs were performed, among which 44 were for RAP group and 40 for CP group. The success rate of cannulating the minor papilla was 97.6% (82/84). The total response rate to endotherapy was 93.3%, with that of 100% (19/19) in RAP group and 81.8% (9/11) in CP group. The 2 patients with no response to endotherapy in CP group underwent surgery. The mean interval of changing pancreatic dorsal duct stent is 3 months (from 2 to 6 months). The mean number of changing dorsal duct stent was 2.3 in RAP group and 3.6 in CP group. ERCP-related complications were mild with a rate of 7.1% (6/84), all of which were managed conservatively. During follow up from 3 to 84 months (mean 38.1 months), all patients had pain relief. In RAP group, 2 patients developed CP with a rate of 10.5%, others showed no more dilation of dorsal ducts. In CP group, all patients had pain relief with few onset of acute pancreatitis, however, they demanded multiple repeated changing dorsal stents with no obvious improvement in pancreatic duct. In both groups, children presented normal in weight, growth and intelligence.
Conclusion: The techniques of Mi-ESCS and Bi-ESCS with ERCP are safe and effective methods to manage s-PD in pediatric patients. It seems very important for such children to undergo endoscopic interventions as early as possible in order to avoid developing CP. Children of PD with CP may present asymptomatic with long term ERCP therapy.
Disclosure: Nothing to disclose

P0201 PANCREATIC DUCT PERFORATION DURING GUIDEWIRE CANNULATION IN THERAPEUTIC BILIARY ERCP

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Introduction: Guidewire (GW) cannulation of the common bile duct (CBD) in ERCP is becoming increasingly widespread. Inadvertent GW passage into the main pancreatic duct (MPD) is relatively common. As a consequence, sometimes involuntary perforation of the MPD occurs.
Aims and Methods: We aimed to evaluate the rate of MPD perforation after unintentional GW access to the pancreas in a series of ERCPs intended for CBD cannulation.
A prospective study was conducted. Endoscopist-controlled GW cannulation was performed in order to gain the CBD. Several marketed types of 0.025" straight tip GWs were used. GWs were loaded into a 4.4 Fr distal tip sphincterotome. When the GW first entered the MPD a small amount of cotrast was injected to verify its correct position. If the GW was stuck in some pancreatic sidebranch or perforation occurred 2 gentle attempts were made to place the GW correctly in the MPD. If this was unsuccessful, the GW was withdrawn from the pancreas. When posible, pancreatic stenting was performed always, as recommended [1]. A straight plastic pancreatic stent, 5 F and 4 cm, without internal flaps was always inserted when the GW was properly positioned along the MPD. Spontaneous expulsion was expected due to lack of internal flaps. Prophylactic NSAIDs were administered to all patients
Results: 174 patients with naïve papilla needing ERCP biliary drainage were included. Inadvertent GW cannulation of the pancreas ocurred in 73 (42.5%) patients. In 55/73 (75.34%) the GW was properly placed along the MPD. MPD perforation was observed in 12/73 (16.4%). In 9 out of these 12 patients the GW could be reinserted to a proper position wihin the MPD. 6 out of these 12 patients had a visible pancreatic contrast leakage. Finally in total, pancreatic stents could be inserted in 64/73 (87.6%) patients having GW cannulation of the pancreas. Post-ERCP pancreatitis rate was 1/64 (1.56 %) in the group of successful pancreatic stenting and 1/9 (11%) in the group in which the GW did not enter properly the MPD and stenting was not posible ($p<0.05$). Both pancreatitis were mild in severity. Pancreatitis was not observed in patients with MPD leakage in whom a pancreatic stent could be placed later on.
Conclusion: In this study a 16.4% rate of MPD perforation was seen after unintentional GW passage into the pancreas. If pancreatic stenting is posible, stents appear to revert damage caused by inadvertent GW perforation. Future improvements to reduce this perforation rate could include comparison between angled vs straight tip GWs and development of GWs with enhanced tip flexibility.
Disclosure: Nothing to disclose

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P0202 EUS-GUIDED PANCREATIC DRAINAGE: A STEEP LEARNING CURVE

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Introduction: Endoscopic ultrasound guided biliary drainage (EUS-PD) is an efficacious, safe option for patients with pancreatic duct obstruction who fail conventional endoscopic retrograde cholangiopancreatography (ERCP). The procedure involves accessing the pancreatic duct using EUS, creating a fistulous tract, and deploying a decompressing stent across the tract. It is a technically challenging procedure, requiring advanced skills in EUS and ERCP. The aim of this study was to define the learning curve for EUS-PD.
Aims and Methods: Consecutive patients undergoing EUS-PD by a single operator with training in therapeutic endosonography, were included from a dedicated registry from May 2003 to September 2017. Demographics, procedure info, adverse events, and follow-up data were collected. Non-linear regression and CUSUM analyses was conducted for the learning curve. Technical success was defined as successful stent placement. Clinical success was defined as resolution of procedural indication.
Results: 55 patients were included (54%M, mean age 58 years). The majority of patients had benign disease (n = 51, 91%): chronic pancreatitis n = 26, anastomotic stricture n = 16, divisum n = 6. The remaining 5 patients had malignant obstruction. 25 patients (44%) had altered anatomy. Technical success was achieved in 47 patients (84%). Stent placement was transluminal in 43 patients (92%) and transpapillary in 4 (9%), antegrade in 36 patients (77%) and retrograde in 11 (23%). All stents were plastic except 1 which was metal. Clinical success was achieved 46/47 (98%) patients who achieved technical success. Adverse events were seen in 13 patients (6 of whom did not achieve technical success) and included bleeding requiring embolization (n = 5), bleeding treated with clips peri-procedurally (n = 1), pancreatitis (n = 5), and a pancreatic fluid collection drained via EUS (n = 2). Median procedure time was 80 mins (range 49–159 mins). CUSUM chart shows 80 minute procedure time was achieved at the 27th procedure indicating efficiency. Apart from 2 outliers, procedure durations further reduced with consequent procedures from 40th onwards reaching a plateau which could be the plateau indicating mastery (nonlinear regression $p<0.0001$)
Conclusion: Endoscopists experienced in EUS-PD are expected to achieve a reduction in procedure time over successive cases, with efficiency reached at 80 minutes and a learning rate of 27 cases. Continued improvement is demonstrated with additional experience, with plateau indicating mastery suggested at the 40th case. EUS-PD is probably one of the hardest therapeutic endosonographic procedure to learn and master.
Disclosure: Michel Kahaleh MD: has received grant support from Boston Scientific, Fujinon, EMcison, Xlumena Inc., W.L. Gore, MaunaKea, Apollo Endosurgery, Cook Endoscopy, ASPIRE Bariatrics, GI Dynamics, NinePoint Medical, Merit Medical, Olympus and MI Tech. He is a consultant for Boston Scientific, Xlumena Inc., Concordia Laboratories Inc, ABBvie, and MaunaKea Tech. -Amy Tyberg MD is a consultant for EndoGastric Solutions. - Prashant Kedia MD is a consultant for Boston Scientific, Endogastric solutions and Apollo Endosurgery. All other authors have nothing to disclose.

P0203 EUS-GUIDED GALLBLADDER DRAINAGE: A LEARNING CURVE MODIFIED BY TECHNICAL PROGRESS

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Introduction: Endoscopic ultrasound-guided gallbladder drainage (EUS-GLB) is an efficacious, safe option for patients with cholecystitis who cannot undergo cholecystectomy. The procedure involves accessing the gallbladder using EUS, creating a fistulous tract, and deploying a stent across the tract. It is a technically challenging procedure, requiring skills in EUS, fluoroscopy, and stent deployment. The aim of this study was to define the learning curve for EUS-GLB.
Aims and Methods: Consecutive patients undergoing EUS-GLB by a single operator were included from a prospective registry from January 2012 to July 2017. Demographics, procedure info, post-procedure follow-up data, and adverse events were collected. Non-linear regression and CUSUM analyses was conducted for the learning curve. Clinical success was defined as resolution of cholecystitis post-procedure.
Results: 48 patients were included (58%M, mean age 76 years). 20 patients (42%) had malignant cholecystitis, the remainder had benign disease. Technical success was 100%. Most patients had lumen-apposing metal stents (LAMS) (15mm, n = 29, 60%; 10mm, n = 8, 17%), 25 of which were cautery-enhanced. The remaining patients had FCSEMS (n = 9, 19%) or plastic stents alone (n = 2, 4%). 1 patient required bridging stents placement. The majority of stents were transduodenal (n = 28, 58%), the remaining transgastric (n = 15, 31%) or transjejunal (n = 4, 8%), and 1 patient had 2 stents placed from transgastric and

transduodenal position during the same procedure. Clinical success was achieved in 36 (86%) of patients. Of the remaining 12, 7 were lost to follow-up and 5 had persistent cholecystitis. 9 patients (19%) had adverse events including bleeding (n = 4), liver abscesses (n = 2), and hypotension post procedure. 2 patients passed away post-procedure due to respiratory failure and peritonitis secondary to ruptured gallbladder wall. 6 patients required re-intervention for stent occlusion with repeat endoscopy or surgical cholecystectomy. The median procedure time was 41 minutes (range 16–121 mins). CUSUM chart shows 41 minute procedure was achieved at the 19th procedure hence indicating efficiency. Procedure durations further reduced with the last 10 procedures being 20 minutes or under (nonlinear regression $p < 0.0001$) indicating continued improvement with experience. This also may be due to the introduction of cautery-enhanced LAMS.
Conclusion: Endoscopists experienced in EUS-GLB are expected to achieve a reduction in procedure time over successive cases, with efficiency reached at 41 minutes and a learning rate of 19 cases. Continued improvement is demonstrated with additional experience and the introduction of cautery-enhanced LAMS.
Disclosure: Michel Kahaleh MD: has received grant support from Boston Scientific, Fujinon, EMcison, Xlumena Inc., W.L. Gore, MaunaKea, Apollo Endosurgery, Cook Endoscopy, ASPIRE Bariatrics, GI Dynamics, NinePoint Medical, Merit Medical, Olympus and MI Tech. He is a consultant for Boston Scientific, Xlumena Inc., Concordia Laboratories Inc, ABBvie, and MaunaKea Tech. -Amy Tyberg MD is a consultant for EndoGastric Solutions. - Prashant Kedia MD is a consultant for Boston Scientific, Endogastric solutions and Apollo Endosurgery. - All other authors have nothing to disclose.

P0204 SINGLE-OPERATOR CHOLANGIOSCOPY REDUCES PATIENT RADIATION EXPOSURE IN THE MANAGEMENT OF DIFFICULT BILE DUCT STONES AND INDETERMINATE BILE DUCT STRICTURES: A SINGLE-CENTRE, HISTORICAL COMPARISON STUDY

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Introduction: Endoscopic Retrograde Cholangio-Pancreatography (ERCP) is a well-established endoscopic procedure for treatment or palliation of a great variety of hepatobiliary and pancreatic diseases, routinely performed using X-ray fluoroscopy. Due to extended fluoroscopy times and increased number of images, patient radiation doses can be high, especially in complex cases. A new digital single-operator cholangioscopy (D-SOC) system (SpyGlass Digital System, Boston Scientific), allows direct visualization of the ducts, targeted biopsies, visual wire manipulation and difficult stone lithotripsy in a radiation-free manner. We investigated whether the SpyGlass platform used adjunctively to ERCP may actually reduce patient radiation exposure.
Aims and Methods: We retrospectively analyzed a prospective database of consecutive patients undergoing D-SOC following failure of ERCP either for difficult-to-treat biliary stones or indeterminate strictures. The overall patient radiation exposure outcomes in terms of Kerma Area Product (KAP), Fluoroscopy time (T) and the total number of films (F) were compared to a historical cohort of patients with difficult stones or indeterminate strictures exclusively managed by conventional ERCP before the era of D-SOC. All procedures were performed by a single, experienced operator
Results: Between 2016 and 2017, a total of 17 patients (10 males, 64 median years old) underwent successful D-SOC management of difficult biliary stones (n = 12) or indeterminate strictures (n = 5). The historical cohort comprised 20 patients (11 males, median 67 years,) with difficult-to-treat stones (n = 12) or indeterminate strictures (n = 8) who were successfully managed by repeat conventional ERCP between 2012 and 2015.
The median KAP, T and F in patients undergoing D-SOC were 11.8 $Gycm^2$, 4.2 min and 1.6 films respectively, compared with 17 $Gycm^2$, 5.8 min, and 2.6 films respectively in the historical ERCP cohort. Statistically significant differences ($p < 0.05$) were found for KAP and T.
Conclusion: Adjunct use of the new SpyGlass cholangioscopy platform appears to significantly reduce radiation exposure in patients with difficult stones or indeterminate strictures in whom conventional ERCP has failed.
Disclosure: Nothing to disclose

P0205 PREDICTIVE MODEL TO DETERMINE THE NEED OF REPEATING ERCP AFTER ENDOSCOPIC TREATMENT OF BILIARY LEAKS

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is the first-line procedure to iatrogenic biliary leaks approach. In patients who have undergone biliary stenting, the timing and optimal method (ERCP or esophagogastroduodenoscopy) of stent removal is controversial.
Aims and Methods: With the present study we aimed to evaluate ERCP efficacy in the treatment of biliary leaks and identify patients in whom repetition of ERCP may be unnecessary. We conducted a retrospective, unicentric analysis of all patients that underwent ERCP with sphincterotomy and biliary stent placement between 2008 and 2017 due to iatrogenic biliary leaks. All patients were submitted to reevaluation ERCP with removal of the stent(s). Factors associated with the *outcome*, resolution of the biliary leak and absence of another pathology in reevaluation ERCP, were identified.
Results: A total of 43 patients were included, 62.8% (n = 27) female, mean age 58.2 ± 17.2 years. The most common etiology of biliary leaks was laparoscopic cholecystectomy (56.8%) and the most common location the cystic duct stump (53.5%). Technical success was 93.3%, with resolution of the biliary leak in 92.9% of those. On multivariate analysis, elective iatrogenic procedure (OR = 209.1, 95% CI 2.18–2050.8), normal total bilirubin (OR = 138.9, 95% CI 1.19–1627.2), ERCP performed in ≤7 days (OR = 32.9, 95% CI 1.08–1004.8) and removal of the stent in ≤12 weeks (OR = 40.7, 95% CI 1.11–1634.9) were independently associated with resolution of the biliary leak and absence of another pathology ($p < 0.05$; $r^2 = 0.71$). The area under the ROC curve of these criteria for *outcome* prediction was 0.93 ($p < 0.001$). When ≥3 criteria were present (42.9% of patients), the model presented specificity of 100%, sensitivity of 58.1%, positive predictive value of 100% and negative predictive value of 45.8% in *outcome* prediction.
Conclusion: We identified criteria that allow selection of 43% of patients in whom repetition of ERCP after treatment of biliary leaks may be unnecessary. These patients can have their biliary stents removed by esophagogastroduodenoscopy, increasing safety and efficiency of healthcare resources utilization.
Disclosure: Nothing to disclose

P0206 EVALUATION OF ENDOSCOPIC SPHINCTEROTOMY WITH ANTITHROMBOTIC THERAPY

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Introduction: The rates of post endoscopic sphincterotomy (EST) bleeding range from 0.3 to 2.0% [1]. Although several studies reported that continuous antithrombotic therapy (ATT) was a risk factor for postoperative bleeding after endoscopic treatment, patients with a higher risk of thrombosis require continuous ATT to prevent thromboembolic events. C.-K. HUI, et al. reported that there was no significant difference in post-EST bleeding between patients who continued to take aspirin until the day of EST and patients who had their aspirin discontinued for 1 week before EST [2].
Aims and Methods: We retrospectively investigated the safety and feasibility of EST with continuous ATT. ERCPs were performed 1933 times from July 2012 to December 2017 at New Tokyo Hospital. Among them, 645 patients were performed with EST. The patients undergoing EST were categorized according to ATT. The bleeding rates were calculated and compared in each group.
Results: The overall rate of postoperative bleeding after EST was 3.9% (25/645). The patients were divided into the following 2 groups: no ATT (n = 365) and ATT (n = 280). ATT included discontinuous ATT (n = 68), continuous ATT (n = 212) subgroups. Furthermore, continuous ATT included continuous antiplatelet therapy (APT, n = 166), continuous anticoagulant therapy (ACT, n = 28), and continuous combination therapy (continuous CT [continuous APT + continuous ACT], n = 18) subgroups. The bleeding rate with ATT (6.1%) was significantly higher than that without ATT (2.2%) (p = 0.013). The bleeding rate with continuous ATT (6.2%) was similar to that with discontinuous ATT (7.4%) (p = 0.570). The bleeding rates were 6.0% in continuous APT, 7.1% in continuous ACT, and 0% in continuous CT. Transcatheter arterial embolization was required for one patient in no ATT group because of severe bleeding.
Conclusion: ATT was associated with post-EST bleeding. However, the bleeding rate with continuous ATT was not statistically different from that with discontinuous ATT. Therefore, continuous ATT administration may be acceptable for EST, although patients should be carefully monitored for possible bleeding.
Disclosure: Nothing to disclose

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P0207 IS THERE AN ASSOCIATION BETWEEN THE MAJOR PAPILLA MORPHOLOGY AND THE SIZE OF THE TERMINAL COMMON BILE DUCT? - A PROSPECTIVE COHORT STUDY

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Introduction: In endoscopic retrograde cholangiopancreatography (ERCP), the risk of adverse events during precut is increased when the terminal bile duct (tBD) is not dilated. Some studies suggest that the major papilla morphology, particularly its width is determined by the prominence of the supra- and intra-duodenal portion of the tBD.
Aims and Methods: The study aim was to assess if the terminal bile duct diameter can be determined by inspecting the major papilla morphology/width during duodenoscopy.
Between July 2017 and January 2018, in 3 hospitals, all consecutive patients with naïve papilla referred for ERCP were eligible for enrollment. The transverse diameter (tD) of the papilla was measured using a comparative measurement technique (biopsy forceps) and a novel software (validity and reliability tested). The papilla morphology was classified into 1 of 4 groups: non-proeminent, proeminent, bulging, distorted. The tBD's diameter was measured in the distal 1 cm (cholangiogram acquired in supine/prone) in a workstation, by an independent researcher. Main outcome was evaluated using a Pearson correlation.
Results: 137 patients were included; 57 males (41.61%), median age of 78 years (26–99). The median tD of the papilla was 6 mm (IQR = 3 mm) and the median tBD's diameter was 8.07 mm (IQR = 4.87 mm). Half (50%) of the papillas were non-proeminent (tBD median = 7.66mm; IQR = 4.473), 32.08% proeminent (tBD median = 8.05mm; IQR = 4.869), 12.26% bulging (tBD median = 8.978mm; IQR = 5.814) and 5.66% distorted (tBD median = 7.533 mm; IQR = 0.832); p[C2 = 2.237)] >0.6923. The correlation between tD and tBD diameters was 0.0245.
Conclusion: Despite what is suggested in the literature, the morphology and the width of the major papilla do not have any association with the diameter of the tBD, and consequently these 2 dimensions should not be taken into account when deciding for a cannulation technique.
Disclosure: Nothing to disclose

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P0208 FEASIBILITY OF A NEW SHORT-TYPE DOUBLE-BALLOON ENDOSCOPE WITH ADVANCED FORCE TRANSMISSION AND ADAPTIVE BENDING FOR PANCREATICOBILIARY INTERVENTION IN PATIENTS WITH SURGICALLY ALTERED ANATOMY: A PROPENSITY-MATCHED ANALYSIS

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Introduction: Recently, short-type double-balloon endoscopes (DBEs) for pancreaticobiliary interventions in patients with surgically altered anatomy have become available in many institutions. However, we previously demonstrated in a multicenter study that endoscopic retrograde cholangiopancreatography (ERCP) using a conventional short-type DBE is a lengthy procedure, requiring approximately 22 minutes to reach the target site and 56 minutes to complete ERCP-related interventions.[1] A new short-type DBE has been developed with a major focus on facilitating scope insertion to the target site for pancreaticobiliary interventions in patients with surgically altered anatomy.
Aims and Methods: We investigated the feasibility of this new short-type DBE by comparing it with a conventional DBE. Data from 885 ERCP procedures using balloon endoscopy were analyzed. We used propensity score matching to adjust for differences between patients who underwent ERCP procedures using the new short-type DBE versus the conventional short-type DBE. The outcomes of interest were the success rate of reaching the target site, the success rate of the pancreaticobiliary intervention, the insertion time required to reach the target site, the overall procedure time, the success rate of cannulation of the papilla of Vater, the time to cannulation of the papilla of Vater, and adverse events during or after the ERCP procedure.
Results: A total of 163 pairs of patients were selected on the basis of propensity score matching. The success rate of reaching the target site was 100% in both the new DBE group and the conventional DBE group (p = 1.0). The new DBE group had a significantly shorter insertion time required to reach the target site than the conventional DBE group (10 min vs. 14 min, p < 0.01). The success rate of the pancreaticobiliary interventions in the new DBE group was as high as that in the conventional DBE group (92% vs. 89% p = 0.35). The overall procedure time decreased from 62 min in the conventional DBE group to 55 min in the new DBE group (p = 0.26). Apart from choledochojejunostomy and pancreaticojejunostomy cases, the success rate of cannulation of the papilla of Vater in the new DBE group was higher than that in the conventional DBE group (96% vs. 87%, p = 0.10). No significant difference in the rate of adverse events was observed between the 2 groups.
Conclusion: A new short-type DBE allows faster insertion to the target site for pancreaticobiliary intervention in patients with surgically altered anatomy.
Disclosure: Nothing to disclose

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P0209 POSITIVE CORRELATION BETWEEN PANCREATIC PARENCHYMAL VOLUME AND PEP

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Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) remains the most common and serious adverse event associated with ERCP. PEP after initial ERCP was reported to have an incidence ranging from 10% to 15% in various studies, and the mortality rate was 0.11%. PEP is considered a high-priority adverse event.
Recently, preventative measures for PEP such as high-dose rectal diclofenac and pancreatic stent placement have been proposed as useful approaches. However, they may not be appropriate for all patients, given the risks involved. Therefore, in order to use these preventive methods more effectively, it is necessary to be able to easily stratify patients into the high- and low-risk groups for PEP.
The three major causes of PEP are patient-related factors, operator-related factors, and technique-related factors. It is difficult to predict the incidence of PEP because there are many potential factors in each category. We considered the importance of predicting PEP based on pre-ERCP findings because it may be possible to increase the safety of the endoscopic procedure.
In a previous study, the degree of pancreatic exocrine function showed a significant positive correlation (p < 0.001) when determined using the ^{13}C-labeled Breath Test and acinar cell area ratio. However, the risk associated with pancreatic parenchymal volume has never been examined as a risk factor for PEP. We hypothesized that a large pancreatic parenchymal volume would increase the risk of PEP. The parenchymal volume of the pancreas was quantified using the volume analyzer SYNAPSE VINCENT® (Fujifilm Medical Co, Tokyo, Japan) in pre-ERCP images and used to evaluate whether it could be a risk factor for PEP.
Aims and Methods: The aim of this study was to investigate the risk factors for PEP by quantification of pancreatic parenchymal volume using pre-ERCP images. Overall, 800 patients were recruited from April 2012 to February 2015 for this study. There were 240 patients who satisfied the inclusion criteria. Measurement of pancreatic parenchymal volume was achieved using the volume analyzer SYNAPSE VINCENT® in all cases and was used to evaluate the risk factors for PEP.
Results: According to the criteria established by the consensus guidelines (Cotton classification), 23 patients (9.6%) were classified as having mild disease, 4 (1.7%) as having moderate disease, and 5 (2.1%) as having severe disease. Multivariate model analysis adjusted for age, female sex, pancreatic duct guidewire cannulation, precut sphincterotomy, and pancreatic injection showed that a large pancreatic parenchymal volume was a significant risk factor for PEP (odds ratio 1.12, 95% confidence interval 1.07–1.17; p < 0.01). In addition, a larger pancreatic parenchymal volume was significantly associated with a higher incidence of PEP (p < 0.001).
Conclusion: A large pancreatic parenchymal volume was identified as a risk factor for PEP. The results of this study suggest that pre-ERCP images might be useful for predicting PEP. Additional caution should be required for patients with larger pancreatic parenchymal volumes to prevent PEP.
Disclosure: Nothing to disclose

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P0210 INITIAL MULTICENTRE DATA FROM THE HUNGARIAN ERCP REGISTRY

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Introduction: The continuous monitoring of quality indicators in gastrointestinal endoscopy became an essential requirement nowadays. Most of these data cannot be extracted from the currently used free-text reports, therefore a

web-based data collecting system, the Hungarian ERCP Registry was developed. Here we present the first multicentre data from the registry.
Aims and Methods: Data collection started in January 2017 at University of Pécs, and a further 4 centres (Szeged, Debrecen, Budapest and Szombathely) started to use the registry from a later date.
Results: 1117 ERCPs of 884 patients were recorded in the database until March 2018 in the 5 participating centres. 30-day follow up data was collected to detect all procedure related late complications, this data is available in 73.5% of the procedures. Native papilla (NP) was detected in 698 ERCPs (62.5% of all procedures), the success rate of biliary cannulation was 90.5% in these patients. Post-ERCP pancreatitis (PEP) developed in 22 cases (3.2% of procedures with NP), clinically significant bleeding was reported in 14 patients (2.0% of cases with NP). Cholangitis was observed in 18 cases (1.6% of all procedures), and perforation occurred in 16 cases (1.4%). Indomethacin suppository was used in 43.8% of the cases, while prophylactic pancreas stent was applied in 9.5% of the procedures to prevent PEP. The data of the participating centres are shown below. Center/ERCP number/30d F/U (%)/ERCP in NP (%)/Success in NP (%)/Complication rate (%): PEP/Bleed/Cholang. /Perf.: Pécs/692/75.1/62.6/89.6/3.2/1.4/0.7/1.9; Szeged/207/67.6/66.2/94.2/4.4/2.9/3.9/1.0; Budapest/151/69.5/55.6/89.3/1.2/1.2/3.3/0; Debrecen/35/85.7/57.1/100/0/10.0/0/0; Szombathely/32/81.3/75.0/83.3/4.2/4.2/0/3.1
Conclusion: These are the first prospectively collected multicentre key performance indicators from the Hungarian ERCP Registry. This web-based registry is a suitable tool to detect the quality of patient care and also can be used for clinical research. Further centres are encouraged and welcome to join this project.
Disclosure: Nothing to disclose

P0211 USE OF THE FORWARD-VIEWING ENDOSCOPE CAN BE A RISK FACTOR FOR POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS: A PROSPECTIVE MULTICENTRE OBSERVATIONAL STUDY

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Introduction: A forward-viewing endoscope is used for endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgically altered anatomy such as Billroth II type or Roux-en Y type reconstruction. Difficulty in procedures with the forward-viewing endoscope may increase the incidence of post-ERCP pancreatitis (PEP). However, there have been few studies directly comparing the incidence of PEP between the forward-viewing and side-viewing endoscopes.
Aims and Methods: We conducted a prospective analysis to compare the incidence of PEP in ERCP with the forward-viewing endoscope with that of the side-viewing endoscope and evaluated the forward-viewing endoscope as a risk factor for PEP. Between May 2015 and May 2016, 2078 patients who underwent ERCP at 5 high-volume hospitals in Japan were enrolled (SOSUI study). We excluded patients with acute pancreatitis, biliary-enteric anastomosis, failure to reach the papilla, altered anatomy other than Billroth II or Roux-en Y reconstruction, and special approach like transgastrostomy. A total of 1877 patients were analysed, including 1814 patients with normal anatomy who underwent ERCP with the side-viewing endoscope and 63 patients with altered anatomy who underwent ERCP with the forward-viewing endoscope. In the present study, the diagnosis of PEP requires the presence of at least 2 of the following criteria: i) abdominal pain persistent for more than 24 hours, ii) elevation in serum amylase to 3 times or greater than the upper limit of normal the following day after ERCP (12 - 20 hours after ERCP), and iii) characteristic findings of acute pancreatitis on computed tomography.
Results: 103 out of 1877 (5.5%) patients developed PEP. The rates of PEP were 5.1% (96/1814) and 11.1% (7/63) for the side-viewing and forward-viewing endoscope groups, respectively. Univariate analysis revealed that the factors significantly correlated to PEP development were the following: use of the forward-viewing endoscope, female sex, naïve papilla,more than 10 trials for selective cannulation, pancreatic duct injection and precut sphincterotomy.
Multivariate analysis identified use of the forward-viewing endoscope as an independent risk factor for PEP (OR 2.78; 95% CI 1.08–6.27), as well as female sex (OR 2.30; 95% CI 1.51–3.53), naïve papilla (OR 3.81; 95% CI 2.14–7.22) and pancreatic duct injection (OR 2.48; 95% CI 1.60–3.89).
Conclusion: Use of the forward-viewing endoscope in ERCP is a risk factor for PEP. The reason for this may be that mechanical injury to the papilla or pancreatic duct can be increased by difficult and prolonged procedures due to the limitations derived from endoscope characteristics and the absence of dedicated devices. When ERCP is performed with the forward-viewing endoscope, some means to prevent PEP and careful observation after ERCP should be considered. In addition, it is desirable that devices dedicated to ERCP with the forward-viewing endoscope should be developed.
Disclosure: Nothing to disclose

P0212 SINGLE-OPERATOR PERORAL CHOLANGIOPANCREATOSCOPY-GUIDED LITHOTRIPSY FOR DIFFICULT BILIARY AND PANCREATIC STONES - A PROSPECTIVE MULTICENTER STUDY

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Introduction: ERCP is the first choice for the removal of biliary and pancreatic stones. In difficult stones, advanced therapeutic techniques, such as electrohydraulic lithotripsy (EHL) and laser lithotripsy (LL) have been proposed. Recently, the availability of single-operator cholangiopancreatoscopy (SOCP) turned these techniques more accessible and easier to perform.
Aims and Methods: We sought to evaluate the clinical efficacy and safety of SOCP guided-lithotripsy using EHL or LL in patients with complex biliary and pancreatic stones.
A prospective study was carried out in 3 hospitals, comprising 30 consecutive patients with complicated biliary and pancreatic stones treated with SpyGlass DS (Boston Scientific, Marlborough, United States) guided-lithotripsy using EHL or Holmium LL. We analyzed the complete cleaning of the ducts, the incidence of adverse events, the impact of the number of stones and its location on clinical success, and the performance of the 2 lithotripsy modalities.
Results: 22 patients (73.3%) had common bile duct/common hepatic duct stones, 2 patients (6.7%) had a single cystic stump stone, 4 patients (13.3%) had pancreatic calculi and 2 patients (6.7%) had intrahepatic stones. 28 patients (93.3%) were successfully treated in one procedure and the remaining 2 patients (6.7%) required additional sessions to obtain cleaning of the ducts. 22 patients were treated with LL and 8 patients with EHL; 2 of the EHL-treated patients required more than 1 probe in the first ERCP; 1 of these patients was submitted to a subsequent ERCP in which LL was opted in, with success. The median duration of each session was 62 minutes (30–110). Complications were mild in 6 patients (20%) and included fever (n = 4), pain (n = 1) and mild pancreatitis (n = 1).
Conclusion: SOCP guided-lithotripsy using EHL or LL in patients with difficult biliary and pancreatic stones is very effective and is associated with transient and mild complications. There is a clear need for comparative studies between EHL and LL.
Disclosure: Nothing to disclose

P0213 DOES THE MORPHOLOGY OF THE MAJOR PAPILLA INFLUENCE BILIARY CANNULATION? - A MULTICENTER PROSPECTIVE STUDY

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Introduction: Selective biliary duct cannulation is an essential prerequisite for biliary ERCP. Some authors suggest that the difficulty of biliary cannulation and the use of rescue techniques (rT) can be conditioned, among other factors, by the papillary morphology.
Aims and Methods: We intend to evaluate if the duration of biliary cannulation, the existence of a difficult cannulation and the use of rT are influenced by the papillary morphology.
This was a multicenter (3) prospective cohort study, including consecutive patients referred for ERCP with naïve papilla between August 2017 and January 2018, performed by experienced endoscopists (> 4000 CPREs). The papillae were classified into 4 types: non-prominent, prominent, bulging and distorted (Leés classification). The transverse, longitudinal papilla diameters and the diameter of the distal bile duct were measured. Primary outcomes: duration of biliary cannulation (tbc), difficult cannulation and rT. The influence of papilla type/dimensions on outcomes was assessed by multiple linear and logistic regressions.
Results: We included 106 patients, 43 men (40.57%), median age = 79 years (26–96). The main indication: suspected obstruction of the biliary tract in 83.02%. The success rate of biliary cannulation was 100%; 29.24% of the cannulations were considered difficult. Rescue access techniques were used in 28.3% of the non-prominent papillae, 41.18% of the prominent ones, 30.77% of the bulging

and 16.67% of the distorted ones. In patients with non-prominent papillae (50%), tbc = 3.35 mins (iqr = 6.84); in the prominent papillae (32%), tbc = 5.08 mins (iqr = 8.53); in the bulging papillae (12.26%), the tbc = 2.25 mins (iqr = 5.66); in the distorted (5.66%), tbc = 2,025 mins (iqr = 7.51). In the multivariate analyzes the papilla type/dimensions did not show to be a predictor of the 3 outcomes evaluated.
Conclusion: Contrary to what is stated in the literature, the type and dimensions of the papilla do not correlate with the difficulty of cannulation nor condition the techniques used.
Disclosure: Nothing to disclose

P0214 THERAPEUTIC ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY

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Introduction: Endoscopic retrograde cholangiography (ERC) is an endoscopic procedure that is globally used for the treatment of biliary disease. However, ERC in patients with surgically altered gastrointestinal (GI) anatomy remains a challenging procedure due to the difficulty of reaching the target site. Consequently, percutaneous interventions or open surgery have been selected in these patients in spite of being more invasive procedures. Today the progression of techniques and devices like a Double-balloon endoscope (DBE) enables us to perform ERC on these patients. The aim of this study is to evaluate the utility and safety of therapeutic ERC in patients with surgically altered GI anatomy (except for Billroth-I reconstruction).
Aims and Methods: A total of 2314 consecutive ERCP procedures were performed at Toranomon Hospital during a 5- year period (2012 to 2016). 105 ERC procedures for biliary disease on 67 separate patients with altered GI anatomy were included in this study. We retrospectively investigated: (1) the success rate of reaching the target site; (2) the success rate of cholangiography; (3) the therapeutic success rate (the success rate of ERC-related interventions); (4) the occurrence of adverse events.
Results: The mean age was 69.7 years, ranging from 37 to 87 years; 43 were male and 24 were female. The most common reconstruction technique was Roux-en-Y reconstruction, which was performed in 54 cases, followed by biliojejunal anastomosis in 48 cases, Billroth-II reconstruction in 12 cases, and bilioduodenal anastomosis in 5 cases. Bile duct stone 59% (n = 62), benign bile duct stenosis 19% (n = 20), pancreatic cancer 9.5% (n = 10), hepatocellular carcinoma 3.8% (n = 4), bile duct cancer 2.9% (n = 3) were major indications. Bile duct stone extraction was performed in 46.7% (n = 49), plastic stent and self-expanding metal stent (SEMS) was positioned for biliary drainage in 42.9% (n = 45) and 1.9% (n = 2), respectively. The results of the above investigations were: (1) 92.4% (97/105), (2) 97.9% (95/97), (3) 83.8% (88/105). Adverse events occurred in 9 cases (8.6%) with perforation 3.8% (n = 4), pancreatitis 1.9% (n = 2), aspiration pneumonia 1.9% (n = 2), and cholangitis 1% (n = 1). They were successfully treated conservatively in all patients with the exception of 1 in whom a perforation developed, requiring emergency surgery. Procedure-related mortality did not occur.
Conclusion: ERC in patients with surgically altered GI anatomy remains a challenging procedure. But today, the number of the successful therapeutic ERCs is increasing in these patients by using DBE or PCF. Successful therapeutic ERC was achieved in 83.8%, a relatively high figure and the rate of adverse events were relatively low in this study. Therapeutic ERC should be performed positively for biliary disease, even if it's a case of altered GI anatomy.
Disclosure: Nothing to disclose

P0215 A MULTICENTER RANDOMIZED TRIAL COMPARING A 25G EUS FINE NEEDLE ASPIRATION DEVICE WITH A NOVEL 20G EUS FINE NEEDLE BIOPSY DEVICE

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Introduction: Several studies have compared Endoscopic Ultrasonography (EUS) fine needle aspiration (FNA) to biopsy (FNB) needles, but none has proven the superiority of 1 needle over the other.
Aims and Methods: As studies were either underpowered or confined to 1 geographical region, we performed an investigator-initiated global randomized controlled trial, to compare the performance of a novel 20G FNB to a 25G FNA needle. 13 EUS-centers from 5 continents randomized consecutive patients with a solid lesion for FNB (ProCore) or FNA (EchoTip Ultra). Primary endpoint was diagnostic accuracy for malignancy and for the Bethesda classification (non-diagnostic, benign, atypical, malignant). Secondary, technical success, safety, and sample quality were assessed. Multivariable and supplementary analysis were performed to adjust for confounders.
Results: 608 patients were allocated to FNA (n = 306) or FNB (n = 302), encompassing 312 pancreatic lesions (51%), 147 lymph nodes (24%), and 149 other lesions (25%). Technical success rate was 100% for FNA and 99% for FNB (p = 0.043), without differences in adverse events. FNB outperformed FNA in terms of histological yield (77% vs. 44%, p < 0.001), accuracy for malignancy (87% vs. 78%, p = 0.002) and Bethesda classification (82% vs. 72%, p = 0.002). This was robust to correction for indication, lesion size, number of passes, and an on-site pathologist (OR 3.53, 95% CI 1.51–8.26, p = 0.004), and did not differ between centers (p = 0.836).
Conclusion: The 20G FNB needle outperforms the 25G FNA needle in terms of histological yield and diagnostic accuracy. This diagnostic benefit was irrespective of lesion type and consistent amongst participating centers, supporting general applicability of our findings.
Disclosure: This investigator-initiated study was supported by means of an unrestricted grant from Cook Medical

P0216 CHOLANGITIS AFTER ENDOSCOPIC ULTRASOUND IN PATIENTS WITH BILIARY STRICTURES AND ASSOCIATED RISK FACTORS

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Introduction: Endoscopic ultrasound (EUS) and EUS-guided fine needle aspiration (FNA) have emerged as an efficient diagnostic tool for pancreatobiliary diseases and have been considered to be a safe modality because of low risk of complications such as bleeding, perforation and pancreatitis. However, the risk of cholangitis after EUS/EUS-FNA in patients with biliary strictures has not

been fully examined. In this study, we examined the rate and the risk factors of cholangitis after EUS/EUS-FNA in these patients.
Aims and Methods: We retrospectively reviewed the data of 138 inpatients with biliary strictures who underwent EUS/EUS-FNA at our institution between April 2012 and September 2017. We excluded 8 patients with percutaneous biliary drainage, 5 patients with difficulty in reaching duodenum and 1 patient who underwent EUS/EUS-FNA and ERCP at the same day. Cholangitis and its severity were diagnosed based on Tokyo Guidelines 2013.
Results: 125 patients (147 cases in total) were included; 59.2% were male; median age was 71. 92 patients (73.6%) were malignant (49 patients, pancreatic cancer; 13 patients, distal cholangiocarcinoma; 18 patients, hilar cholangiocarcinoma; 2 patients, intrahepatic cholangiocarcinoma: 3 patients, gallbladder cancer; 7 patients, the others) and 33 patients were benign (13 patients, IgG4-related disease; 1 patient, primary sclerosing cholangitis; 2 patients, tumor-forming pancreatitis; 17 patients, the others). The location of biliary strictures was 106 cases in distal (72.1%), 30 in hilar (20.4%), 4 in intrahepatic (2.7%) and 7 in spreading (4.8%). Endoscopic biliary stenting (EBS) had been already performed before EUS/EUS-FNA in 86 cases (58.5%). Median time from EBS to EUS/EUS-FNA was 21 days (range; 1–125 days). EUS-FNA was performed in 57 cases (38.8%). Cholangitis was observed in 4.1% (6/147). The severity was mild in 2, moderate in 3 and severe in 1 case. The patient who suffered from severe cholangitis underwent urgent endoscopic nasal biliary drainage at the day of EUS. The incidence of cholangitis in the cases with EBS was significantly higher than those without EBS (7.0% (6/86) vs. 0% (0/61), $p = 0.042$). Other statistically significant risk factors of cholangitis were gamma-GTP levels ($> 1.5 \times$ upper limit of normal (ULN) (7.2%, 6/83) vs. $< 1.5 \times$ ULN (0%, 0/64), $p = 0.030$) and ALP levels ($> 1.5 \times$ ULN (10.7%, 6/56) vs. $< 1.5 \times$ ULN (0%, 0/91), $p = 0.003$). Age, gender, malignant/benign disease, the location of biliary strictures, endoscopic sphincterotomy, examination time, examination with/without EUS-FNA, WBC, CRP, AST and ALT were not significant risk factors. In the cases with higher ALP levels, cholangitis occurred in 16.7% of the cases with EBS (6/36), while no cholangitis occurred in the cases without EBS (0/20).
Conclusion: The rate of cholangitis after EUS/EUS-FNA was 4.1% in the cases with biliary strictures. The use of prophylactic antibiotics might be beneficial in these cases, especially the cases with EBS and biliary enzyme elevation.
Disclosure: Nothing to disclose

P0217 EFFICACY AND SAFETY OF ENDOSCOPIC RADIOFREQUENCY ABLATION FOR METASTATIC PANCREATIC RENAL CELL CARCINOMA: A MONOCENTRIC EXPERIENCE

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Introduction: Glandular metastasis (GM) from metastatic renal cell carcinoma (mRCC) are rare but associated with good prognosis and pancreas metastasis (PM) is the more frequent site. The management of PM only, is surgery or tyrosine kinase inhibitor (TKI). Endoscopic radiofrequency ablation (ERFA) is a very innovative approach to control metastasis and have never been reported to treat PM from mRCC.
Aims and Methods: We report a monocentric, prospective analysis for local control and toxicity of patients (pts) treated by ERFA for progressive PM from mRCC. ERFA was performed under general anesthesia, with a linear EUS scope and a 19 G RFA needle; time of ablation was short (30sec –1 mn), 1 or 2 shots were needed to ablate a 2 cm lesion.
Results: 6 pts from Paoli Calmettes Institute (France) were recruited between May 2017 and January 2018. Median age was 72y (69–73), 4/6 female, ECOG 0 (100%). The median time from diagnosis to PM was 14 years (9.98–22.18), median number of PM was 2 (1–3), 5/6 was documented by histology and all were classified as progressive before ERFA. PM localizations was: head in 40%, body 40%, tail 20% and average size was 19.6 mm. 80% of pts (4/6) had other mRCC spread, 4/6 received systemic treatment and 2 of them were on therapy at ERFA time (1 TKI, 1 Nivolumab). 2 pts had ERFA as the only treatment for oligometastatic RCC. Median number of ERFA sessions was 2 (1–3). With a median follow up of 6.6 months (0.5–9.3), 5/6 pts had local control (with 2 CR). 1 patient treated by TKI during procedure, developed a paraduodenal abscess 2 months after ERFA and was drained endoscopically. Pancreatitis or diabetes were not reported and no toxicity was observed for pt treated with nivolumab.
Conclusion: ERFA is feasible and displays an excellent local control for PM without any major side effect. However TKI should be stop before the procedure to avoid complications. ERFA could be a valuable option, less morbid than pancreas resection for progressive PM.
Disclosure: Nothing to disclose

P0218 GRANULOMATOUS LYMPHADENITIS - TO REACH A DEFINITIVE DIAGNOSIS IN INDIAN POPULATION. A PROTOCOL-BASED STUDY

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Introduction: In India mediastinal and abdominal lymphadenopathy is widely seen. In cases where EUS-guided FNA reveals granulomatous disease, to identify the real cause we devised a specific protocol.
Aims and Methods: Retrospective analysis of last 1 year data of EU FNA and FNB with a specified protocol to reach a final diagnosis in granulomatous lymphadenitis in India.
Protocol: from September 2016 to October 2017. 6 passes for each node sampling with a 22 G Aquire needle. 2 passes - cytology, 2 passes- Core biopsy for histopathology and Immunohistochemistry, 2 passes- Core biopsy in saline for Gene Xpert and SOS AFB Culture. If granuloma found on cytology -subjected to Gene Xpert and AFB Culture. If malignant on cytology- excluded. Only with granulomas on smear - caseating or non caseating were included.
Results: No of cases of lymphadenopathy that underwent EUS-guided FNA in a period of 1 year from October 2016 to October 2017 - 38 Granulomatous lymphadenitis on FNA cytology found - 26 (68.4%) Cases which had other diagnosis than granulomas - 12 (31.6%) Gene Xpert was done in 24 /26 cases - 92.3% TB culture was done in 21/26 cases - 80.7% Positive either for gene Xpert or TB culture or both - 12/26 - 46.1% Out of 12 positives: Gene Xpert positive - 7 /11 (63.6). Xpert was not done in one case Culture positive - 7 /10 (70%). Culture was not done in 2 cases Xpert negative but positive on culture - 4 cases (33.3%) TB CULTURE - correlated with presence of caseation in smears &/or biopsies caseous necrosis - identified in 7/12 positive cases (58.3%) Cases positive on Xpert or culture and showed non caseating granuloma on cytology & histology - 5 (41.6%) Granulomatous lymphadenitis which were negative on culture & Xpert were evaluated clinically - 14 Raised ACE levels- 1 (7.1%) - Diagnosed as sarcoidosis Empirical ATT & were followed up for response - 13 (92.8 %) Responded to ATT - 13 (100%).
Conclusion: In our region (India and the Asian nations) - Granulomatous Lymphadenitis is major cause lymphadenopathy. Of the positive granulomatous nodes - a definitive diagnosis of tuberculosis was obtained in around half the cases only with all expensive tests. But of the remaining cases, almost 93% responded to Anti Tubercular Treatment when followed up clinically. Only 1 case of all the granulomatous cases turned out to be sarcoidosis. Therefore, if we see granuloma on smear of any lymph node during FNA, giving a trial of ATT sounds prudent. However further studies are warranted to confirm this. Clinical setting will impact our diagnosis. Should look for non-responders to ATT and do ACE levels to rule out sarcoidosis. Of course a culture and sensitivity should be done all cases that we can rule any drug resistance.
Disclosure: Nothing to disclose

P0219 WHICH APPROACH IS BETTER FOR PANCREATIC NECROSECTOMY - COMPARING DATA IN A TERTIARY REFERRAL CENTRE IN INDIA

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Introduction: Minimal access techniques have gained popularity for the management of necrotizing pancreatitis, but only few studies compared open necrosectomy with a less invasive treatment.
Aims and Methods: We aimed to evaluate the outcomes of minimally invasive treatment including endoscopic methods for necrotizing pancreatitis in comparison with open necrosectomy in our own data.
Our data were compared in 3 groups - Surgery, Minimal Access Surgery and EUS Guided Drainage for management of walled of necrosis.
Total Number of patients with acute pancreatitis between October 2010 to March 2017: **1860,** Number of patients with necrotizing pancreatitis: **572 (30.7%),** Number of patients with Walled of Necrosis: **266 (46.5%),** Procedures Offered: **Open surgery, Endoscopic transgastric approach & Minimal access Necrosectomy (MAN)** - Including (Retroperitoneal Videoscopic Approach, Laparoscopic approach, Transgastric approach, Laparoscopic transabdominal, Hybrid- open surgery + retroperitoneal approach).
Number of Sessions in Open Surgery: 1 in 44 of 48 (91.7%), Repeat Sessions in Open Surgery: 4 of 48 (8.3%), Number of Sessions in MAN: 56 of 56 (100%), Number of sessions in Endoscopy: Average 4. Average time for first session was 25 min with plastic stents, 15 minutes with metal stents. Average time for the second session and third was 20 min, Outcome and data in all 3 groups compared. Follow up –6 years to 3 months. All the patients tolerated the procedures well,
Bleeding: 3 patients in endoscopy & Open surgery each and 1 in MAN. Endoscopic procedures were abandoned and patients were subjected to laparoscopic transabdominal surgery, all 4 patients were angioembolized from the bleeding vessel of which 1 patient died.
Wound infections - 42 vs 8 in open and MAN
Intestinal fistulae 4 vs 1 in open and MAN (Controlled retroperitoneal fistula treated without ileostomy); 4 were treated with Laparotomy and ileostomy.
Pulmonary complications were 24, 6 and 2 in open, MAN & Endoscopy

Average length of ICU stay in MAN group was 3.57 vs 8.14 days in case of open vs 2.04 days in Endoscopy.
The average length of hospital stay after ICU - 11.33 vs 12.7 vs 11.8 days in open vs MAN vs endoscopy respectively.
Mortality - (0.6%) in Endoscopy vs 3 (5.35%) in MAN vs 12 (25%) in open
Incisional hernia - 8 vs 3 patient in open vs MAN.
Average time of doing intervention in Endoscopy was 45th day (32 - 75days), while MAN was 34th day (24 to 50 days) and Open was 33rd (18 to 40 days) day of illness.
Results: Endoscopic necrosectomy - 162, Trans gastric surgery - 18, Laparoscopic surgery - 10, Retroperitoneal minimal access surgery - 20, Retroperitoneal Videoscopic + laparoscopic/open - 8, Conventional open surgery - 48
Conclusion: Later the necrosectomy better the outcome. No statistical difference in clearance of the necrosis when all groups were compared head to head.
Endoscopic necrosectomy with plastic or SEMS (LAMS Excluded) - technically feasible in upto 50% necrosis- should be preferred whenever possible.
More necrosis - minimally access necrosectomy - better technique compared to open & endoscopy not possible.
Open surgical techniques - More risk of fistula formation than minimal access group and least with endoscopic group.
More bleed in conventional open and transgastric approach.
Endoscopic approach - limitation- Not useful in early days.
Pulmonary complications are more in the open.
ICU stay - more in open and minimal access group.
More mortality in open and MAN groups.
Mortality in endoscopy group - 1. Due to serious septic complications. Salvage open lavage done but succumbed.
Disclosure: Nothing to disclose

P0220 ROLE OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION OF PORTAL VEIN THROMBUS IN THE DIAGNOSIS AND STAGING OF HEPATOCELLULAR CARCINOMA

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Introduction: Portal vein thrombosis (PVT) is being increasingly diagnosed. Presence of neoplastic thrombus serves as an important determinant of tumor staging, as well as prognosis, and influences treatment selection. In some cases, it may be the initial sign of an undetected HCC. Therefore, accurate differentiation of bland from neoplastic thrombus is crucial for patient treatment.
Aims and Methods: This is a prospective study that included 11 cirrhotic patients with PVT which don't fulfill the criteria of malignancy by imaging techniques; either with or without hepatic mass or undergone local treatment following a diagnosis of HCC and develop PVT during their follow-up. Under EUS guidance, the main, left and right portal veins were identified and a 22-gauge EUS-FNA needle was advanced from the duodenum into the portal vein, 1–2 passes through portal vein thrombus were taken. The puncture site was monitored under EUS for complications. To assess the ease, safety, and efficacy of EUS-FNA in characterizing the nature of the PVT which don't fulfill the criteria of malignancy via imaging techniques.
Results: Out of 11 patients; 7 patients (64%) were males. 6/11 were cirrhotic without liver masses, 4/11 HCC and 1/11 developed PVT during follow-up after TACE for HCC. EUS-FNA was done using 22G needle from main portal vein in 9 patients and from right portal vein in 2 patients. Pathological examination was malignant in 1 patient with HCC and non-enhancing PVT by CT abdomen. No complications were reported in any case.
Conclusion: EUS-FNA is an effective and safe method in characterizing the nature of PVT which don't fulfill the criteria of malignancy via imaging techniques. We believe that EUS-FNA should be utilized more frequently in the diagnosis and staging of HCC.
Disclosure: Nothing to disclose

P0221 EVALUATION OF THE ROLE OF ENDOSCOPIC ULTRASOUND-GUIDED GASTRIC BOTULINUM TOXIN INJECTIONS IN THE TREATMENT OF OBESITY

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Introduction: Obesity is an important public health concern. In rats, botulinum toxin A (BTA) injected subserosally into the antrum resulted in significant decreases in caloric intake and body weight. Subsequent open-label human studies have reported conflicting results, finding little or no body weight loss after gastric BTA injection. We hypothesized that EUS guidance would help to assure injection of BTA in the gastric muscularis propria and subserosal layers.
Aims and Methods: To assess the safety, feasibility and efficacy of EUS-guided gastric Botulinum toxin A injections in obese subjects to reduce body weight. This is a pilot study that included 16 subjects with obesity (BMI > 30). Under EUS guidance, BTA injections (100U) were made with 25G needle. A ring of 5 injections were made into the antral muscularis propria; 2–3 cm proximal to the pylorus. During a 16 weeks follow-up period, subjects were weighed and completed the Gastrointestinal Symptom Rating Scale (GSRS) 2 weeks before and weekly after injection. Nutrient drink tests 1 week before and at 4 and 16 weeks after injection. No behavioral or dietary interventions were offered to study subjects.
Results: Out of 16 subjects; 15 subjects (93.7%) were females. Mean age was 34.5 years (21–43) and mean BMI was 41.5 (33–50). In a follow-up period of 16 weeks, weight loss ranged from 7 to 25 kg. Nutrient drink tests decreased from a baseline value 1200 cc (600–1800) to 420 cc (240–600) at 4 weeks. Mild elevation of the GSRS score was found in 2 subjects who reported diarrhea at 1–4 week in 1 subject and at 5–7 week in another 1. No vomiting, abdominal pain or any complications were detected in any subject.
Conclusion: EUS-guided botulinum toxin injection is an effective method for weight reduction which can be performed safely with minimal adverse events. However, further studies are still warranted.
Disclosure: Nothing to disclose

P0222 PROSPECTIVE MULTICENTER STUDY OF EUS-GUIDED THROUGH-THE-NEEDLE BIOPSY FOR THE EVALUATION OF PANCREATIC CYST: AN INTERIM ANALYSIS

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Introduction: The primary aim was to evaluate the safety and feasibility of EUS-TTNB of PCLs. The secondary aim was to assess the potential incremental diagnostic yield of TTNB of mucinous cysts.
Aims and Methods: The primary aim was to evaluate the safety and feasibility of EUS-TTNB of PCLs. The secondary aim was to assess the potential incremental diagnostic yield of TTNB of mucinous cysts. Prospective multicenter study of consecutive patients undergoing EUS fine-needle aspiration (FNA) and TTNB for PCLs $\geq$ 15 mm in size between June 2016 to November 2017. Technical success by FNA or TTNB was defined as successful tissue acquisition of a specimen adequate for cytohistopathological evaluation. Cyst fluid CEA was used to initially categorize cysts as nonmucinous (CEA < 192ng/mL) or mucinous (CEA $\geq$192ng/mL). A cyst was determined to be mucinous on cytology or histology by the presence of mucinous pancreatic cystic epithelium.
Results: A total of 49 patients (mean age 64.4 ± 15.2 years; 51% women) were included in the interim analysis. Mean PCL size was 36.2 mm, range 15–200 mm. Technical success was significantly higher with TTNB (77.6%) compared to EUS-FNA (36.7%) ($p<0.001$) for PCL sampling. For cysts with insufficient amount of fluid for CEA ($n=14$) or CEA < 192 ng/mL ($n=24$), the cumulative incremental diagnostic yield of a mucinous cyst was significantly higher with EUS-TTNB (44.7%) compared to EUS-FNA (2.6%) ($p<0.001$). In all, there were 2 cases of self-limited intracystic bleeding (4.1%) that did not require additional interventions. There was 1 case (2%) of mild acute pancreatitis reported 48 hours after the procedure.
Conclusion: This interim analysis of our multicenter prospective study suggests that EUS-TTNB is safe and effective for the evaluation of PCLs. EUS-TTNB represents an additional tissue acquisition method that may help increase the diagnostic yield of pancreatic mucinous cysts during EUS.
Disclosure: Nothing to disclose

P0223 PROSPECTIVE MULTICENTER STUDY OF EUS-GUIDED THROUGH-THE-NEEDLE BIOPSY FOR SOLID LESIONS: AN INTERIM ANALYSIS

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Introduction: EUS-FNA is standard practice for tissue acquisition of solid lesions adjacent to the gastrointestinal tract. An EUS-guided through-the-needle microforceps is a novel tissue acquisition device.
Aims and Methods: The aim of our study was to evaluate the safety and feasibility of EUS through-the-needle biopsy (TTNB) of solid lesions using the microforceps. Prospective multicenter study of consecutive patients undergoing EUS fine-needle aspiration (FNA) and TTNB of solid lesions $\geq$ 15 mm in size between June 2016 to November 2017. Demographics, size, location and final diagnosis were recorded. Technical success by FNA or TTNB was defined as successful tissue acquisition of a specimen adequate for cytohistopathological evaluation.

Results: A total of 45 patients (mean age 64.2 ± 15.3 years; 60% men) were included in the interim analysis. Mean lesion size was 44.1 mm, range 18–222 mm. The following sites were sampled: pancreas (n = 25; 55.6%), gastric/duodenal subepithelial lesion (n = 12; 26.7%), lymph nodes (n = 6; 13.3%), retroperitoneum (n = 1; 2.2%) and liver (n = 1; 2.2%). Technical success (adequate cellularity for cytohistopathological analysis) was similar between FNA (n = 42; 93.3%) and TTNB (n = 39; 86.7%) (p = .48). Diagnostic yield with FNA was 83.3% compared to 89.7% with TTNB (p = 0.5). There were no intra-procedural or post-procedural adverse events reported with FNA and TTNB.
Conclusion: This interim analysis of our multicenter prospective study suggests that EUS-TTNB is a safe and feasible technique for tissue acquisition of solid lesions. The diagnostic yield with TTNB was similar to that of FNA. EUS-TTNB represents a novel tissue acquisition method for the evaluation of solid lesions adjacent to the GI tract.
Disclosure: Nothing to disclose

P0224 SURVEY STUDY ON THE PRACTICE PATTERNS OF THE EVALUATION AND MANAGEMENT OF INCIDENTAL PANCREATIC CYSTS

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Introduction: Various gastrointestinal societies have released guidelines on the evaluation of asymptomatic PCs. These guidelines differ on several aspects, which creates a conundrum for clinicians.
Aims and Methods: An electronic survey distributed to members of the American Society for Gastrointestinal Endoscopy (ASGE). Main outcomes included practice setting (academic vs. community), preferences for evaluation, management, and surveillance strategies for PCs. An electronic survey distributed to members of the American Society for Gastrointestinal Endoscopy (ASGE). Main outcomes included practice setting (academic vs. community), preferences for evaluation, management, and surveillance strategies for PCs.
Results: 172 subjects completed the study (52% academic-based endoscopists). 86 (50%) and 138 (80%) of the participants responded that they would recommend EUS surveillance of incidental PCs measuring less than 2 cm and 3 cm, respectively. Nearly half of the endosonographers (42.5% community and 44% academic; p = 1.0) would routinely perform FNA on PCs without any high-risk features. More academic-based endoscopists (57% academic vs. 32% community; p = 0.001) would continue incidental PC surveillance indefinitely.
Conclusion: There is significant variability in the approach of incidental PCs among clinicians, with practice patterns often diverging from the various GI societal guideline recommendations. Most survey respondents would routinely recommend EUS-FNA and indefinite surveillance for incidental PCs without high-risk features. The indiscriminate use of EUS-FNA and indefinite surveillance of all incidental PCs is not cost-effective, exposes the patient to unnecessary testing, and can further perpetuate diagnostic uncertainty. Well-designed studies are needed to improve our diagnostic and risk stratification accuracy in order to formulate a consensus on the management of these incidental PCs.
Disclosure: Nothing to disclose

P0226 CHRONIC PANCREATITIS FINDINGS BY ENDOSCOPIC ULTRASONOGRAPHY IN THE PANCREATIC PARENCHYMA OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM AND PANCREATIC CANCER CONCOMITANT WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM

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Introduction: Despite evidence suggesting a role of chronic pancreatitis (CP) in pancreatic carcinogenesis, its relationship with invasive intraductal papillary mucinous neoplasm (invasive IPMN) and pancreatic cancer (PC) in concomitant with IPMN (PC with IPMN) remains unclear. Endoscopic ultrasonography frequently reveals evidence of CP (EUS-CP findings) in the background pancreatic parenchyma of patients with IPMNs.
Aims and Methods: We investigated whether EUS-CP findings were associated with a higher incidence of invasive IPMN or PC with IPMN. This study included 104 patients who underwent preoperative EUS and surgical resection for IPMN (N = 86: IPMA N = 62, Invasive IPMN N = 24) and PC with IPMN (N = 18) between January 2010 and August 2016. The association of EUS-CP findings (total number of EUS-CP findings; 0 vs. ≥1) with invasive IPMN or PC with IPMN was examined. The association of EUS-CP findings with pathological changes of the background pancreatic parenchyma (atrophy/inflammation) was also examined.
Results: EUS-CP findings were significantly more frequently observed in Invasive IPMN (for Invasive IPMN vs IPMA: multivariable odds ratio [OR] = 2.8, 95 % confidence interval [CI] = 1.08–7.72, p = 0.03), but not in PC with IPMN (for PC with IPMN vs. other IPMNs: OR = 0.4, 95 % CI = 0.09–1.29, p = 0.12). In addition, EUS-CP findings were also associated with higher-grade pancreatic atrophy and inflammation (EUS-CP findings absent vs. present: 13.1%(8/61) vs. 25.6%(11/43), p = 0.13, 8.2%(5/61) vs. 25.6%(11/43), p = 0.02, respectively).
Conclusion: Detection of EUS-CP findings in the background pancreatic parenchyma was associated with a higher prevalence of invasive IPMN, but not with PC with IPMN.
Disclosure: Nothing to disclose

P0227 EUS-DIRECTED TRANSGASTRIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (EDGE): THE FIRST LEARNING CURVE

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Introduction: EUS-directed transgastric endoscopic retrograde cholangiopancreatography (EDGE) is a minimally invasive option for ampullary access or head of pancreas access in patients with roux-en-y anatomy. The procedure involves creating a fistulous tract between the remnant stomach or jejunum and the bypassed stomach with deployment of a lumenapposing metal stent (LAMS), followed by advancement of an endoscope through the LAMS to perform an ERCP or EUS. It is a technically challenging procedure, requiring skills in EUS, fluoroscopy, and LAMS deployment. The aim of this study was to determine the learning curve for EDGE.
Aims and Methods: Consecutive patients undergoing EDGE by a single operator were included from a prospective registry from Aug 2014 to Oct 2017. Demographics, procedure info, post-procedure follow-up data, and adverse events were collected. Nonlinear regression and CUSUM analyses was conducted for the learning curve. Technical success was defined as successful creation of fistulous tract. Clinical success was defined as successful EUS or ERCP via the LAMS.
Results: 19 patients were included (21%M, mean age 58.7 years). Indication included symptomatic biliary stricture (n = 6, 32%), choledocholithiasis (n = 5, 26%), pancreatitis (n = 3, 16%). Technical success was 100%. All patients had a 15mm LAMS placed, 3 (16%) had cautery-LAMS. Clinical success was achieved in 18/19 (95%) patients. 14 patients had an ERCP, 1 patient had an EUS, and 3 patients had both. 5 patients had the EUS or ERCP performed during the same session as fistula creation; the remaining 14 were separated by 2–3 weeks. 13 patients had their LAMS removed and fistula closed. 1 patient had bleeding requiring EGD with clipping post-procedure; 3 patients required a bridging stent, 1 for tamponade and 2 for misdeployment. No other adverse events were noted. Median procedure time was 54.5 mins (range 31 - 88 mins). CUSUM chart shows 54 minute procedure time was achieved at the 9th procedure hence indicating efficiency. Apart from 2 outliers, the procedure duration further reduced with consequent procedures with the last 3 being under 40 minutes indicating at that after 25–35 procedures a plateau may be reached indicating mastery (nonlinear regression p < 0.0001)
Conclusion: Endoscopists experienced in EDGE are expected to achieve a reduction in procedure time over successive cases, with efficiency reached at 54.5 minutes and a learning rate of 9 cases. After 25–35 procedures, a plateau may be reached indicating mastery
Disclosure: Michel Kahaleh MD: has received grant support from Boston Scientific, Fujinon, EMcison, Xlumena Inc., W.L. Gore, MaunaKea, Apollo Endosurgery, Cook Endoscopy, ASPIRE Bariatrics, GI Dynamics, NinePoint Medical, Merit Medical, Olympus and MI Tech. He is a consultant for Boston Scientific, Xlumena Inc., Concordia Laboratories Inc, ABBvie, and MaunaKea Tech.-Amy Tyberg MD is a consultant for EndoGastric Solutions.- Prashant Kedia MD is a consultant for Boston Scientific, Endogastric solutions and Apollo Endosurgery.- All other authors have nothing to disclose.

P0228 NEWLY DEVELOPED MODEL FOR TRAINING EUS-FNA AND PSEUDOCYST DRAINAGE PROCEDURE

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Introduction: Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) has become a indispensable examination in the clinical fields. Furthermore, therapeutic EUS such as pseudocyst drainage, EUS-biliary drainage, and EUS-pancreatic duct drainage, etc. have become popular year by year. Generally, it is important to learn EUS-anatomy by books and DVDs at first. And it has been believed that the learning of EUS-FNA takes a long time and a certain number of case experiences are essential, in order to become a good endosonographer. On the other hand, clinical cases are not enough for training young endosonographers and hands-on training with models are able to reduce the number of performing clinical EUS-FNA on training programs. Therefore, we have developed newly designed model for training EUS-FNA and therapeutic EUS-FNA procedure and investigated its usefulness and limitations.
Aims and Methods: We have made a model for EUS-FNA with Olympus Co. and pseudocyst model by non-rupture-balloon (Sumitomo Bakelight Co., Tokyo) which is 8cm in diameter. This balloon is filled with lubricant, and these models are puts into water tank. We have tried this model at Kitasato hands-on training workshop with 16 attendees who have experienced 100 to 700 diagnostic EUS examinations and 0 to 50 EUS-FNA procedures. We have investigated whether all attendees can complete EUS-FNA of the pancreas and pseudocyst drainage or not, and how long it takes to complete the procedure. Furtheremore, we have checked their impression of this model. We have employed UCT-260 (Olympus Co., Tokyo), 19G EUS-FNA needles and 7Fr plastic stent as a drainage tube.
Results: All attendees have found the pancreas which is located behind the stomach and performed EUS-FNA in the target of the pancreas. Concerning about pseudocyst model, attendees firstly have to look for a good position for pseudocyst drainage. Secondly, attendee punctures the balloon with 19G needle and put a 0.035 inch guidewire in pseudocyst model. Thirdly, attendee pushes a dilator into the pseudocyst model and finally puts a 7 Fr drainage tube in the model. All attendees completed pseudocyst dranage with 6.5 minutes in average. No balloons have not ruptured during these procedures and all kept the balloon size, in spite of some leakage. According to their impression, resistance of puncture and putting in a stent is less, compared with clinical cases, however it is very useful to understand EUS-guided pseudocyst drainage and EUS-FNA.
Conclusion: We concluded that newly designed pseudocyst model is useful to train the beginner, in order to understand the procedure. Furthermore, using this model, we can do hands-on training everywhere and there is no necessity of animal laboratory because of dry model.
Disclosure: Nothing to disclose

P0229 THE FEASIBILITY AND EFFICACY OF ENDOSCOPIC ULTRASOUND-GUIDED LIVER BIOPSY USING A CORE NEEDLE FOR HEPATIC SOLID MASSES

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Introduction: Evaluate feasibility and efficacy of EUS-guided fine-needle biopsy (FNB) using a core needle for hepatic solid masses (HSMs). Also, assess the factors that influence diagnostic accuracy of EUS-FNB for HSMs.
Aims and Methods: A retrospective analysis of patients who underwent EUS-FNB for the pathological diagnosis of HSMs between January 2013 and July 2017 was conducted. The procedure was performed with core needles of different calibers. The variable evaluated were mass size, route of puncture, needle type, and number of needle passes.
Results: During study period, 58 patients (23 female; mean age, 68.0 ± 11.5 years [range, 42–86]) underwent EUS-FNB for pathologic evaluation of HSMs with a mean size of 21.4 ± 9.2 mm. EUS-FNB with 20G (n = 14), 22G (n = 29) or 25G core needle (n = 15) was performed (right lobe: n = 16, left lobe: n = 39, caudate lobe: n = 3). The median number of needle passes was 2.6 ± 0.8 (range, 1–5). The diagnostic accuracy were 89.7%, but both specimen adequacy for histology and available immunohistochemistry stain was 91.4%. The sensitivity and specificity of EUS-FNB were 89.7 and 100%, respectively. Additional information regarding cytology results increased sensitivity, and diagnostic accuracy of 93.1%, respectively. There was 1 bleeding complication, but well-controlled with endoscopic hemostasis. The median score of the procedure related pain using visual analog scale (VAS) was 1.76 ± 0.68 and 50 patients (86.2%) had a pain score of less than 2. No variable were independently associated a correct final diagnosis according to the multivariate analysis.
Conclusion: EUS-FNB with core biopsy needle is a safe and highly accurate diagnostic option for assessing HSMs. There was no variable factors associated with diagnostic accuracy.
Disclosure: Nothing to disclose

P0230 A MULTI-CRITERION, FULLY AUTOMATED, HIGH-PERFORMANCE, RAPID TOOL ASSESSING THE MUCOSAL VISUALIZATION QUALITY OF STILL IMAGES IN SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Capsule endoscopy (CE) is the preferred method for small bowel (SB) exploration. Its diagnostic yield can be reduced by poor mucosa visualization secondary to the presence of residues, bile, bubbles in the digestive luminal, or due to insufficient or excessive brightness. An electronic evaluation, image by image, is likely to be more efficient and reproducible than human evaluation of full length videos. The main objective of this study was to evaluate diagnostic performances of 3 computerized parameters, isolated and then combined, to assess quality of SB mucosa visualization for 3rd generation CE still images: (a) red/green ratio pixels of the image (1); (b) an index reflecting the abundance of the bubbles based on a gray-scale co-occurrence matrix (GLCM) (2); (c) an index reflecting the image's brightness.
Aims and Methods: 600 still images were randomly extracted from 30 full and normal SB-CE. 3 experimented CE readers evaluated these images according to an assessment grid with 5 items and 10 points, based on the quantitative scale by Brotz et al (3): mucosa visibility (2 points), brightness of the picture (2 points), bubbles abundance (2 points), bile and chime abundance (2 points), liquids and residues abundance (2 points). An image was judged to be of good visual quality when the mean score was $\geq$ 7/10. These images were analyzed electronically according to the 3 pre-cited parameters (ratio of red/green pixels, abundance of bubbles, brightness). A random forests methodology was used for machine learning and testing. Performances of the electronic analysis, using the expert's analysis as reference, were compared for each of the 3 electronic parameters individually and then combined.
Results: Combination of the 3 parameters on the computerized analysis of the 600 images compared to the experts' evaluation achieved the highest diagnostic performances, to discriminate between adequately and inadequately cleansed still frames. Sensitivity was of 90.01% (95% CI [84.12–95.88]) and specificity 87.73% (95% CI [81.63–94.37]), positive and negative predictive values were respectively of 81.10% (95% CI [73.31–88.69]) and of 93.70% (95% CI [88.94–98.46]). The mean time required to electronically analyze a still image using the 3 criteria test method was 34 ± 2 milliseconds using the MATLAB©software. An extrapolation on 50,000 images suggests a 28 minutes analysis of a full-length CE video.
Conclusion: We propose a novel, efficient, perfectly reproducible, automatic and rapid multi-criterion electronic score to determine the level of cleanliness of SB-CE still frames. This tool will be able to serve in clinical practice (to determine if the quality of preparation of SB-CE is acceptable) and research (testing different modalities of bowel preparation). A European patent is pending.
Disclosure: Xavier Dray has acted as a consultant for Boston Scientific, Fujifilm, Medtronic, and Pentax. Sarra Oumrani, Aymeric Histace, Einas Abou Ali, Olivia Pietri, Aymeric Becq, Guy Houist, Isabelle Nion-Lamurier, Marine Camus, Christian Florent disclose no conflicts of interest related to this subject.

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P0231 A NEURAL NETWORK ALGORITHM FOR DETECTION OF GASTROINTESTINAL ANGIODYSPLASIA DURING SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Capsule endoscopy (CE) has become a standard non-invasive tool for small bowel (SB) examination. However, with an average number of 50,000 SB still frames per CE video, lesions can be missed and CE reading remains a time-consuming activity. Therefore, the development of computer-aided algorithms for lesions' detection has become an active research area in CE. Gastrointestinal angiodysplasias (AGD) are the most common SB vascular lesions with an inherent risk of bleeding. This study aimed to develop a computer-assisted diagnosis (CAD) tool for SB-AGD detection in CE.
Aims and Methods: A French national database (CAD-CAP) was created: 4166 deidentified third-generation SB-CE videos (Pillcam® SB3 system, Medtronic) were collected from 13 centers; 6013 pathological still frames were extracted from 1354 SB-CE with at least 1 pathological findings; 20,000 normal (control) still frames were extracted from 200 normal SB-CE videos. 600 still images with typical AGD were selected from the database by expert readers. 600 normal still frames were randomly extracted as controls. The 600 selected AGD were annotated on each individual pathological frame, as ground truth reference. 2 sets of 600 SB-CE still frames (300 normal frames and 300 frames with AGD per set) were created. Different learning-based algorithms were tested including color-based approaches and deep feature extraction. The first set of still frames was used for the machine learning process and the second set for the validation process.
Results: Among the tested algorithms, the 1 with the best diagnostic performance characteristics used a semantic segmentation images approach associated with an artificial convolutional neural network (CNN) for deep feature extraction (figure 1 from left to right: original image, annotated image, CNN approach, CNN approach on original image). This algorithm reached a 100% sensitivity, a 96% specificity, a 96% positive predictive value, and a 100% negative predictive value for AGD detection. Reproducibility was perfect (Kappa = 1.0).
Conclusion: This study shows that a computed algorithm based on a CNN has very good reproducibility, diagnostic sensitivity (100%), and specificity (96%), for detection of AGD on still frames. This study opens the way to automated SB-CE reading softwares, and calls for prospective evaluations of CNN at the video level. The CAD-CAP project is founded by the French National Society of Gastroenterology (SNFGE), and endorsed by the French Society of Digestive Endoscopy (SFED).
Disclosure: Xavier Dray is a consultant for Boston Scientific, Fujifilm, and Medtronic. Gabriel Rahmi is a consultant for Medtronic. Jean Christophe Saurin is a consultant for Capsovision, Medtronic and Intromedic. Sylvie Sacher Huvelin is a consultant for Medtronic.

P0232 CAD-CAP: A 26000 IMAGES DATABASE SERVING THE DEVELOPMENT OF ARTIFICIAL INTELLIGENCE FOR CAPSULE ENDOSCOPY

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Introduction: Capsule Endoscopy (CE) is preferred method for small bowel (SB) exploration. With a mean number of 50,000 SB frames per video, SBCE reading is time-consuming and tedious (30 to 40 minutes per video). We describe herein a large, multicentric, public database named CAD-CAP (Computer-Assisted Diagnosis for CAPsule Endoscopy, CAD-CAP). This database aims to serve the development of CAD tools, from the initial steps (machine learning) to the last preclinical steps (assessment and comparison of performances).
Aims and Methods: 13 endoscopy French centres were involved, together with a research group specialized in signal treatment and analysis in medicine. All available Pillcam® SB3 (Medtronic) SB-CE videos were retrospectively selected from these centres and deidentified. Any pathological frame selected from the initial reading was extracted and included in the database. Manuel annotation was performed by premed students trained and supervised by an expert reader. All annotated lesions were then read again by a panel of 3 expert readers Any inadequate annotation was revised. Lesions were then classified both by type and clinical pertinence. An automated extraction process was also developped to create a dataset of normal, control images from normal, complete, SB-CE videos. For any extracted still frame (with or without a lesion), a short video sequence was also captured (9 secondes long, with 25 frames upstream and downstream of the index frame).
Results: 4,166 SB-CE were included. 1,127 videos (27%) containing at least 1 pathological frame were selected. 6,103 pathological frames (with their short video sequences) were extracted and annotated: 691 frames with fresh blood, 2946 frames with vascular lesions, 1676 frames with inflammatory lesions, and 790 frames with miscellanous lesions (including tumors and polyps). 20,000 normal frames (controls, with their short video sequences) were extracted from 206 SB-CE normal videos. CAD-CAP has already been used for the development of an automated angiodysplasia detection tool, with sensitivity of 100% and specificity of 96% (1). International challenges between research groups specialized in signal treatment and analysis in medicine have been organized, using the CAD-CAP database (2,3).
Conclusion: The CAD-CAP database is an innovative tool, serving the developement of artificial intelligence for SB-CE reading. Requests from academic research groups to use CAD-CAP will be made possible on www.sfed.org in September 2018.
Disclosure: Xavier Dray is a consultant for Medtronic. Gabriel Rahmi is a consultant for Medtronic. Jean Christophe Saurin is a consultant for Capsovision, Medtronic and Intromedic. Sylvie Sacher Huvelin is a consultant for Medtronic.

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P0233 DIABETES MELLITUS AND VIDEO CAPSULE ENDOSCOPY: SOME OF THEM JUST NEED MORE TIME

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Introduction: Video Capsule Endoscopy (VCE) is commonly used for evaluation of small bowel in patients with iron deficiency anemia. Patients undergoing VCE are typically instructed to end the recording after 8 hours. Due to limited recording time the presence of delayed gastrointestinal transit often leads to incomplete examination. The influence of Diabetes Mellitus (DM) on VCE is controversial - 1 study found prolonged gastric transition time and increased VCE failure rate in DM, while others didn't demonstrate correlation between the 2.
Aims and Methods: The aim of the study was to evaluate the influence of DM, with or without end-organ damage, on gastric and small bowel transit times, and on VCE examination completion rate.
In single center, retrospective study we investigated the records of patients who underwent VCE (PillCam, Given Imaging,Israel) for evaluation of iron deficiency during the period of 2010–2017. Only outpatient examinations were included. Patients with history of gastric/colonic/small bowel surgery, Parkinson's disease, Crohn's disease, chronic laxative use and active non-prostate malignancy were excluded. Demographic and VCE examination related data were collected. VCE was considered complete if the capsule reached cecum within the examination allotted time. DM-variables of interest included duration of the disease, use of insulin, presence of end-organ damage, average and peak HgA1c within the past 3 months prior to the VCE.
Results: A total of 254 patients met the inclusion criteria. 47% had type 2 DM. Patients with diabetic neuropathy had significantly prolonged small bowel transition time (SBTT) compared both to non-DM patients (5.24+/−1.18 VS 4.38+/−1.34 hours, p = 0.02) and to patients with DM without end-organ damage (5.24+/−1.18 VS 4.08+/−1.48 hours, p = 0.005). Likewise, patients treated with insulin had significantly prolonged SBTT compared to DM patients without insulin treatment (5.32+/- 1.19 VS 4.23+/−1.59, p = 0.007). Retinopathy and

nephropathy alone did not significantly influence SBTT. No correlation was found between average and peak HgA1c levels and SBTT.
Gastric transit time (GTT) was similar between the DM and non-DM cohorts (0.54 +/−0.67 hours VS 0.6 +/−0.82 hours, p = 0.55), and no correlation was found between GTT and either the presence of end-organ damage, HgA1c levels within 3 months from VCE, peak Hga1c or the duration of the disease.
VCE completion rate was significantly lower in DM patients with neuropathy compared to to those without end organ damage (87.5% VS 98%, p = 0.03). There was a trend towards lower VCE completion rate in patients treated with insulin or with multiple effected end-organs, however it didn't reach statistical significance. VCE completion rate was similar between non-DM patient and DM patients without end-organ damage (94% VS 98%, p = 0.11).
Conclusion: SBTT is significantly prolonged in DM patients with neuropathy or insulin treatment, and might lead to lower VCE completion rate in those patients. An *a priori* longer VCE recording time should be considered for patients with these conditions. For DM patients without end-organ damage or insulin treatment, bowel transition times and VCE completion rates are similar to those without DM, thus examination time adjustments are not needed.
Disclosure: One of the authors (Dr. Stein Assaf) is also a member of R&D team, Medtronic, Yokneam site, Israel

P0234 VIDEOCAPSULE ENDOSCOPY IN UNEXPLAINED IRON DEFICIENCY ANEMIA: A RETROSPECTIVE COHORT STUDY

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Introduction: Iron deficiency anemia (IDA) may affect 1–2% of all adults. After conventional endoscopy, the cause of IDA remains unknown in up to 40% of patients. Video-capsule endoscopy (VCE) represents the cornerstone of investigation for unexplained IDA in subjects with strong suspicion of obscure bleeding. We aimed to investigate the prevalence of VCE-detected small bowel injury and associated risk factors in a cohort of inpatients with IDA and obscure small-bowel bleeding.
Aims and Methods: We included inpatients with IDA (hemoglobin levels < 12.0 g/dl in women and < 13.0 g/dl in men), showing obscure bleeding demonstrated by fecal occult blood test (FOBT) and negative upper endoscopy and colonoscopy. Cirrhosis and inherited polyposis syndromes were exclusion criteria. A complete medical history and laboratory tests were collected. All subjects received VCE (PillCam SB2/SB3) and Lewis score was calculated. Comparison between continuous variables was performed by unpaired t-test and between categorical variables by Fisher's exact test. Variables with statistical significance at univariate analysis were evaluated by a multivariate binomial or linear regression analysis. The risk was expressed with Odd Ratio (OR) and 95% confidence intervals (CI).
Results: 109 (female/male ratio 53/56, aging 63.4 ± 18.9 years) were recruited according to exclusion and inclusion criteria. All patients had hemoglobin levels < 10 g/dl and a strong suspicion of obscure bleeding. 80 (73.4%) presented 1 or more small bowel lesions at VCE (11 petechiae, 13.7%; 29 erosions, 36.2%; 7 hemorrhagic areas, 8.75%; 3 denuded areas, 3.75%; 5 strictures, 6.25%; 15 neoplasms, 18.75% and 25 angiodysplasiae, 31.25%; 14 patients had multiple lesions, 18.75%).
52 patients (65%) showed a mild Lewis score (<135), 25 (31.2%) had a moderate score (135 to 790), and only 3 (3.8%) showed a score >790. The mean Lewis score in patients with lesions was 193 ± 198. We did not find a significant correlation between hemoglobin levels and severity of damage: Pearson's r = 0.10, p = 0.41.
When compared to patients without small bowel injury, subjects with lesions had a longer small bowel transit time (6.2 ± 2.9 versus 5.2 ± 2.1 hours), had used non steroidal anti-inflammatory drugs for at least 2 weeks (17.5% versus 0%, p = 0.01) and used more frequently oral anticoagulants (20% versus 6.9%, p = 0.10) at univariate analysis. None of the factors statistically significant in univariate analysis was associated with the presence of small bowel injuries at multivariate analysis (table 1).
Age (b = 1.05, 95% CI 0.76–0.98, p = 0.10), small bowel transit time (b = 1.26 95% CI 1.05–1.86, p = 0.09), and PPI use (b = 5.81 95% CI 4.54–7.45, p = 0.09) showed a favorable trend, correlating directly with the severity of the lesion at univariate analysis. In the multivariate analysis, only the use of PPI correlate with the severity of the lesion (b = 4.56 95% CI 4.12–5.77, p < 0.001).

	OR (95% confidence interval)	P value (univariate)	OR (95% confidence interval)	P value (multivariate)
Small bowel transit time	0.88 (0.76–0.98)	0.049	0.86 (0.72–1.03)	0.09
NSAIDs assumption for at least 2 weeks	12.86 (0.74–223.1)	0.01	2.15 (0.44–10.50)	0.34
Oral anticoagulants	3.38 (0.73–15.70)	0.10	2.50 (0.46–4.56)	0.36

[Table 1. Estimation of risk, expressed as odd ratio (OR), for presence of lesions detected at VCE, both in univariate and multivariate analysis (binom]

Conclusion: VCE can reveal a source of obscure bleeding in unexplained IDA in up to 73.4% of subjects. Old age is the main risk factor for small bowel lesions. In about the 26.6% the cause of anemia could be not linked to gastro-intestinal bleeding despite a positive FOBT.
Disclosure: Nothing to disclose

P0235 A ROPEWAY CAPSULE ENDOSCOPY FOR EXPLORING THE ENTIRE GASTROINTESTINAL TRACT WITH A NON-PER OS PREPARATION AND A SHORTER EXAMINATION TIME

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Introduction: Capsule endoscopes are designed for screening a long tube organ such as the small intestine or colon. Though they are non-invasive, they have various drawbacks compared to conventional endoscopes, such as inadequate observation in the esophagus and stomach, an unacceptable amount of preparation solution for colon screening and a long examination time.
Aims and Methods: Our aim was to realize an entire gastrointestinal (GI) tract examination with high accuracy, easy preparation and a short examination time. Our system was composed of a current colon capsule endoscope (CCE: PillCAM colon2, Covidien, USA), a length of carbon thread attached to the CCE and a 7.5 Fr. catheter with a tilting function at the tip (Smart touch: Biosense Webster, USA). At first a 0.04mm carbon thread was inserted into the nose and taken out through the mouth using a magnet. After the AFR function was turned on, a CCE was attached to the thread and swallowed. After confirming the CCE's position in the stomach, the catheter was inserted into the stomach along the thread. The examiner used the catheter to control the volume of air in the stomach or to flash water through it if the stomach needed cleansing. After observing all parts of the stomach, the CCE was navigated into the duodenum. The capsule was detached from the tip of the catheter by pulling on the thread. After the detachment, the catheter was used for injecting a large volume (over 2 liters) of preparation solution into the small bowel quickly to accelerate the CCE's movement and cleanse the colon easily. To evaluate this method, 15 volunteers were enrolled in a pilot study.
Results: 1) We could observe all the parts of the stomach easily and manipulation of the catheter was the same as a current endoscope. Image quality was not inferior to conventional gastroscopy. 2) The preparation solution was injected into the duodenum through the catheter at a speed of 10cm/sec, which meant that we could inject 3 liters in 300 seconds. 3) The chief adverse reaction was abdominal distention (3/15). 4) The average examination time for the small bowel transit time was 12 minutes and the colo-rectal transit time was 33 minutes. 5) The cleanliness was similar to or better than the current colon capsule endoscopy preparation. 6) The VAS scores for acceptability were better than the scores for current colon capsule endoscopy.
Conclusion: We have developed a simple, inexpensive and practical method for examining the entire GI tract with only one CCE.
Disclosure: Nothing to disclose

P0236 CAPSULE ENDOSCOPY: IS THE SOFTWARE TOP 100 A RELIABLE TOOL IN MID-GASTROINTESTINAL BLEEDING?

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Introduction: Capsule endoscopy (CE) is the gold standard for diagnosing mid-gastrointestinal bleeding (MGIB). In 2017 emerged a new functionality in the RAPID Reader® the TOP100, that performs the automatic selection of the 100 most distinct images that may contain abnormalities.
Aims and Methods: We aimed to compare the concordance of findings between the classical CE reading (CR) and the use of TOP 100 in suspected MGIB.
Retrospective study including consecutive patients submitted to CE for suspected MGIB. 2 experienced readers performed CR and reported the most important findings. Another experienced reader, blinded to the CR results, reviewed all SBCE videos using TOP100 and reported the most important findings, excluding false positive results. In MGIB the relevant findings were defined as the presence of P2 lesions, namely angioectasias, ulcers or tumors.
Results: 69 patients were included, 56.5% females, with mean age 60 ± 18 years. 62 patients (89.9%) performed CE for anemia and 7 (10.1%) for obscure-overt gastrointestinal bleeding. The overall diagnostic yield was 42% and the P2 lesions more frequently observed were angioectasias (34.85) followed by ulcers (11.6%). No tumors of the small bowel were observed.
TOP100 detected 53/66 (80.3%) of the P2 lesions, in particular 45/48 (93.75%) of the angioectasias and 8/18 (44.4%) of the ulcers. The TOP 100 identified all active bleeding.

All images that were false positives selected by the TOP 100 were easily identified by an experienced reader.
Conclusion: The TOP100 identified all active bleeding, as well as the vast majority of significant lesions (80%), in particular, detected about 94% of angioectasias. Although CR remains the gold standard in the EC review, these findings demonstrate that TOP100 allows a quick reading with early identification of the most important findings in MGIB, constituting an extraordinary tool in an urgent context.
Disclosure: Nothing to disclose

P0237 SIGNIFICANCE OF INCIDENTAL FINDINGS IN VIDEO CAPSULE ENDOSCOPY

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Introduction: Video Capsule Endoscopy (VCE) is the procedure of choice for the investigation of small bowel pathologies. VCE examinations also provide limited views of the esophagus, good visualization of the stomach/proximal duodenum, and some visualization of the colon. Incidental gastrointestinal pathologies in the upper gastrointestinal tract and colon are often seen during VCE but there is limited data regarding the significance of incidental findings. These pathologies, may not be directly linked to the patient's presenting complaint, may not be clinically significant and can lead to unnecessary investigations and consumption of health care resources.
Aims and Methods: The aim of this study is to evaluate if incidental pathologies found during VCE have any effect on patient outcome. 2 experienced gastroenterologists consultants prospectively reviewed the upper GI segment and colonic segments of VCEs performed over a 5-year period and identified those with UGI and colonic findings. These patients were then reviewed in the electronic databases for follow up visits, investigations, and treatments up to a year following their VCE procedure.
Results: We identified 103/733 (14.15%) patients with incidental findings, of which, 51 patients (49.5%) had completed charts that allowed for analysis. Incidental upper GI pathologies were identified in 45/103 (43.7%) patients in the original VCE reports, and 88/103 (85.4%) in the prospective dedicated VCE reading ($p < 0.001$). Incidental colon pathologies were identified in 7/103 (6.8%) patients in the original reports, and 19/103 (18.4%) in the prospective dedicated VCE reading ($p = 0.012$). 40 (38.8%) patients had only incidental upper GI and/or colon VCE findings without small bowel findings. 32 out of 51 (62.7%) patients with incidental VCE findings were seen for follow up. 19 of 51 (37.3%) patients had further investigations related to pathologies outside the small intestine; 9 underwent repeat EGD only, 4 underwent repeat colonoscopy only, and 6 underwent both repeat EGD and repeat colonoscopy. 5 out of 15 (30%) documented follow up EGDs attributed to a positive incidental finding on VCE were found to have significant findings that were not documented in their respective pre-VCE EGD reports. 2 out of 10 (20%) documented follow-up colonoscopies attributed to a positive incidental finding on VCE were found to have significant findings which were not documented in their respective pre VCE colonoscopy reports. No patients had recorded repeat hospitalizations, required blood products, or invasive interventions during the follow-up period.
[Pertinent Results of VCE Study Outcome]

	Initial VCE Report	Prospective Dedicated VCE Reading	P-value
Upper GI Incidental Pathologies	45/103 (43.7%)	88/103 (85.4%)	<0.001
Colonic Incidental Pathologies	7/103 (6.8%)	19/103 (18.4%)	0.012
New Endoscopic Pathologies Found in Follow Up (n = 9)			
Small Gastric Duodenal Polyps			3/7 (42.9%)
Gastric Erosions			2/7 (28.6%)
Gastric Blood			1/7 (14.3%)
Colonic Polyps			2/2 (100%)

Conclusion: Dedicated readings of additional segments (upper GI and colon) may identify significantly more incidental pathologies compared to current practices. Many of these findings are significant enough to warrant further follow-up. Upper GI and colonic segments of small bowel VCE should be reviewed routinely. Any incidental pathologies should be clearly documented and suggestions for follow up should be made within the VCE reports.
Disclosure: Nothing to disclose

P0238 THE EFFECTIVENESS OF IMPROVED USE OF CHEWING GUM IN INFLUENCING CAPSULE ENDOSCOPY TRANSIT TIME - A PROSPECTIVE RANDOMIZED, CONTROLLED PILOT STUDY

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Introduction: Capsule endoscopy (CE) is a powerful tool in the assessment of small bowel pathology. However, approximately 1 in 5 CEs does not visualize the entire small bowel at completion of the examination by the end of the recording time. Data suggest that chewing gum during the whole examination time, simulating sham feeding, may increase CE completion rate, but decrease the small bowel transit time (SBTT) that may be positive correlated with its diagnostic rate.
Aims and Methods: The aim of this study is to determine the effect of chewing gum, during the first 1 hour of examination in patients undergoing CE for GTT and SBTT time and the proportion of cases with complete small bowel examination.
Consecutive patients 16 years of age and older undergoing small-bowel CE from November 2017 to April 2018 were assessed for eligibility. Patients chewed 1 piece of gum for approximately 15 min every 30 min at the first hour of the examination. 2 blinded gastroenterologists examined all studies. The completion rate of CE that reached the caecum within 10 h, gastric transit time (GTT) and small bowel transit time (SBTT) were evaluated in all patients.
Results: 52 consecutive patients were randomized either to use chewing gum ($n = 26$) or not ($n = 26$). The mean age was 47.5 ± 18.3 years and 48.0 ± 19.0 respectively. The GTT in the chewing-gum group was significantly shorter than control [35.5 min (interquartile range: 35.25) vs. 65.5 min (interquartile range: 44.75) ($p = 0.000$)]. There was no significant difference in SBTT between the 2 groups [350.0 min (interquartile range: 236) vs. 384.0 min (interquartile range: 221) ($p = 0.701$)]. The CE percentage passed into the caecum was no difference in the chewing gum group compared with those in the control (88.5% vs. 76.9% respectively, $p = 0.271$).
Conclusion: Chewing gum at the first hour during CE examination could significantly reduce GTT but not SBTT. Its use might improve the likelihood of the diagnostic yield of CE by the unaltered small bowel transit during the procedure.
Disclosure: Nothing to disclose

P0239 ENDOSCOPIC ULTRASOUND-GUIDED TRANSMURAL GALLBLADDER DRAINAGE USING ELECTROCAUTERY-ENHANCED LUMEN-APPOSING METAL STENT VERSUS STANDARD TUBULAR METAL STENT

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Introduction: In high-risk patients, EUS-guided gallbladder drainage (EUS-GBD) is a validated alternative to percutaneous transhepatic gallbladder drainage (PT-GBD) based upon the 2018 Tokyo guidelines. The use of electrocautery-enhanced lumen-apposing metal stent (ECE-LAMS) have recently and rapidly disseminating into interventional EUS practice.
We compare in this French study the clinical outcomes of endoscopic ultrasound-guided gallbladder drainage with standard tubular fully covered metallic stents (FCMS) versus ECE-LAMS as a treatment for patients with acute cholecystitis who are unfit for surgery.
Aims and Methods: We performed this retrospective single center study between June 2014 and March 2018. A total of 40 patients (22 women) with acute cholecystitis (25 acalculous) underwent EUS-GBD with FCMS ($n = 19$) or LAMS ($n = 21$). FCMS procedures were executed under general anesthesia with endotracheal intubation and fluoroscopy guidance. Access was achieved with a 19G EUS needle. A.035-inch guidewire was passed through then a 8Fr cystotom was used to create the fistula before we place the FCMS then a plastic double-pigtail stent of 7Fr (stent in stent technique). ECE-LAMS procedures were performed without endotracheal intubation and access was achieved directly and by using only EUS guidance. Data were collected on technical success (stent placement), clinical success (resolution of symptoms within 3 days) and adverse events.
Results: EUS-GBD with FCMS was performed in 19 patients (11 women) with a median age of 77 years (range, 66–92), most with acalculous cholecystitis ($n = 13$; 68.4%). In the ECE-LAMS group, 21 patients (11 women) with a median age of 79 (48–99) were treated for cholecystitis, acalculous in 12 cases (57.1%). Stent placement was technically successful in 38 patients (95%), 18/19 with FCMS and 20/21 with LAMS. 2 of the failure cases required immediate surgery. Resolution of cholecystitis was observed in 37 of 38 patients (97.3%). The medium time of procedure was 22mn (range, 10–40) in the FCMS group and 7mn (range, 3–30) in the ECE-LAMS one. There were 4 adverse events in the FCMS group (15.8%) and 1 in the LAMS group (4.7%). No bleeding occured. We observed 2 late stent migrations and 2 patients had recurrent cholecystitis in the FCMS group, none in the LAMS group with a median follow-up of 267 days (range, 3–1206). Removal of a FCMS was attempted successfully in 1 case at 4 months before a now possible cholecystectomy. The mean postprocedure pain score (2/10) and length of stay in the hospital (4 days) were the same in both groups.
Conclusion: EUS-GBD technique with FCMS or ECE-LAMS appear as a feasible and efficient technique with similar technical (95%) and clinical success (97%) in both group. This results are equivalents to thoses of the PT-GBD and better to thoses of the transcystic endoscopic drainage. The ECE-LAMS has the benefits of a simpler and faster method with less adverse events. We

also observe no stent migration and no recurrence of cholecystitis with the ECE-LAMS, which is contrary to the litteracy.
Disclosure: Privat J.: consultant for Boston Scientific.

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P0240 STENT PATENCY ACCORDING TO THE CHEMOTHERAPY AND ITS REGIMEN

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Introduction: Jaundice and subsequent biliary infection caused by tumor can be detrimental for the patients with pancreatic cancer. Therefore, stent insertion for biliary decompression is necessary for the patients with biliary obstruction by pancreatic cancer and it is important to keep the stent patent as long as possible. However, few studies have compared stent patency according to chemotherapy itself and chemotherapy regimen.
Aims and Methods:.Therefore, in this study, we aimed to evaluate the difference of stent patency according to chemotherapy and the factors associated with better stent patency. Between January 2015 and May 2017, 102 patients with pancreatic cancer who underwent biliary stent insertion with metal stent for the first time were retrospectively analyzed. The relationship between chemotherapy and stent patency were assessed. Additionally, factors for better stent patency and stent patency according to the chemotherapy regimen were also assessed.
Results: Median stent patency was 163 days for patients with best supportive care, 338 days for patients with chemotherapy, respectively. ($p = 0.041$) Univariate analysis showed that chemotherapy itself and chemotherapy regimen stent were significantly associated with better stent patency. Compared with patients who received best supportive care only, patients who underwent chemotherapy after stent insertion had better stent patency in multivariate analysis (OR 0.494; CI 0.247–0.988; $p = 0.046$). FOLFIRINOX also showed better stent patency than gemcitabine-based chemotherapy in multivariate analysis (OR 0.318; CI 0.113–0.900; $p = 0.031$).
Conclusion: Compared with patients who received best supportive care only, patients who underwent chemotherapy after stent insertion had better stent patency. Better stent patency can be expected for the patients with FOLFIRINOX.
Disclosure: Nothing to disclose

P0241 DRAINAGE OF THE RIGHT LIVER UNDER EUS: BRIDGE TECHNIQUE WITH HEPATICOGASTROSTOMY ALLOWING DRAINAGE OF THE RIGHT LIVER THROUGH THE LEFT LIVER INTO THE STOMACH

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Introduction: EUS (Endoscopy ultrasonore)-guided biliary drainage is now a comparable technique to percutaneous drainage. This drainage can also be performed in cases of complex drainage of the hilum, mainly described for salvage therapy to drain the left liver. In cases of inaccessible papilla or altered anatomy, EUS-guided biliary for hilar stenosis of the liver could be used as the first approach. The limitation of EUS drainage is the drainage of the right liver.
In this feasibility study, we reported the drainage of the right liver using the bridge technique and hepaticogastrostomy.
Aims and Methods: The study is a retrospective work based on a prospective registry from January 2013 to February 2017. Inclusion criteria were patients with inaccessible papilla due to altered anatomy or duodenal invasion and drainage by EUS guidance and bridge technique without previous biliary drainage. The bridge technique was used to place an uncovered biliary stent between the right liver and the left liver. The left liver was drained by performing a hepaticogastrostomy.
Results: 12 patients were included. Stenosis was type II for 9 patients, IIIB for 2 patients, and type IV for 1 patient. Technical success was 100%, and clinical success was 80%. Morbidity was 33% (4 patients), including 3 patients with abdominal pain managed conservatively and 1 patient with a percutaneous salvage drainage. Postoperative mortality was 8% (uncontrolled sepsis). Mean survival was 6 months. Chemotherapy could be administered in 70% of patients in cases of clinical success (7 patients).
Conclusion: The bridge technique under EUS-guidance could be a first alternative for draining malignant hilar stenosis in cases of inaccessible papilla.
Disclosure: No conflict of interest

P0242 FULLY COVERED SELF-EXPANDABLE METALLIC STENT, AS SUPERIOR TREATMENT OPTION FOR BILIARY ANASTOMOSIS STRICTURE AFTER LIVER TRANSPLANTATION COMPARED TO PLASTIC STENTS: A CASE-CONTROL STUDY

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Introduction: Fully covered self-expandable metallic stent (FCSEMS) was reported as endoscopic treatment option for biliary anastomotic stricture (AS) after liver transplantation (LT). However, there were only few studies compared FCSEMS to conventional plastic stent insertion to biliary strictures. The aim of this case-control study was to evaluate resolution rate of biliary AS and 1-year recurrence rate after stent removal between FCSEMS and plastic stents in LT patient.
Aims and Methods: 35 cases with biliary AS after LT were enrolled between 2012 and 2016. There were 20 patients in plastic group and 15 in FCSEMS group. ERCP were repeated every 3 months for evaluate stent function and AS resolution. Stent was removed if AS resolution was confirmed with radiologic remission. Patients were followed up until 1yr after stent removal for evaluate AS recurrence.
Results: There were no significant differences between groups in age, gender, and other baseline characteristics. The median stent indwelling period was 4.7 vs. 8.9 months in FCSEMS and plastic group ($p = 0.039$). The numbers of ERCPs were 2.3 in FCSEMS group and 3.1 in plastric group ($p = 0.065$). The mean number of inserted stents and ballooning during treatment period were lower in FCSEMS group ($p = 0.004$ and 0.007). The AS resolution rate was superior in FCSEMS group to plastic group (100% vs. 65%, $p = 0.012$). The 1-year AS recurrence rate were lower in FCSEMS group than plastic group (0 of 15 vs. 4 of 13, $p = 0.042$). Complication rate associated with stent insertion was 20% in FCSEMS group and 45% in plastic group ($p = 0.190$).
[Table 1. Comparison of plastic versus Kaffes stent for anastomosis stricture after liver transplantation]

	Plastic (N = 20)	FCSEMS (N = 15)	P-value
Male gender, N (%)	16 (80.0%)	11 (73.3%)	0.700
Age, mean ± SD	53.1 ± 13.9	57.7 ± 4.8	0.183
AS onset from LT, mo., median (range)	12.4 (0.4–76.4)	12.8 (0.17–112.8)	0.482
AS duration, mo., median (range)	12.4 + 27.6	16.2 + 18.6	0.633
Number of ERCPs, mean ± SD	3.1 ± 1.8	2.3 ± 0.6	0.065
Number of stents, mean ± SD	2.6 ± 2.0	1.1 ± 0.3	0.004
- Lenth of FCSEMS, cm		4.9 ± 1.0	
- Width of FCSEMS, mm		6.9 ± 1.0	
Number of ballooning, mean ± SD	1.7 ± 1.8	0.6 ± 0.6	0.017
Stent indwelling period, mo., median (range)	8.9 (0.5–48.5)	4.7 (3.3–11.9)	0.039
Stricture resolution, N (%)	13 (65.0%)	15 (100.0%)	0.012
1-year Recurrence, N (%)	4/13 (28.6%)	0/15 (0%)	0.042
Complication during treatment, N (%)	9 (45.0%)	3 (20.0%)	0.190

Conclusion: FCSEMS was superior compared to plastic stent in aspect of AS resolution rate of and 1year-recurrence rate without increasing complication rate. In addition, stent indwelling period, number of stents and ballooning procedure were reduced in FCSEMS group than plastic group. The FCSEMS is safe and effective treatment option for biliary AS after LT.
Disclosure: Nothing to disclose

P0243 IN VIVO EVALUATION OF A NOVEL ANTIREFLUX BILIARY METAL STENT

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Introduction: The efficacy of antireflux valve (ARV) biliary stent has not been well established and previous studies showed mixed results. ARV metal stents may be ineffective due to morphological change of the ARV. A novel ARV metal stent is a graft of 2 different stents, and each part has a different radial force. Distal part, ARV area, can be freely bent in multiple directions and has an unchanging stent lumen.

Aims and Methods: The aim of this *in vivo* animal study was to evaluate the efficacy of a novel ARV metal stent. The ARV metal stents and control metal stents were evenly inserted into the 10 mini-pigs. After 2 weeks, contrast media was injected in all mini-pigs at the duodenal bulb to evaluated for duodenobiliary reflux (contrast injection test), and histopathologic examination was performed to access the degree of duodenobiliary reflux.
Results: Stent placement was technically successful in all mini-pigs. After 2 weeks, 2 of control stents and 2 of ARV stents were distally migrated from the biliary ducts. Morphological change of ARV was not found in all ARV metal stent. In contrast injection test, duodenobiliary reflux was not found in all mini-pigs of ARV stent group, but found in all mini-pigs of control stent group. In histopathologic examination, the severity of inflammation was significantly attenuated in ARV stent group.
Conclusion: The novel ARV metal stents can be resistant to morphologic change and duodenobiliary reflux that can improve ARV dysfunction and stent patency.
Disclosure: Nothing to disclose

P0244 INTRA-DUCTAL MIGRATION OF BILIARY AND PANCREATIC STENTS, HOW TO MANAGE SUCH COMPLICATION? MONO-CENTERED EVALUATION OF A RETRIEVAL TECHNIQUE USING RAT-TOOTH FORCEPS

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Introduction: Intra-ductal stent migration is a common adverse even, and could be difficult to manage. In the major series, the frequency is estimated around 5% for the pancreatic stents and 3.5% for biliary stents.
Several techniques have been proposed for removing those stents, but to date, none has been objectively assessed in terms of technical success and complication rate. Thus, we propose a study with the aim to evaluate the outcomes of the stent removal using rat-tooth forceps.
Aims and Methods: This was a retrospective observational monocentered study. All the patients with intra-ductal stent migration, biliary or pancreatic, with a removal attempted using rat-tooth forceps were included. For each case, the procedure was consisting of first catheterizing the involved duct with a guide wire pushed along the stent, then advance forceps up to the distal tip of the stent, and finally open it for grasping the stent to pull it back outside of the duct. A balloon dilation or an enlargement of sphincterotomy could be applied in association to help for extracting the stent.
The age, sex, pathology of the patients, the indication for ERCP, the location, the type of stent, the presence of a stricture and stones, and the associated techniques have been recorded. The main objective was to document the technical success of stent removal using intra-ductal rat-tooth forceps. The secondary objectives were to elucidate the need for additional technique and the complication rate.
Results: In total, 2152 ERCPs with biliary or pancreatic stenting have been performed between 2009 and 2017. The overall migration rate was 5%, with 2.5% intra-ductal representing 55 patients. Among them, 40 patients had an attempt of stent extraction using rat-tooth forceps, and were kept for analysis. There were 22 men and 18 women, with a mean age of 53 ± 15 years-old. The main pathology indication a stenting was a calcified chronic pancreatitis in 21 cases. The other pathologies were idiopathic or genetic pancreatitis ($n = 4$), cholangitis ($n = 4$), a biliary duct stricture ($n = 4$), an ampulloma ($n = 2$), a pancreas divisum ($n = 2$), or others ($n = 3$).
The migration was involving biliary duct in 19 patients (47.5%), from whom 74% ($n = 14$) were covered self-expandable metallic stents, with a stricture associated in 32% of cases. It was involving the pancreatic duct in 18 patients (45%), from whom 83% were plastic stents, with a stricture associated in 50% of the cases as well as stones. Finally, 3 patients (7.5%) had a double migration in both ducts.
The removal success rate was 90% (17/19) for the intra-biliary migrations, in 3 cases requiring in addition a dilation or an enlargement of sphincterotomy, and 89% for the intra-pancreatic migrations, requiring a dilation in 4 cases or an enlargement of sphincterotomy in 1. An extraction balloon was used as prior technique in 5 cases. In case of double migration, the 2 stents could be removed in 1 case only. The overall technical success rate was 85% (34/40). In case of failure, an additional stent was placed in parallel to the other 1, the 2 stents being removed during the next session in 100% of the cases.
In terms of adverse events, there were 2 sepsis and 2 low grade pancreatitis with quickly favorable evolution. There was only 1 case of necrotic and severe acute pancreatitis. There was no mortality related to this procedure.
Conclusion: The removal of intra-ductal migrated stents using rat-tooth forceps is an effecitve approach in 85% of the cases in 1 single endoscopic session. This technique is also safe, with a low morbidity rate.
Disclosure: Nothing to disclose

P0245 URGENT ERCP AND PANCREATIC DUCT STENTING FOR THE MANAGEMENT OF POST-ERCP PANCREATITIS

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Introduction: Post-ERCP pancreatitis (PEP) is the most common and dreadful complication of ERCP, with reported 2–15% incidence rate among patients (pts.). Traditional methods of treatment of acute PEP like surgical approach or conservative treatment are well known, meanwhile endoscopic treatment, in particular duct stenting, are still controversial.
Aims and Methods: to evaluate the results of endoscopic stenting of the main pancreatic duct (MPD) as a new perspective treatment method of PEP.
From 01.01.2009 till 01.01.2016 we performed 3366 endoscopic interventions on major duodenal papilla (MDP). Complications occurred in 57 (1.7%) cases and PEP originated in 33 (0.98%) of them (29 f. and 4 m.; range: 25 - 86 years; mean age 59.7 ± 11.1). The indication for primary endoscopic interventions was jaundice in all cases, caused by stenosis of the MPD and microlithiasis (21), choledocholithiasis (7), duodenal parapapillary diverticulum (2), polyps of the MDP (2) and restenosis after previously performed EPT (1). Acute pancreatitis developed after failed ERCP in 3% (1/33), after balloon papillodilation with extraction of bile stones in 3% (1/33), after biopsy of MDP tumor in 3% (1/33) and after EPT in other 90.9% (30/33) patients, including nonselective EPT in 10 cases and additional pancreatic sphincterotomy in 4, extraction of bile duct stones in 11. PEP diagnosis was confirmed by laboratory (33 cases, level of amylasemia from 882 to 18502 un/l, mean level 4637 ± 3028 un/l) and instrumental methods (abdominal ultrasound in 23 pts. (69.7%), abdominal computer tomography - 8 (24.3%). Frequency of risk factors in patients with PEP was as following. The most frequent risk factors were female gender (29) and stenosis of terminal part of common bile duct (24), the equally often risk factors were young age, nonselective EPT, pancreaticography/cannulation of MPD - 12 cases to each other. The most common combinations of risk factors in patients with PEP were conjunction of 2 (21%), 3 (31%), and 4 (21%) risk factors.
Results: Promptly after confirmation of the diagnosis of acute PEP we tried to perform stenting of the MPD in 25 out of 33 patients, and succeeded in 22 (88.0%) of them. Complications of pancreatic stenting have not been revealed; all patients recovered. Inserted stents were short length, 5 and 7 Fr diameter with perforations on the sides, pig-tail and straight type with flaps by both ends. Pancreatic stents were removed in 5–12 days after their placement. The average time of pancreatic stenting was 11.2 ± 3.2 days. The average length of hospitalization was 10.4 ± 3.7 days. Other 11 (33.3%) pts., including 3 pts. with failed attempts of stenting, underwent medical therapy and 2 of them - surgical intervention afterwards. There were 2 (18.2%) lethal outcomes in this subgroup. The average time of hospitalization was 22 ± 17.1 days.
Conclusion: Endoscopic stenting of the MPD is technically feasible in 88.0% (22/25) of patients with acute PEP and it leads to recovery in all cases. Urgent pancreatic stenting should be done as fast as it is possible, but not more than 24 hours after the primary endoscopic retrograde intervention. Successful stenting is effective and safe method of treatment of this dangerous complication of ERCP. Moreover using pancreatic stenting reduces length of hospitalization by 71.5%, which brings economical benefits. Meanwhile in the subgroup of pts. where pancreatic stenting was not performed or failed, mortality reached 18.2% and average time of hospitalization was in 2 times longer. Prospective randomized trial is needed to prove these promising results.
Disclosure: Nothing to disclose

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P0246 MAGNETIC RESONANCE IMAGING OF THE COLON - AN ANALYSIS OF FECAL VOLUME AND STOOL DRYNESS

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Introduction: Opioids are known to affect motility, but their effect on fluid absorption and secretion in humans is poorly investigated.
Aims and Methods: This study is aimed at investigating the effect of oral-administered oxycodone on colonic fecal volume and stool dryness by using a novel magnetic resonance imaging (MRI)-based technique. We hypothesized that experimental opioid-induced constipation increases fecal volume and stool dryness. In a randomized, double-blinded, cross-over study, 25 healthy male volunteers were treated for 5 days with prolonged-release oxycodone or placebo, separated by 52 ± 10 days (mean ± SD). Dixon-type Liver Accelerated Volume Acquisition MRI-scans of the abdomen were obtained on day 1 and day 5 in each treatment period. Data were divided in 4 colorectal segments and analyzed with semi-automatic Matlab-based software (Sandberg *et al*., 2015). Fecal volume was quantified excluding gas volume and colon wall. Stool dryness was assessed using

MRI signal intensity (SI) as a biomarker for water content, where higher values means less water.
Results: After oxycodone treatment, total colonic fecal volume was significantly increased [mean 101 mL, 95% CI 15 to 187 mL] compared to placebo treatment [mean −14 mL, 95% CI −74 to 46 mL] ($p = 0.001$), with the largest difference (24%) observed in the ascending colon/cecum ($p = 0.001$). Stool dryness increased after oxycodone treatment [mean 0.09 SI, 95% CI 0.01 to 0.17 SI] compared to placebo [mean −0.02 SI, 95% CI −0.08 to 0.04 SI] ($p = 0.001$).
Conclusion: The MRI analysis methods showed differences in colonic fecal volume and stool dryness after treatment with oxycodone compared to placebo. The MRI-based method for non-invasive analysis of colon content have the potential to characterize gastrointestinal symptoms in general, such as in constipation.
Disclosure: Nothing to disclose

Reference

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P0247 THE SAFETY TRIAL OF SONODYNAMIC THERAPY FOR UNRESECTABLE INTRACTABLE CANCER

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Introduction: High-intensity focused ultrasound (HIFU) is expected to be the new and improved advanced therapy for unresectable intractable cancer (UIC) like pancreatic cancer (PC). The combination of HIFU therapy and chemotherapy can be used to effectively control the locally advanced tumor of unresectable intractable cancer by the site-direct manner. HIFU therapy has showed effectiveness of anti-tumor effect for unrespectable PC. From that, we have developed the new method, Sonodynamic therapy (SDT) in order to enhance anti-tumor effect and limit the damage done to the normal tissues during treatment. SDT is a novel therapeutic method of cancer treatment deriving from the cytotoxicity reaction, which is based on preferential uptake of sonosensitizer with anticancer drug in tumor tissues and subsequent activation of drug by ultrasound irradiation form an extracorporeal.
Aims and Methods: We have evaluated the safety and clinical tolerability of SDT in UIC. This is the prospective exploratory clinical non-random sampling and a series of registration studies. We have treated UIC patients using SDT, with whom an agreement was obtained in adequate IC, from May 2017 in our hospital. This study had received approval from the members of the ethic society of our hospital, and obtained research support from the Japan Agency for Medical Research and Development (AMED). The participants of the study were 12 UIC patients, i.e. 11 of pancreatic cancer and 1 of cholangiocellular carcinoma of Stage IV. The average age of the participants was 63.7 years old. The performance status was PS 0:6 and PS 1:6 patients. 11 of whom have had chemotherapy previously and 1 had no therapy. The HIFU device used was MS-2 (joint production equipment by Hitachi, Ltd., Denso, Inc., Tohoku Universities and Tokyo Women's Medical University, Japan, which was provided by Tokyo Woman's Medical University. The drug used for the study was epirubicin-conjugated polymer micelles; NC-6300 (manufactured by NanoCarrier Co., Ltd. And supplied by Kowa Company, Ltd., Japan). NC-6300 was administered intravenously before 24 ± 2 hours before HIFU treatment. HIFU mode used was the high strength pulse irradiation addition to the usual continuous-wave radiation, and performed HIFU irradiation by the triggered HIFU sequence which induces a cavitation and heightens the SDT effect. 3+3 design for increase in quantity of four steps of HIFU power and doses of NC-6300 was performed. The safety and therapeutic effect of 7 and 30 days after SDT was evaluated.
Results: Side effects of NC-6300 after administration were not seen in which step of [1] $30mg/m^2$+75W; 3 cases, [2] $30\ mg/m^2$+150W; 3 cases, [3] $80mg/m^2$+HIFU75W; 3 cases, and [4] $80mg/m^2$+150W; 3 cases. Treatment data was followed; mean total treatment time: 22.3 min, mean total number of irradiation: 17.4 shots. The effects of HIFU therapy were the following; the rate of complete tumor coagulative necrosis was 33%, the rate of partial tumor coagulative necrosis was 42%, mean tumor reduction rate was 40%, the rate of primary disease control rate (DCR) was 64%, and the rate of symptom relief effect was 33%. No adverse events more than grade 3 were seen during and 7 and 30 days of after treatment. The tolerability of NC-6300 dose was $80mg/\ m^2$ and HIFU power 150W was confirmed.
Conclusion: This study has shown that SDT will be a promising new cancer treatment that is effective and secure which can be done in a lesser time with less risks. It is expected to be a topical therapy for UIC, and the next stage of clinical trial for therapeutic effect is also going to start in the very near future.
Disclosure: This study obtained research support from the Japan Agency for Medical Research and Development (AMED).

P0248 SAFETY AND EFFECTIVENESS OF EUS-GUIDED HEPATICOGASTROSTOMY (EUS-HGS) COMPARED WITH PTBD IN PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION

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Introduction: EUS-guided hepaticogastrostomy (EUS-HGS) is recognized as an alternative treatment for biliary drainage.
Aims and Methods: We aimed to evaluate the outcome of EUS-HGS and Percutaneous transhepatic biliary drainage(PTBD) treatment, and consider the possibility of EUS-HGS treatment about continuity and further compatibility. We conducted a retrospective study among 13 patient who underwent EUS-HGS and 46 patients who underwent PTBD with malignant biliary obstruction from January 2016 to December 2017. The success rate of the procedure, the response rate of the treatment, short-term complication rate, the length of hospital stay after treatment, the ratio of re-hospital events, and the survival time after treatment were examined.
Results: On PTBD vs. EUS-HGS, the median age was 68 years (38–88 years) vs. 69 years old (43–76 years), male 72% vs. 38% ($p < 0.05$), the primary disease were pancreatic cancer/biliary tract cancer/Gastric cancer/Other 17/10/11/8 vs. 7/6/0/0 ($p < 0.05$). The reasons for choosing PTBD were 17 cases of poor EBD effects, 12 reconstructed intestinal anastomy, 11 EBD failures due to gastrointestinal stricture, 3 ERCP complications, 1 poor treatment effect of EUS-HGS, 2 others. The reasons for choosing EUS-HGS were 5 poor EBD effects, 5 EBD incapacitations due to gastrointestinal stricture, 1 PTBD refractory, 2 PTBD intolerance cases. The success rate of the procedure was 95.7% vs. 100%, the response rate was 83.0% vs. 92.3%, and the complication rate within 2 weeks after the treatment was 10.6% vs. 15.3%. The median length of hospital stay after treatment was 21 days (3–129 days) vs. 11 days (3–22 days), the ratio of re-hospitalization events was 30% vs. 30.7%, the median time from treatment to the event occurrence was 92 days (12–305 Day) vs. 77 days (24–252 days), BSC cases was 43.5% vs. 92.3% ($p < 0.05$), median post survival time was 112 days vs. 89 days.
Conclusion: Most of the EUS-HGS were administered to the patients with biliary and pancreatic cancer premised on BSC cases. Since it has the same degree of safety as PTBD, it seemed possible to continue performing EUS-HGS more positively in terms of QOL. Also, it seemed possible to expand EUS-HGS indication for the cases with any other organ cancer than pancreatic or biliary cancer before chemotherapy, but it is necessary to verify the safety of EUS-HGS in the future.
Disclosure: Nothing to disclose

P0249 ROLE OF INTERVENTIONAL RADIOLOGY IN PEDIATRIC GASTROINTESTINAL DISEASES - A LARGE TERTIARY CENTER EXPERIENCE

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Introduction: Interventional radiology (IR) is an indispensable component of multidisciplinary care in various gastrointestinal (GI) diseases. The available literature on safety and utility of IR is limited in children with GI disorders.
Aims and Methods: In this study, we aim to analyze the outcomes of IR in various pediatric GI diseases.
The data of children (<18 years) who underwent radiological intervention for various GI disorders during study period (2009–2017) were analyzed, retrospectively. The indications for interventions included vascular (Budd Chiari syndrome, pseudoaneurysm) and nonvascular (pancreatic fluid collections, cholangitis and anastomotic biliary strictures). All the interventions were performed with standard technique. The indications for intervention in children with pancreatic fluid collections included unsuitability of endoscopic drainage or collections at multiple sites. Percutaneous transhepatic biliary drainage was carried out in children in whom endoscopic retrograde cholangiopancreaticography was unsuccessful or not feasible. The outcomes of radiological intervention including success and adverse events were assessed.
Results: A total of 93 children (mean age 13.45 ± 4.09) underwent radiological interventions for vascular (chronic Budd Chiari syndrome 14, pseudoaneurysm 28) or non-vascular (pancreatic fluid collections 33, hepaticojejunostomy strictures or leaks 12, cholangitis 6) indications. Of 33 children who underwent percutaneous drainage of pancreatic fluid collections, clinical success was noticed in 32 children during a mean follow-up of 32.4 ± 21.66 months. 11 children developed persistent pancreaticocutaneous fistula of which 8 children were managed with endoscopic pancreatic ductal stenting and 3 underwent internalization of transgastric drain. In children who underwent stenting of hepatic vein or inferior vena cava for Budd Chiari syndrome, mean stent patency was 78.57% during a follow-up of 24.1 ± 13.78 months. Adverse clinical outcomes were noticed in 4 children (28.57%) including persistence of ascites (1 child), requirement of re-intervention (1 child), and death (2 children: re-occlusion and intracranial

bleeding). In children with pseudoaneurysms, angioembolization with glue and or coils was successfully performed in 92.8% patients. The sites of pseudo-aneurysms were splenic artery in 8, gastroduodenal artery in 7, hepatic artery in 5, superior mesenteric artery in 3, renal artery in 1 and right gastroepiploic artery in 1 child. Re-bleeding was noticed in 2 children. 1 child was managed conservatively and one required re-intervention. Percutaneous transhepatic biliary drainage was performed in 18 children. Resolution of hepaticojejunostomy strictures, leaks and cholangitis was noticed in all the children during a follow-up of 36.1 ± 13.73 months.
Conclusion: Interventional radiology is safe and effective in the management of various pediatric GI diseases. The role of angiotherapy in children with chronic Budd Chiari syndrome needs to be evaluated in future.
Disclosure: Nothing to disclose

P0250 PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE HAS LOW CLINICAL SUCCESS AND HIGH COMPLICATION RATE IN PATIENTS WITH MALIGNANT BILIARY STRICTURES

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Introduction: Patients with malignant biliary strictures carry a poor prognosis and the majority present with unresectable disease. Biliary drainage is achieved by endoscopic retrograde cholangiopancreatography (ERCP) in over 75% of cases. Percutaneous transhepatic biliary drainage (PTBD) is commonly employed as second-line method of obtaining biliary drainage in cases of failed ERCP. The aim of this study is to evaluate the efficacy and safety of PTBD for malignant biliary strictures.
Aims and Methods: This is a retrospective study of consecutive patients who underwent PTBD for malignant biliary strictures at an academic tertiary referral centre between 2005 and 2016. Clinical, laboratory, endoscopic and radiological data were obtained from electronic medical records. Technical success was defined as successful biliary cannulation and treatment of obstruction. Clinical success was defined as a 50% reduction in serum bilirubin 7 days post-procedure, or a 75% reduction at 4 weeks post-procedure.
Results: During the study period 205 patients underwent 564 PTBS (61% male, median age 69 years [IQR 59–77]). Causes of malignant stricture included: cholangiocarcinoma in 71 (35%), metastatic disease in 64 (31%), pancreatic adenocarcinoma in 55 (27%), hepatocellular carcinoma in 7 (3%), gallbladder cancer in 6 (3%), ampullary cancer in 1 (0.5%) and lymphoma in 1 (0.5%). The stricture was hilar in 76/205 (37%), distal in 100/205 (48%) and both hilar and distal in 29/205 (14%). Most patients 130/205 (63%), had failed ERCP prior to PTBD. The median serum bilirubin at time of PTBD was 159 μmol/L (IQR 86-271).
The median number of procedures for each patient was 2 (IQR 1-3). Interventions performed included: stenting (154 (75%) including; 105 (51%) covered metal, 26 (13%) uncovered metal, 21 (10%) plastic, and 2 (1%) partially covered metal), balloon dilatation 165 (86%) and external drainage 189 (92%). 63 (33%) of the patients with external drainage had drain removal prior to discharge. Technical success was achieved in 198/205 (96%) and clinical success was achieved in 111/205 (54%). The likelihood of clinical success was significantly lower for strictures with a hilar component when compared to those with distal strictures only (51% vs. 71%, $p = 0.006$). Patients with strictures involving the hilum also required an increased number of procedures compared to those with distal only (3 vs. 2.4, 95%CI 0.02–1.2, $p = 0.04$). Complications occurred in 109/205 (53%) patients and included pain requiring analgesia in 51 (25%), haemobillia in 29 (14%), cholangitis in 27 (13%), bile leak in 21 (10%), non-biliary bleeding in 21 (10%), peritonitis in 3 (1%), and 14 (7%) other. There was 1 case of procedure related mortality at 4 weeks follow-up.
Conclusion: PTBD is unsuccessful in 46% of patients with malignant biliary strictures and complications are seen in 53%. Malignant strictures with a hilar component had significantly reduced clinical success and required more procedures compared with distal lesions. Other techniques should be explored to improve patient outcomes in this setting.
Disclosure: Nothing to disclose

P0251 OUTCOMES AND SAFETY OF PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE AFTER LIVER TRANSPLANTATION

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Introduction: Biliary complications are a common cause of morbidity and mortality in liver transplantation (LT) recipients occurring in 10–25% of patients. Most can be managed successfully with endoscopic retrograde cholangiopancreatography (ERCP) or double-balloon enteroscopy assisted ERCP (depending on the type of anastomosis). Percutaneous transhepatic biliary drainage (PTBD) remains second-line treatment for biliary complications after ERCP failure at most centres. However, its use in patients after cadaveric LT has not been well studied. We aimed to determine the outcomes and safety of PTBD in this setting.
Aims and Methods: This is a retrospective study including all patients who underwent PTBD post-cadaveric LT at a tertiary referral centre between 2005 and 2016. Clinical, laboratory, endoscopic and radiological data were obtained from electronic medical records. Technical success was defined as successful biliary cannulation and treatment of obstruction. Clinical success was defined as a 50% reduction in serum bilirubin 7 days post-procedure, or a 75% reduction at 4 weeks post-procedure. Patient were analysed according to clinical success or failure using standard statistical methods for group comparisons.
Results: During the study period, 44 LT patients underwent 164 PTBDs (89% male, median age 56 years [IQR 52–62]). Causes of liver disease included: hepatitis C (12/44; 27%), PSC (11/44; 25%), alcoholic liver disease (6/44; 14%), hepatitis B (5/44; 11%) and other (13/44 30%). 19 patients had a duct-to-duct anastomosis while 25 patients had a roux-en-Y anastomosis. 4 (9%) patients had more than 1 prior LT. Indications for PTBD were: 22/44 (50%) for anastomotic stricture, 7 (16%) for bile leak, 6 (14%) for focal non-anastomotic strictures, 3 (7%) for ischaemic biliopathy, 3 (7%) for recurrent PSC and 2 (5%) for choledocholithiasis. 15 (34%) patients had failed ERCP and 15 (34%) had failed double balloon enteroscopy assisted-ERCP (DB-ERCP) prior to PTBD, whereas 14 (32%) underwent primary PTBD. The median time from LT to PTBD was 25 months (IQR 3-67). The median serum bilirubin at time of PTBD was 41 μmol/L (IQR 18-103).
Technical success was achieved in 43/44 (98%) and clinical success was achieved in 29/44 (66%) of patients. The median number of procedures for each patient was 3 (IQR 2-6). Patients with clinical success had a lower median time post transplantation; 9 vs. 94 months ($p = < 0.001$) and lower median bilirubin 31 vs. 57 μmol/L ($p = 0.01$). The clinical failure group had no procedures performed for bile leak 0/15 (0%) vs. 7/27 (24%) ($p = 0.04$). There were no other differences observed in baseline characteristics between the clinical success and failure groups including indication for PTBD, number of procedures, prior ERCP and aetiology of liver disease.
Serious adverse events occurred in 25/44 (57%) patients which included: cholangitis in 15 patients (34%), haemobilia in 9 patients (20%), bleeding outside the biliary tree in 6 patients (14%) and bile leak in 5 patients (11%). 10 patients required ICU admission post-procedure (23%). There was no procedure related mortality at 4 weeks follow up.
Conclusion: Although technical success for PTBD for post-LT is high, clinical success is modest at 66% with multiple procedures being generally required. PTBD carries a significant risk of adverse events of 57% in this population and hence should remain a second-line procedure.
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00–17:00
Surgery I - Hall X1____

P0252 RISK FACTORS OF LYMPH NODE METASTASIS IN PATIENTS WITH EARLY PURE AND MIXED SIGNET RING CELL GASTRIC CARCINOMAS

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Introduction: Early gastric carcinoma (EGC) with pure signet ring cell (pSRCC) histology limited to the mucosa has been reported to have favourable prognosis and low risk of lymph node metastasis (LNM). However, risk factors for lymph node metastasis(LNM) and clinicopathological features of early mixed signet ring cell gastric (mSRCC) remain poorly investigated.
Aims and Methods: The aim of this study was to identify risk factors of LNM and compare clinicopathological characteristic and prognosis of early pSRCC with early mSRCC.
This retrospective study was conducted at our center between 2005 and 2015 in 796 radical gastric cancer gastrectomies. A total of 160 early signet-ring cell carcinoma (ESRCC) radication resections were reviewed, in which 79 cases were early pSRCC and 81 cases were early mSRCC. Risk factors of LNM and clinicopathologic features of these 2 groups were statistically compared, including age, gender, tumor location, gross pattern, size, invasion depth, lymphovascular invasion (LVI), helicobacter pylori (Hp) infection, atrophic gastritis, and LNM. Patients were follow-up for post-resection survival. The 5-year survival rate and disease-specific survival were estimated with the Kaplain-Meier method with a log-rank test and compared between the two groups.
Results: The overall 5-year survival rate for ESRCC was 96.25%. Univariate analysis reviewed LVI and tumor size as the risk factors of LNM in the mERCC groups but only LVI as the risk factor in the pERCC group. Compared to the pERCC group, the risk factors of LNM in the mERCC included the male gender ($p < 0.0001$), ulcerated gross pattern ($p < 0.05$), LVI ($p < 0.01$), and Hp infection ($p < 0.01$). Multivariable analysis revealed 2 independent risk factors in the mERCC group: 1) tumor size (the odds ratio of 2.075; 95% confidence interval: 1.049 - 4.105) ($p < 0.05$), and 2) LVI (the odds ratio: 22.215 (95% confidence interval: 4.786 - 103.112) ($p < 0.0001$). There was no significant difference in the overall survival and disease-specific survival between the 2 groups.
Conclusion: Although with similar post-resection survival, the independent risk factors of LNM in the mERCC group, compared to those in the pERCC group, included large tumor size and LVI.
Disclosure: Nothing to disclose

P0253 OUR EDUCATIONAL ACTIVITY FOR PERCUTANEOUS TRANS-ESOPHAGEAL GASTRO-TUBING

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Introduction: We developed the percutaneous trans-esophageal gastro-tubing (PTEG) technique in 1994 in Japan for patients in whom it was difficult to create a percutaneous endoscopic gastrostomy (PEG). Initially, PTEG was routinely used for quite a while as a palliative treatment for gastrointestinal decompression in patients with gastrointestinal obstruction due to carcinoma. Then, PTEG began to be used routinely for enteral nutrition. We believe that the establishment of a system to teach the PTEG procedure is essential because we would like PTEG to become a general technique all over the world. Here, we describe our educational activities for PTEG.

Aims and Methods: The PTEG procedure was constructed from 2 existing general techniques. We also developed a rupture-free balloon (RFB) for the standard PTEG technique procedure in 1997. 1 technique was puncturing of the esophagus with a RFB under ultrasonic control. The other was tube placement via the puncture site under fluoroscopic control. The standard PTEG procedure was thus a nonvascular interventional radiological technique that did not require an endoscope. The Japan Association for PTEG (JA-PTEG) was established in 2002, and annual- meetings of JA-PTEG were held every year. From 2005, under the guidance of the Ministry of Welfare, a clinical trial for PTEG was undertaken for 6 years in Japan, which confirmed its safety and efficacy. The Ministry of Welfare approved support for PTEG by Japanese national health insurance in 2012. Hands-on seminars with simulators for the PTEG procedure were held twice a year from 2014. In 2018, JA-PTEG initiated a system to technically certify physicians performing PTEG.

Results: PTEG has been performed in over 25,000 patients in Japan from 1994 to the present. We have also performed PTEG as an educational procedure in 341 patients in 62 institutions. JA-PTEG was formed with 186 individual members, 52 authorized institutions, 43 faculty members and 32 attending physicians. To date in 2018, JA-PTEG certified 8 physicians as those authorized to perform the standard PTEG procedure.

For patients with intractable nausea and vomiting due to gastrointestinal obstruction caused by carcinoma, PTEG as a palliative treatment can quickly and effectively improve a patient's quality of life. PTEG is also highly efficacious in enteral nutrition as an alternative to PEG. PTEG was originally born as a Japanese technique in 1994, and currently, it is still only performed within Japan.

Conclusion: We believe that the PTEG technique should be disseminated safely and effectively throughout the world.

Disclosure: Nothing to disclose

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P0254 INTENSITY OF ESOPHAGEAL PERISTALSIS IS A FACTOR IN PROLONGED POSTOPERATIVE PAIN BEFORE PERORAL ENDOSCOPIC MYOTOMY

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Introduction: Peroral endoscopic myotomy (POEM) is a minimally invasive and curative treatment for esophageal dysmotility (1,2). However, significant pain persists in some cases.

Aims and Methods: This single-center study retrospectively investigated risk factors for pain after POEM.

This study included consecutive patients who underwent POEM and high-resolution manometry (HRM) at the Okayama University Graduate School of Medicine between January 2016 and December 2017. A numerical rating scale (NRS) was used for pain assessment. A pain group (P-group: 3 days to achieve NRS < 1) and a non-pain group (NP-group: < 3 days) were compared. Demographic information, disease, symptoms, and histological findings were obtained from medical records. All study participants provided informed consent. The local ethics review committee granted approval.

Results: Of 22 patients who underwent POEM, 2 were excluded because preoperative HRM was not performed, and 11/20 (55%) had prolonged pain after POEM. There was no significant difference in sex, age, and the amount of analgesic required during hospitalization between the P-group and NP-group. In univariate analysis, high distal contractile integral (DCI) median value on HRM and classification as a straight-type were risk factors for prolonged postoperative pain. In multivariate analysis, high DCI was a risk factor for prolonged postoperative pain.

Conclusion: The intensity of esophageal peristalsis before POEM may be a factor in prolonged postoperative pain.

Disclosure: Nothing to disclose

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P0256 ENDOSCOPIC PAPILLECTOMY IN TREATMENT OF PATIENTS WITH AMPULLARY NEOPLASMS: A SINGLE-CENTER EXPERIENCE

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Introduction: Benign tumors of the ampulla of Vater occur in 0.4% −0.12% of all tumors of the gastrointestinal tract (GI tract). However, malignant transformation occurs in 60–65% of cases, so the common tactic of treatment is their removal. Regardless of the pathohistological structure of the tumor, endoscopic papillectomy is considered reasonably safe and most effective method compared to a more radical interventions such as pancreatoduodenal resection (PDR), transduodenal resection.

Aims and Methods: 37 endoscopic papillectomies were performed at the Moscow Clinical Research Center between April 2014 and January 2018. In most cases, the tumor was detected during a routine examination for other diseases.

The preoperative examination protocol included duodenoscopy with biopsy, endosonography, CT or MRI, which excluded the presence of malignant lesions and the intraductal spread of the adenoma more than 1 cm. The sizes of the adenomas ranged from 1 cm to 5 cm. The aim of the study was to evaluate the effectiveness of endoscopic papillectomy in the treatment of patients with neoplasm of the ampulla of Vater.

Results: 37 patients underwent endoscopic papillectomy, including 16 men and 21 women. Median age: 54 years (26–73). The average time of surgery was 85 minutes. In 26 cases, the removal of the adenoma was performed 'en bloc' (59.5%). In 11 cases, due to the presence of lateral spread of the tumor, fragmentation was performed (40.5%). Pancreatic stenting was successful in 31 patients (83.7%). Stenting was of the common bile duct in 9 patients (24.3%). In all cases there was R0 resection. Morbidity included bleeding in 8 patients (21.6%), 2 cases of intraoperative perforation (5.4%), 1 of them was conservatively treatment. The other was operated in volume: laparotomy, suturing a perforation, drainage of the abdominal cavity. In 2 patients, the postoperative period was complicated by cicatricial stenosis of the bile duct opening (5.4%). The ERCP with the stenting of the common bile duct was performed. No death occured.

Conclusion: Endoscopic papillectomy is characterized by lower morbidity and mortality and a shorter period of hospitalization. Compared with surgery, endoscopic ampullectomy appears to be a preferred treatment modality for small benign ampullary tumors with high success rate of tumor eradication.

Disclosure: Nothing to disclose

P0257 ENDOSCOPIC VACUUM THERAPY FOR TREATMENT OF UPPER GASTROINTESTINAL ANASTOMOTIC LEAKAGES: FIRST EXPERIENCE

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Introduction: Surgical interventions on the esophagus belong to the group of 'high-risk' operations, as they can lead to such formidable complications as insolvency, bleeding and the formation of postoperative fistulas and strictures. The results of systematic analysis of the largest series of clinical cases published in the last 20 years show the incidence of postoperative anastomotic leakage about 3% after open and 2.1% after laparoscopic surgery without significant differences determined by the type of surgical access. However, analysis of the cumulative world experience shows the average incidence of anastomotic leakage at the level of 7–8%. These reports suggest that postoperative mortality rates in this patient group reach 30% and have no significant improvement toward reduction. Aggressive approaches to the treatment of patients with traditional surgical interventions lead to an increase in mortality from 20 to 64%, which determines the use of minimally invasive technologies as a priority. Since 2006, a new method of endoscopic vacuum therapy in management of anastomotic leaks has become available in clinical practice.

Aims and Methods: From March 2015 to March 2018, anastomotic leakage of the esophagus was diagnosed in 12 patients (5 women, 7 men), including 9 patients with failure of esophagogastric anastomosis, 3 patients with failure of

esophagojejunal anastomosis. The average age was 67.5 years. Size of anastomotic perforation ranged from 0.8 to 3 cm.
Strategy of treatment for all patients include adequate nutritional support by enteral feeding through the nasogastric tube, parenteral administration of combined nutrients, enterostomy, or a combination of several methods. Early antibiotic therapy is necessary for the prevention and treatment of already developed mediastinitis and septic complications.
The complications were detected on the 1–7 days after surgery. Anastomotic leak was confirmed by radiological and endoscopic methods. Endoscopic vacuum therapy was performed on the day of leakage detection (2–4 days after the surgery). Thus no additional sanation and draining interventions were required due to early diagnosis and adequate drainage of the anastomosis area.
Polyurethane spongy system, slightly smaller diameter or corresponding to the diameter of the esophagus, was mounted on a thermoplastic gastric probe and installed at the level of the perforation. Immediately after installation, the system was connected to a vacuum aspirator with a pressure of 100 - 125 mm Hg. Replacement of the system was carried out every 3–13 days. To fully close the insolvency, it took from 1 to 7 procedures. The decision to complete the therapy was carried out based on the results of endoscopic and X-ray examination in the absence of data for the presence of fistula.
Results: In total 57 procedures were performed: the number of replacements - 4 (1–7), the interval between procedures - 6 days (3–13 days), the duration of treatment -13 days (1–66 days). The success rate was 75%.
There were 3 lethal outcomes, including 2 due to progressive cardiovascular failure with positive dynamics of local treatment. 1 patient died of multiple organ failure.
Conclusion: Endoscopic vacuum therapy is considered to be valuable and cost-effective method of treatment of anastomotic leaks and perforations of the upper GI tract.
Disclosure: Nothing to disclose

P0258 THE SMART APPROACH TO SURGICAL TREATMENT FOR GASTRIC AND DUODENAL GISTS BASED ON PREOPERATIVE EUS-TYPING

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Introduction: Surgical treatment is the treatment of choice for the resectable GISTs with objective of surgery being complete R0 resection. No need for extended resections and lymphadenectomy makes minimaly-invasive techniques the treatment of choice.
Aims and Methods: We aimed to develop and demonstrate different surgical techniques of laparoscopic or endoscopic resection for GISTs **based on classification of EUS-typing for optimal choice of treatment**. By the 'smart' approach we imply the approach which allows us to make a surgery less invasive and more accurate, including more functional results with no increase of complications.
The EUS-classification of GISTs was created based on the analysis of treatment of 80 patients with gastric and duodenal GISTs. The principles of classification included the following criteria:
Location of tumor base in relation to GI layer
Size of the tumor base (''growing point'')
Type of growth in relation to GI lumen
The EUS-typing includes Type I, Type II, Type III (a,b,c,d) tumors
Optimal approach for type I
Endoscopic removal of tumor by means of:
Endoscopic submucosal dissection (large size)
Endoscopic mucosal resection (small size)
Type II
Endoscopic enucleation of tumor after resection of covering mucosa
Endoscopic tunneling dissection
Type IIIa
Endoscopic tunnneling dissection
Type IIIb
Laparoscopic atypical resection after gastrotomy (duodenotomy)
Endoscopic tunneling dissection (advanced endoscopic surgeon and small tumor size)
Laparo-endoscopic hybrid procedures
Type IIIc
Laparoscopic atypical (wedge) resection
Type IIId
Laparoscopic enucleation of tumor
Laparoscopic atypical stapler resection.
Results: Patients with gastric and duodenal GISTs underwent laparoscopic resection - 62, endoscopic intraluminal resections - 18 patients (tunneling resection - 7, endoscopic submucosal dissection or endoscopic enucleation of tumor after resection of covering mucosa - 11). Median operation time was 150 min. Recovery was uneventful and median post-op hospital stay was 5 ± 2.4 (2–8) days. The pathology showed R0 resection in all cases. Histology and immunohistochemistry confirmed GIST. 4 patients received adjuvant target therapy and were prescribed Gleevec for 1–2 years. The mean follow-up period was 42 months (range 3–74 months) with no local or distant recurrence or stenosis at the site of surgery.
Conclusion: The classification of GISTs based on EUS-typing allows to select the optimal approach individually for each patient to perform surgery more accurate and less invasive.
Disclosure: Nothing to disclose

P0260 A COMPREHENSIVE COMPARISON OF THE FIVE LEADING SCORINGS SYSTEMS FOR PERITONEAL CARCINOMATOSIS FROM COLORECTAL ORIGIN TO SELECT CRS/HIPEC CANDIDATES WITH MRI

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Introduction: Multiple surgical scoring systems have been developed to assess the extent of peritoneal carcinomatosis in colorectal patients. These scoring systems are used as important predictors of surgical outcome in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC). Diffusion weighted magnetic resonance imaging (DW-MRI) could allow for the assessment of these surgical scores preoperatively and non-invasively.
Aims and Methods: The purpose of the study is to compare the performance of these scoring systems determined on MR images, for predicting whether a complete resection was feasible in CRS/HIPEC candidates with colorectal cancer.
Between February 2016 and October 2017, colorectal cancer patients considered for CRS/HIPEC who underwent DW-MRI were included. The DW-MRI images were, retrospectively and independently, assessed by 2 abdominal radiologists. Both radiologists were blinded for the clinical parameters. Clinical parameters were obtained from the patient files. 5 most-used models were selected, namely the Peritoneal Surface Disease Severity Score (PSDSS), Region Count, Simplified Peritoneal Cancer Index (SPCI), Peritoneal Cancer Index (PCI), and the Colorectal Peritoneal Metastases Prognostic Surgical Score (COMPASS). The performance of the scoring systems was assessed by receiver operator characteristics (ROC) analysis for predicting complete resection and the area under the curve (AUC) was calculated for every model.
Results: In 82 patients, the scores could be accurately constructed for all 5 methods. The mean age was 62.80 (± 10.53) and 46/82 of the patients were female. Of these patients 70% (58/82) had undergone a successful surgical procedure with a curative intent, of which 84% (49/58) underwent a CRS/HIPEC procedure. In 20 patients, an inoperable amount of peritoneal carcinomatosis was determined at surgery. ROC curve analysis for predicting a complete resection showed AUCs of 0.79, 0.79, 0.82, 0.83, and 0.89 for PSDSS, Region Count, SPCI, PCI, and COMPASS, respectively.
Conclusion: This study shows that DW-MRI might be used for less invasive and preoperative patient selection of colorectal patients considered for CRS/HIPEC. The COMPASS model was the best model to select CRS/HIPEC candidates with MRI.
Disclosure: Nothing to disclose

P0261 DEVELOPEMENT OF 3D MODEL OF PERIANAL DISEASE IN CD. SINGLE-CENTRE EXPERIENCE

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Introduction: Preoperative evaluation of MR images may not be sufficient for precise planning the anal fistulas surgery nor the stem cell therapy. 3D printing allows to obtain spatial structures in 1:1 scale with unprecedented precision.
Aims and Methods: Optima MR360 Advance 1.5T (GE Healthcare) with a 16-channel TOTAL BODY coil was used. The imaging protocol consisted of high-resolution axial and coronal T2-weighted images with a matrix size 512 × 512, a slice thickness of 2 mm and zero spacing scans. DICOM images were imported into 3D Slicer v.4.8.0. Firstly anal fistula was modelled on the basis of axial images. Fistula locations, anus and anal canal were marked with a different color marker. The last step was to mark the skin that was connected to the anus and contact areas of the fistula with the skin. The prepared model was then exported to an STL format file. Blender 2.77a was used to smooth the edges of the model, then 3D program allowing the color to be assigned to individual model element was used. The final version of the model contained 958 layers. The anal fistula model was printed using the 3D ProJet 460 Plus printer (3D Systems). The development of the model, including printing took approx. 9 hours.
Results: Acessability of rotatable 3D before surgery allows more precise detection of the location and the degree of the perianal disease. Moreover, this may also lower the inter-observer bias connected with the different skills to interpret complex MR imaging before planned surgery.

Conclusion: The proposed use of 3D printing technology in the case of anal fistula will allow to effective surgery planning.
Disclosure: Nothing to disclose

P0262 THE POTENTIAL OF HUMAN FOETAL GUT MESOANGIOBLATS-LIKE CELLS FOR ENTERIC SMOOTH MUSCLE REGENERATION

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Introduction: Severe gastrointestinal disorders including chronic intestinal pseudo-obstruction affect the neuromuscular compartment of the small intestine. Very little is known, however, about the repair and regeneration of damaged or dysfunctional smooth muscle.
Aims and Methods: Our study aims to investigate the potential of human foetal gut mesoangioblast-like cells for enteric smooth muscle regeneration as a possible treatment for enteric myopathies and related disorders.
Mesoangioblasts-like cells (MABS), isolated from human foetal midgut (under ethical approval from the UK-Human Developmental Biology Resource at UCL Great Ormond Street Insitute of Child Health), were expanded and TGFß used for 7 or 14 days to induce smooth muscle differentiation *in vitro*. Immunohistochemistry, FACS analysis and calcium imaging were performed to characterise MABS and smooth muscle-derived cells. After eGFP-lentiviral labelling, MABS were transplanted *in vivo* into terminal ileum of NOD-SCID mice (under UK licence, PPL 70/7622) and cell engraftment assessed with immunohistochemistry after 4 weeks.
Results: Immunohistochemistry and FACS analysis showed that foetal gut MABS have high proliferative capacity (~55% of cells are $Ki67^+$) in culture, are positive for mesenchymal markers CD90 and CD146 (~98% for both markers) and for pericyte markers NG2 and PDGFRß (~90% and ~20–30% respectively). After 7 days in culture with TGFß-treatment, MABS expressed smooth muscle proteins SM22 and calponin, and showed intracellular calcium transients in response to carbachol. After 14 days MABS also expressed smoothelin, a marker of mature smooth muscle. *In vivo*, transplanted MABS were able to engraft, distribute in the muscle layers of the ileum and differentiate into SM22 positive smooth muscle cells.
Conclusion: Here we demonstrate that MABS can be successfully isolated from human foetal gut. *In vitro* and with TGFß-treatment MABS showed an increasing ability to generate smooth muscle cells able to respond to carbachol stimulation, thus supporting their functional potential. The ability of MABS to differentiate into mature smooth muscle cells *in vitro* and engraft *in vivo* provides proof of principle for their potential use as a treatment of enteric smooth muscle disorders.
Disclosure: Nothing to disclose

P0263 IMAGE-GUIDED PATHOLOGY FOR EVALUATION OF RESECTION MARGINS IN LOCALLY ADVANCED RECTAL CANCER USING THE NEAR-INFRARED FLUORESCENT TRACER BEVACIZUMAB-800CW

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Introduction: Negative circumferential resection margins (CRM) are the cornerstone for curative treatment of patients with locally advanced rectal cancer (LARC). Unfortunately, perioperative techniques for evaluation of resection margins are lacking, whereas standard histopathological examination is time-consuming. In this study, we evaluated the feasibility of optical molecular imaging as a tool for evaluation of resection margins at the surgical theater, i.e. Image-Guided Pathology (IGP), to improve clinical decision making.
Aims and Methods: Fluorescence imaging data of fresh surgical specimens and subsequent bread-loaf slices from patients with LARC (NCT01972373) were analyzed as a side study. All patients were administered intravenously with 4.5 mg of the fluorescent tracer bevacizumab-800CW 2–3 days prior to surgery. 7 patients met the inclusion criteria for correlation of fluorescence intensities in fresh surgical specimens with histology, to evaluate resection margins. For analysis of bevacizumab-800CW localization in bread-loaf slices, sufficient data was available from 17 patients. A receiver operating characteristics (ROC) curve was plotted to determine the mean fluorescence intensity (MFI) cut-off value for tumor detection.
Results: Using IGP, in one patient a histologically confirmed tumor-positive CRM was predicted correctly at the surgical theater. Tumor-negative CRMs were predicted correctly in 4 patients using IGP. 1 tumor-positive CRM could not be detected; however, this positive margin was based on the presence of only an isolated microscopic tumor deposit in the CRM. 1 close CRM (1.4 mm) was identified as tumor-positive. Optical imaging enabled a clear differentiation between tumor and surrounding tissue in the bread-loaf slices ($n = 42$) of all 17 patients *ex vivo*. In our limited sample size, an optimal MFI cut-off value of 5085 was determined based on the ROC curve, with a sensitivity and specificity of 98.2% and 76.8% respectively.
Conclusion: We demonstrate for the first time the potential of IGP for identification of positive resection margins directly after surgery in patients with LARC. Clearly, this might change current peri-operative decision making with regard to additional targeted resections or intraoperative brachytherapy. Based on the initial results from this study, a standardized methodology was developed to confirm these findings in a subsequent larger IGP study.
Disclosure: Nothing to disclose

P0264 SNAPSHOT STUDY ON MRI RESTAGING AFTER CHEMORADIOTHERAPY AND INTERVAL TO SURGERY IN RECTAL CANCER; INFLUENCE ON SHORT AND LONG-TERM OUTCOMES

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Introduction: The time interval between CRT and surgery in rectal cancer patients is still subject of debate and concerns exist regarding increased postoperative complication and local recurrence rates after longer waiting.
Aims and Methods: To evaluate the impact on short and long-term outcomes of variation in practice related to MRI restaging and time interval between neoadjuvant chemoradiotherapy (CRT) and surgery in rectal cancer patients. Patients were selected from a collaborative rectal cancer research project including 71 Dutch centers. Patients were subdivided into 2 groups according to the time interval from the start of preoperative CRT to surgery (<14 and ≥ 14 weeks).
Results: From 2095 registered patients, 475 patients received preoperative CRT. MRI restaging was performed in 79.4%, with a median CRT-MRI interval of 10 (IQR 8–11) weeks, and median MRI-surgery interval of 4 (IQR 2–5) weeks. Short and long interval groups consisted of 224 and 251 patients, respectively. Pathological complete response rate ($n = 34$ (15.2%) vs. $n = 47$ (18.7%), $p = 0.305$) and CRM involvement (9.7% vs. 15.9%, $p = 0.145$) did not significantly differ. 30-day surgical complications were similar (20.1% vs, 23.1%, $p = 0.943$). No significant differences were found for local- and distant-recurrence rates and disease-free and overall survival.
Conclusion: These real-life data reflecting routine daily practice in the Netherlands showed substantial variability in use and timing of restaging MRI after preoperative CRT for rectal cancer, as well as time interval to surgery, but with similar short- and long-term outcomes.
Disclosure: Nothing to disclose

P0265 LAPAROSCOPIC VENTRAL RECTOPEXY FOR OBSTRUCTED DEFECATION FUNCTIONAL RESULTS AND QUALITY OF LIFE

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Introduction: Laparoscopic ventral mesh rectopexy (LVR) is gaining wider acceptance as the preferred procedure to correct internal as well as external rectal prolapse associated with obstructed defecation syndrome (ODS) and/or faecal incontinence.
Aims and Methods: The aim of our study was to analyse functional outcome and quality of life (HRQL) after laparoscopic ventral rectopexy for symptomatic internal prolapse and/or rectocele with ODS. Prospectively collected data on LVR for internal rectal prolapse were analysed in 46 consecutive female patients operated between January 2011 to April 2018. Mean age was 62 years (range 25 -

79). All patients had internal rectal prolapse (grade 3 or 4) confirmed at the defecogram study and 29 of them an associated rectocele. Functional results of LVR were evaluated in terms of constipation as measured with the Wexner Constipation Score, and HRQL as measured by SF-36, were analysed before the operation and after at least 3–6 months. Finally, HQRL results of LVR patients were compared with sex and age matched healthy controls. Non parametric statistics was used.
Results: Mean operative time was 151 min (range 75 - 240). Conversion rate to open technique was 10,8 %. There was no post-operative mortality or major complications. Median post-operative length of stay was 4 days (range 3 - 28). After a mean follow-up of 26 months (range 3 - 71 months), we observed no recurrence of prolapse or rectocele. Comparing Wexner score before and after LVR we observed an improvement in painful evacuation effort ($p = 0.001$), minutes in lavatory attempt ($p = 0.008$), feeling incomplete evacuation ($p = 0.017$) and abdominal pain ($p = 0.017$). Moreover, the global Wexner score was significantly improved from 13.60 to 10.18 ($p = 0.000$). Similarly, SF-36 items improved after the surgery, especially in term of Physical Functioning ($p = 0.005$). The comparison of preoperative SF-36 score with matched healthy controls demonstrated a significant difference in particular in Physical Functioning ($p = 0.001$) and Bodily Pain ($p = 0.023$). On the contrary, the comparison of post-operative SF-36 scores and healthy controls scores showed a significant difference only in terms of Bodily Pain item ($p = 0.035$). No worsening of continence status, constipation or sexual function was observed. No significant improvement was observed in urinary incontinence. None patient experienced persistence or recurrence of the prolapse.
Conclusion: LVR appears to provide a sustained improvement in HRQL, constipation and incontinence in patients with ODS without worsening constipation with low morbidity and recurrence.
Disclosure: Nothing to disclose

P0266 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) VERSUS TRANSANAL ENDOSCOPIC MICROSURGERY (TEM) FOR THE TREATMENT OF EARLY RECTAL CANCER: COMPARISON OF LONG-TERM OUTCOMES

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Introduction: Methods for the local treatment of early rectal cancer have been developed in the recent years. In this scenario, the transanal endoscopic microsurgery (TEM) and the endoscopic submucosal dissection (ESD) have played an important role. Both have their own advantages and drawbacks, but there are still few studies comparing them. Previous studies have shown that both techniques have similar short term outcomes (1). Studies assessing long-term outcomes, however, are scarce.
Aims and Methods: To compare long-term outcomes between ESD and TEM for the treatment of early rectal cancer.
From Jun/2008 to Dec/2017, 103 procedures were performed (either ESD or TEM). Lesions submitted to ESD were previously assessed by magnification chromoendoscopy and lesions with high risk of deep submucosal invasion were referred to surgical resection. Lesions treated by TEM were assessed by 3D endorectal ultrasound before the procedure.
Data regarding age, surgical risk, early and late complication rates, recurrence and anatomopathological report were collected retrospectively. Qualitative variables were submitted to a chi-square analysis and the quantitative ones, to a t-Student test.
Results: The mean follow-up of these patients was 34 months, 74 of them (71.8%) were submitted to ESD and 29 to TEM (28.2%). The average age in the ESD group was 65.5 years and 51.3% of those patients were female. Among the patients submitted to TEM, the mean age was 66.51 years and 58.6% of them were female. The surgical risk was equivalent in both groups ($p = 0.97\%$).
The lesions removed by ESD were significantly larger than the ones removed by TEM - 68.9mm against 44.79mm, respectively ($p = 0.002$). The mean procedure duration was 176 min for the ESD and 195 min for the TEM ($p = 0.4$).
In the ESD group, 7 patients (9.46%) had early complications, 2 of which were Clavien I, 3 Clavien II and 2 Clavien III. In the TEM group, 5 patients had complications (17.2%), of which 2 were Clavien I, 1 Clavien II, 1 Clavien III and 1 Clavien IV ($p = 0.19$).
The average days of hospitalization was 3.4 among the ESD patients and 6.9 among the TEM ($p = 0.015$).
During the first post-operative month, 10 patients (13.5%) from the ESD group presented mucorrhea, fecal urgency and/or incontinence and anal stricture requiring dilatation. By the end of 18 months, all patients were asymptomatic. Among the patients undergoing TEM, 7 (24.13%) had rectal pain, diarrhea or fecal incontinence. After 18 months, 6 were asymptomatic and 1 persisted with rectal pain.
The lesions removed either by ESD or TEM had similar rates of en-bloc resection - 89.2% and 96.5%, respectively ($p = 0.23$) and R0 resection - 85.13% and 82.6%, respectively ($p = 0.742$). The anatomopathological analysis of the lesions removed by ESD showed 27% of adenomas, 64.86% of intramucosal adenocarcinoma, 4% sm1 adenocarcinoma and 4.05% of sm≥2 adenocarcinoma (non-curative resection). In the TEM group, 31% were adenomas, 44.8% of intramucosal adenocarcinoma, 7% of sm1 adenocarcinoma and 17.2% of sm≥2 adenocarcinoma. Therefore, the ESD had a higher percentage of curative resections ($p = 0.002$).
Among the patients undergoing TEM, there was a 24.13% recurrence rate, against 1.3% in the ESD group ($p = 0.0001$).
Conclusion: The ESD, compared with the TEM, showed better results, enabling the treatment of significantly larger lesions, with a higher curative rate, less hospitalization days and lower recurrence rates.
Disclosure: Nothing to disclose

Reference

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MONDAY, OCTOBER 22, 2018 09:00–17:00
IBD I - Hall X1

P0267 CROSSTALK BETWEEN SEROTONIN AND ENDOCANNABINOID SYSTEMS IN THE GUT CONTRIBUTES TO THE ABDOMINAL PAIN IN COLITIS

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Introduction: Abdominal pain is one of the most common symptoms of inflammatory bowel diseases (IBD). However, its molecular basis has not been fully characterized yet. It has been previously shown that chronic elevation of luminal serotonin increases visceral pain and that elevated secretion of this neurotransmitter in the gut leads to the exacerbation of inflammation. On the other hand, it is well established that inhibited endocannabinoid signaling in the gut lowers pain threshold and endogenous cannabinoid receptor agonists reverse this effect and exhibit antinociceptive and anti-inflammatory properties.
Aims and Methods: The aim of this study was to test the hypothesis that chronic administration of serotonin causes disruption of the cannabinoid signaling leading to visceral pain in the course of colitis.
Methods: We used 3% DSS in drinking water to induce colitis in mice. Serotonin was systemically administered for 5 days starting from day 3 post-DSS and each day visceromotor response to colorectal distention (CRD) was measured. Selective 5-HT_3 and 5-HT_4 receptor antagonists were used to examine the mechanism of action of serotonin. Macroscopic evaluation of the colonic damage was performed. Expression of cytokines, serotonin and cannabinoid (CB) receptors as well as enzymes responsible of biosynthesis and degradation of endocannabinoids were investigated. Moreover, serotonin as well as endocannabinoid levels were assessed in all experimental groups by ELISA and mass spectrometry.
Results: DSS caused severe intestinal inflammation represented by increased macroscopic score as well as upregulation of TNFα, IL-1β and IL-6. Chronic, systemic treatment with serotonin led to significant increase in the concentration of this hormone in the colon and simultaneous decrease of the endocannabinoids, anandamide and 2-arachidonylglycerol. The visceromotor response to CRD was significantly higher in the serotonin-treated animals compared to the vehicle group and this effect was dependent on 5-HT_3 but not 5-HT_4 receptors. Moreover, chronic serotonin administration led to the downregulation of CB1, but not CB2, and decreased N-acyl phosphatidylethanolamine-specific phospholipase D (NAPEPLD), which is responsible for synthesis of anandamide and other *N*-acylethanolamines, and these effects were reversed by the 5-HT_3 receptor antagonist graniserton.
Conclusion: Here we present a novel mechanism that may be responsible for the increased visceral pain in intestinal inflammation. Our study suggests that pharmacological blockade of serotonin signaling in the gut might be of benefit in severe cases of abdominal pain in IBD patients.
Disclosure: Nothing to disclose

P0268 UROTENSIN II RECEPTOR EXPRESSION IN ULCERATIVE COLITIS: RELATIONSHIP WITH ENDOSCOPIC AND HISTOLOGICAL ACTIVITY OF THE DISEASE

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Introduction: Urotensin II (U-II) is a vasoactive peptide that interacts with a specific receptor, UTR (1). Recently our group has demonstrated increased UTR expression both in adenocarcinoma cell lines and adenomatous polyps and even greater in colon carcinoma samples when compared to healthy colon samples of the same patients. We also showed that an UTR agonist induced an

increase in colon adenocarcinoma cells growth in vitro, while the UTR block with a specific antagonist caused an inhibition of their growth and an inhibition of about 50% both of motility and cell invasion (2).
Aims and Methods: There are no UTR expression data in the ulcerative colitis (UC), and we therefore evaluated the expression of UTR in ill colon biopsy and in healthy colon biopsies of patients with UC and colon biopsies of healthy patients. We enrolled, prior informed consent, 7 patients (4 males and 3 females, age range 29–78 years, median 55) with first UC diagnosis compared to 7 healthy controls (3 males and 4 females, age range 30–75 years, median 52). 5 patients had a left colitis and two had a proctitis. All patients had histologic examination of moderate to severe disease activity. We have therefore sampled flogistic and healthy tissue. We therefore also have colic tissue samples taken in these subjects. Evaluation of receptor expression was performed by RT-PCR. The ANOVA test ($p < 0.05$) was used for statistical analysis.
Results: We found a) increased expression of UTR in patients with ill mucosa biopsies compared to healthy controls in 5 of the 7 patients ($p < 0.05$); b) increased expression of UTR in ill colon biopsy of UC patients compared to healthy colon biopsies of the same patients in 5 of the 7 patients ($p < 0.05$); c) increased UTR expression in healthy colon biopsy specimens of patients with UC compared to healthy controls in 5 of the 7 patients ($p < 0.05$); d) correlation of UTR expression with endoscopic and histological activity of disease in most study patients. We found a greater expression of UTR in patients with a Mayo Endoscopic Score 2 and with severe histologic only in 4 patients.
Conclusion: UTR could be considered as an inflammatory disease marker. UTR up-regulation in ill mucous is correlated with endoscopic and histological activity of disease in most patients.
Disclosure: Nothing to disclose

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P0269 DS-1093A, A NOVEL HYPOXIA-INDUCIBLE FACTOR PROLYL HYDROXYLASE INHIBITOR, HAS A THERAPEUTIC POTENTIAL IN INFLAMMATORY BOWEL DISEASE

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Introduction: Tissue hypoxia is predominated in inflammatory intestinal lesions. Hypoxia inhibits hypoxia-inducible factor prolyl hydroxylase (HIF-PH), which stabilizes HIF and induces HIF downstream gene expression in the colon. HIF-1, a complex consisting of inducible HIF-1 alpha and constitutive HIF-1 beta, induces the expression of protective barrier genes in colon epithelial cells and plays a critical role in protecting against inflammatory bowel disease (IBD). HIF-PH inhibitors are thought to have the potential to enhance mucosal barrier function through HIF-1 alpha stabilization. We found out that DS-1093a, a HIF-PH inhibitor, might have the potential to be a novel IBD drug with mucosal healing activity.
Aims and Methods: To elucidate the effect of DS-1093a on IBD, we administered DS-1093a to colitis mice. Experimental colitis was induced in male BL/6 mice by dissolving Dextran Sodium Sulphate (DSS) in their drinking water for 8 days. DS-1093a was administered to DSS mice in the feed for 8 days or by intra-rectal administration (IRA) once a day until day 7. The disease conditions (colon length, body weight, and diarrheal score), histopathology (HE staining, AB-PAS staining, and HIF-1 alpha immunohistochemistry) of colon, and haematological parameters were analysed on day 8. Colon and serum of each mouse were also collected on day 8. The mRNA expression was analysed by qRT-PCR. IRA was conducted by administering the solution between the cecum and the rectum via a catheter through the anus.
Results: DS-1093a improved total body conditions, as shown by body weight, colon length, and diarrheal score in DSS colitis mice. In the histopathological analysis, colitis mice showed intestinal tissue injury; however, treatment of DS-1093a reduced the mucosal injury and increased normal tissue region. AB-PAS (mucin) stained section of the colon showed DS-1093a normalized mucus production in colitis mice. DS-1093a prevented the activation of immune cells by colitis. DS-1093a also suppressed inflammatory cytokine gene expression in the colon epithelial cells. DS-1093a induced HIF-1 alpha accumulation in the nucleus of mucosal epithelial cells.
In contrast, DS-1093a induced excess erythropoiesis by 8-day feeding administration. IRA of DS-1093a led to lower systemic exposure and erythropoiesis than with oral administration. IRA of DS-1093a improved disease conditions and normalized intestinal mucosa in colitis mice.
Conclusion: DS-1093a improved disease conditions, prevented mucosal injury, and normalized the intestinal mucosa of colitis mice. DS-1093a is suggested to maintain the functional integrity of colon epithelial cells. Owing to mucosal barrier improvement, DS-1093a prevented immune cell activation by colitis, suppressed inflammatory cytokine gene expression in colon epithelial cells. Mucosal normalization effect was correlated with the stabilization of HIF-1 alpha. These results suggested that DS-1093a had a strong efficacy for IBD in colitis mice with novel mechanisms for normalizing colitis mucosa. Moreover, topical exposure of DS-1093a to the colon can widen the efficacy margin between IBD and erythropoiesis.
Disclosure: Nothing to disclose

P0270 LOWER FECAL BACTERIAL ABUNDANCE IS ASSOCIATED WITH DISEASE RECURRENCE ONE YEAR AFTER ILEOCAECAL RESECTION IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Dysbiosis has been proposed to be a key antigenic driver for the inflammation in Crohn's disease (CD). However, the role of the fecal microbial composition for the post-operative disease course in CD patients remains to be established.
Aims and Methods: Our aim was to determine if the fecal microbial composition at the time of ileocaecal resection or 1 year after surgery was associated with endoscopic disease recurrence in CD patients 1 year after surgery.
Patients with CD who had undergone ileocaecal resection were included in the study. Approximately 1 year after surgery, clinical evaluation by ileocolonoscopy was performed. The mucosa in the neoterminal ileum and ileocolonic anastomosis was assessed according to Rutgeerts' scoring system. 5 or less aphtoid lesions were considered as remission (i,0-i,1), and >5 aphtoid lesions, lesions or ulcers confined to the anastomosis or diffuse inflammation were considered as endoscopic disease recurrence (i,2-i,4).
Fecal microbial composition was analyzed using the Genetic Analysis GA-map Dysbiosis test, which consists of 54 DNA probes targeting ≥300 bacteria on different taxonomic levels.
Logarithmic data were analyzed in SIMCA using orthogonal partial least squares discriminate analysis (OPLS-DA) to identify discrimination between groups. Bacteria with the strongest discriminatory power were further analyzed by univariate analysis (Mann-Whitney U-test).
Results: In total, 22 CD patients from Southwestern Sweden (8 women) with median age 30 (17–63) years and median disease duration of 3 (0–11) years at the time of resection was included. At inclusion, 8 patients were treated with 5-aminosalicylic acid (5-ASA), 14 with corticosteroids, 11 with thiopurines, 1 with anti-tumor necrosis factor, and 4 patients had none of the treatments above. At the one year follow up, 9 patients were treated with 5-ASA, 2 with corticosteroids, 6 with thiopurines, and 8 patients had no treatment.
Stool samples were collected by 9 patients at the time of resection and by 21 patients at the 1 year post surgery follow-up. At the 1 year follow up, 13 patients were in endoscopic remission (i,0-i,1) and 9 patients had endoscopic recurrence (i,2-i,3).
At the time of resection, fecal microbial composition discriminated patients whom at the 1 year post surgery follow-up were in endoscopic remission or with recurrence, respectively, although the predictive ability was low ($R2 = 0.94$, $Q2 = -0.1$; i,0-i,1: $n = 5$; i,2-i,3: $n = 4$). Similarly, fecal microbiota at the 1 year post surgery follow-up discriminated patients in endoscopic remission from those in recurrence, yet with low predictability ($R2 = 0.71$, $Q2 = -0.47$; i,0-i,1: $n = 13$; i,2-i,3: $n = 8$).
The OPLS-DA models at the time of resection and at 1 year post surgery follow-up demonstrated that endoscopic remission was associated with a higher bacterial abundance, both among the Firmicutes and Bacteroidetes, as compared to patients with recurrence. In addition, univariate analysis showed that patients in remission one year after surgery tended to have higher abundance of Pseudomonas spp at the time of surgery ($p = 0.06$) and Parabacteroides spp at the 1 year post surgery follow up ($p = 0.08$), as compared to patients with recurrence.
Conclusion: Our results suggest that CD patients with endoscopic disease recurrence 1 year after ileocaecal resection have lower fecal bacterial abundance, both at the time of resection and 1 year after surgery, as compared to patients in remission. Thus, a lower intestinal bacterial abundance may be a contributing factor to disease relapse in these patients.
Disclosure: Nothing to disclose

P0271 RELATIONSHIP BETWEEN BIOPSY LOCATION, HISTOLOGICAL DISEASE ACTIVITY, AND MRNA EXPRESSION IN ENDOSCOPICALLY ACTIVE CROHN'S DISEASE

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Abstract No: P0271

Segment/ Location	NHI	RHI	GHAS	CD31	S100A9	IL-23 (p19)	IL-23 (p40)	IL-6	IL-8
Colon 1	3.3 (2.7,3.8)[1,3]	19.5 (14.7,24.4)[1,3]	10.1 (8.5,11.7)[1,3]	−2.1 (−2.3,−1.8)[1,3]	−1.4 (−1.8,−0.9)[1,3]	−5.7 (−6.1,−5.3)[1,3]	−8.7 (−9.2,−8.2)[1,3]	−4.3 (−4.9,−3.6)[1,3]	−2.6 (−3.2,−2.0)[1,3]
Colon 2	1.2 (0.7,1.8)	5.8 (2.6,9.0)	5.2 (3.4,6.9)	−2.7 (−2.9,−2.5)	−3.2 (−3.6,−2.8)	−6.6 (−6.9,−6.3)	−9.8 (−10.2,−9.4)	−7.1 (−7.7,−6.5)	−5.3 (−5.8,−4.7)[4]
Colon 3	0.9 (0.4,1.4)	4.8 (2.3,7.4)	4.2 (2.5,5.8)	−2.7 (−3.0,−2.5)	−3.4 (−3.8,−3.0)	−6.7 (−7.0,−6.4)	−9.9 (−10.3,−9.5)	−7.2 (−7.6,−6.7)	−5.9 (−6.4,−5.3)[2]
Ileum 1	2.7 (2.1,3.2)[1,3]	14.2 (10,18.3)[1,3]	8.3 (6.9,9.6)[1,3]	−2.2 (−2.4,−1.9)[2,3]	−1.6 (−2.0,−1.2)[1,3]	−5.7 (−6.0,−5.3)[1,3]	−8.6 (−9.0,−8.2)[1,2]	−4.9 (−5.5,−4.4)[1,3]	−2.7 (−3.2,−2.1)[1,3]
Ileum 2	1.3 (0.8,1.8)[4]	6.6 (3.7,9.5)[4]	5.1 (3.6,6.6)[4]	−2.6 (−2.8,−2.4)[4]	−3.0 (−3.3,−2.7)[4]	−6.8 (−7.0,−6.5)	−9.7 (−10.1,−9.3)	−7.3 (−7.8,−6.8)	−5.2 (−5.7,−4.7)
Ileum 3	0.7 (0.3,1.2)	3.4 (1.1,5.7)	3.1 (1.6,4.6)	−2.9 (−3.1,−2.7)	−3.3 (−3.6,−3.0)	−6.7 (−7.0,−6.5)	−9.5 (−9.9,−9.1)	−7.6 (−8.0,−7.2)	−5.6 (−6.1,−5.1)

Within segment pairwise comparison with location 2, [1]$p<0.001$, [2]$p<0.05$; and location 3, [3]$p<0.001$, [4]$p<0.05$

NHI, Nancy Histological Index; RHI, Robarts Histopathology Index; GHAS, Global Histological Activity Score; IL, interleukin

Introduction: The appropriate biopsy location for assessment of histological disease activity and mRNA expression in patients with Crohn's disease (CD) is unknown.

Aims and Methods: We aimed to identify the location adjacent to existing ulcers corresponding to the maximal histologic disease severity rating and mRNA expression level. This prospective multicenter (Belgium, Netherlands, Slovenia) study enrolled 51 patients with CD with ulcers (>0.5 cm) in the colon and/or (neo)terminal ileum. 2 biopsy specimens were obtained from the ulcer edge (location 1) and non-ulcerated mucosa at distance of 1 (7–8 mm [location 2]) and 3 open forceps (21–24 mm [location 3]) perpendicular to the edge of the largest ulcer in the ileum in 19, colon in 15, and ileum and colon in 17 patients. Ileocolonoscopy videos were centrally assessed to confirm correct biopsy procurement and to score endoscopic disease activity with the Simplified Endoscopic Score-CD (SES-CD). Histological disease activity was blindly assessed in digitized biopsy images with the Global Histological Disease Activity Score (GHAS), and the Robarts Histopathology (RHI) and Nancy Histological (NHI) indices. Expression of interleukin (IL)-6, -8, -23, CD31 and S100A9 mRNA levels were determined by quantitative polymerase chain reaction, normalized against housekeeping genes (β-actin and cyclophilin) and expressed as log-transformed data. The relationship between biopsy location and histological activity/mRNA expression level was analyzed using a mixed model with location, segment and location-segment as fixed effects and an unstructured variance-covariance matrix.

Results: The mean (standard deviation) SES-CD score of the patients was 11 (7.5). A linear relationship was observed between biopsy location and histological disease activity and mRNA expression in both segments ($p<0.05$). All histological disease activity ratings and mRNA expression levels were highest at the ulcer edge (**Table 1**). Significant ($p<0.0001$) differences were observed for all comparisons between the ulcer edge and the other biopsy locations in both segments. Although histological disease activity was statistically different ($p<0.05$) between locations 2 and 3 in the ileum, most other comparisons were not (**Table 1**).

[Table 1. Histological disease activity and mRNA expression (estimates and 95% confidence intervals) according to segment and biopsy location]

Conclusion: Biopsy procurement at the edge of an ulcer in patients with CD yields the greatest histological disease activity and mRNA expression.

Disclosure: GN, TS, PB, BS, and GRVDB have nothing to disclose. TVV and JJ are employees of, and NVC, LS, RK, WJS, BGF, RP, VP, and GDH have received consulting fees from Robarts Clinical Trials, Inc.

P0272 NEUTROPHIL EXTRACELLULAR TRAPS SUSTAIN INFLAMMATORY SIGNALS IN ULCERATIVE COLITIS

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Introduction: In Ulcerative colitis (UC), mucosal damage occurs in areas, which are infiltrated with neutrophils, a subset of innate immune cells involved in the defense against pathogens. The anti-microbial function of neutrophils relies in part on the formation of extracellular web-like structures, named neutrophil extracellular traps (NETs) through a process called NETosis. Aberrant NETs formation and/or clearance have been associated with several immune diseases.

Aims and Methods: We examined whether UC-related inflammation is characterized by aberrant formation of NETs and investigated the role of such structures in the control of mucosal inflammation. To this end, we evaluated the expression of PAD4, a key enzyme in the formation of NETs, in intestinal samples of patients with UC and controls by Western blotting and immunohistochemistry. The expression of NET-related proteins such as neutrophil elastase (NE), myeloperoxidase (MPO) and citrullinated histone H3 (citH3) was investigated by Western blotting and immunofluorescence. PAD4 and NET-associated proteins expression was further investigated by immunohistochemistry and immunofluorescence in colonic samples of UC patients before and after anti-TNFα (infliximab) treatment. Furthermore, we tested the capacity of neutrophils to produce NETs *in vitro* upon activation with various inflammatory stimuli. Lamina propria mononuclear cells isolated from the inflamed intestine of UC patients were cultured in presence or absence of NETs and then cytokines expression was evaluated by real-time PCR and ELISA and activation of mitogen-activated protein kinases was assessed by Western blotting. Finally, we assessed whether administration of a specific PAD4 inhibitor to mice reverted dextran sodium sulfate (DSS) colitis.

Results: NET-associated proteins were over-expressed in inflamed colon of UC patients as compared to Crohn's disease patients and normal controls. Circulating neutrophils of UC patients produced NETs in response to TNF-α stimulation, and reduced expression of NET-related proteins and diminished NETs formation were seen in patients receiving anti-TNF. Treatment of UC lamina propria mononuclear cells with NETs activated extracellular signal-regulated kinase-1/2, thus enhancing TNF-α and IL-1β production. NETs were induced in mice with DSS colitis and *in vivo* inhibition of NETs formation attenuated colitis.

Conclusion: Data show that NETosis is induced in UC and suggest a role for NETs in sustaining mucosal inflammation in this disorder.

Disclosure: Nothing to disclose

P0273 THE SYSTEMIC INFLAMMATORY PROTEIN PROFILES DEVIATE BETWEEN PATIENTS WITH INFLAMMATORY AND FUNCTIONAL GASTROINTESTINAL DISEASES

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Introduction: Patients with ulcerative colitis (UC) may suffer from irritable bowel syndrome (IBS)-like symptoms during periods of remission. Due to the low-grade immune activation repeatedly reported in IBS, it has been suggested that the underlying inflammatory mechanisms of the 2 diseases overlap or are part of the same spectrum.

Aims and Methods: We aimed to determine if the systemic protein profiles (SysPP) differ between UC and IBS patients, and if SysPP are linked to presence of inflammation and/or functional symptoms. Patients with active ulcerative colitis (UCA), UC patients in remission with IBS-like symptoms (UCR+IBS), UC patients in remission without IBS-like symptoms (UCR-IBS), IBS patients (IBS) and healthy subjects (HS) were included. UCA patients had an endoscopic Mayo score ≥2 and UCR patients had an endoscopic Mayo score = 0 with no relapse during the previous 3 months. UCR+IBS and IBS patients met Rome III criteria with predominant diarrhea or mixed symptom profiles. Serum samples were analyzed using Olink Proseek Multiplex Inflammation panel including 92 proteins (normalized protein expression (NPX)). Logarithmic data were analyzed in SIMCA using principal component analysis (PCA) and orthogonal projection least square discriminate analysis (OPLS-DA) with a Variable Importance for the Projection (VIP) cut-off of >0.7 to identify proteins discriminating between groups. Univariate analyses were performed using Mann-Whitney U test and false discovery rate analysis.

Results: In total, 166 subjects (UCA, n = 40; UCR-IBS, n = 45; UCR+IBS, n = 20; IBS, n = 40; HS, n = 21) were included in the study. PCA of SysPP of all groups revealed 2 clusters; 1 cluster composed of IBS patients and HS, and 1 cluster composed of all UC patients, irrespective of disease activity or presence of IBS-like symptoms. Variables most important for the clustering were higher levels of co-stimulatory molecules such as CD40 and tumor necrosis factor superfamily member 14 (TNFSF14), cytokines such as interleukin (IL)-8 and IL-6, oncostatin-M (OSM), chemokines such as chemokine ligand 3 (CCL3), other inflammatory markers such as extracellular newly identified receptor for advanced glycation end-products (EN-RAGE), sulfotransferase 1A1 (ST1A1), axin 1 (AXIN1), and an apoptotic marker, caspase-8 (CASP8), among UCA/UC+IBS/UC-IBS as compared to IBS/HC.

When comparing IBS and UCR+IBS patients based on the SysPP, OPLS-DA discriminated the 2 groups with high predictability ($R^2Y = 0.92$, $Q^2 = 0.82$).

UCR+IBS was associated with lower levels of IL-7 ($q < 0.01$) and higher levels of CASP8, ST1A1, AXIN1, TNFSF14, OSM, IL8 and EN-RAGE (all $q < 0.0001$) as compared to IBS. Further, when comparing UCR+IBS and UCR-IBS patients the SysPP discriminated the groups, yet the predictive value was low ($R^2Y = 0.68$, $Q^2 = 0.24$). In more detail, UCR+IBS were associated with higher levels of osteoprotegerin (OPG) and TNF-β, while UCR-IBS was associated with higher levels of proinflammatoy cytokine IL-17A and chemokine ligand 9. The SysPP also discriminated UCA and UCR+IBS patients although with low predictability ($R^2Y = 0.52$, $Q^2 = 0.24$). IBS patients and HS could not be discriminated by SysPP ($R^2Y = 0.20$, $Q^2 = 0.10$).
Conclusion: The systemic protein profiles differentiate between UC patients, irrespective of presence of inflammation or functional symptoms, and IBS patients. This suggests that the systemic protein profiles reflects different underlying mechanisms of the 2 diseases rather than presence of functional symptoms.
Disclosure: Nothing to disclose

P0274 TISSUE REMODELLING IN TERMINAL ILEAL STRICTURING CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is a chronic inflammatory condition with multiple phenotypes of which the fibrostenotic type carries significant morbidity and risk of surgery. We have shown that stenotic segments are characterised by expansion of several layers of the intestine which can be quantitated by a novel scoring system (1).
Aims and Methods: We aimed to look at histological changes in resected terminal ileal (TI) specimens using this novel scoring system. We identified all patients undergoing surgery for TI CD secondary to symptomatic stricturing disease using the histopathology database at Queen Elizabeth Hospital in Birmingham, United Kingdom, between 2012 and 2017. Phenotypic data were recorded and the resection specimens were reviewed and the most representative section of the stenotic segment was used for microscopic assessment. 2 independent pathologists applied the semi-quantitative scoring system. Data was analysed using the %PMTS (possible maximum total score) recorded by the pathologists.
Results: Among 48 patients (M = 25; median age 45 years, range 21–72 years), 41 were Caucasian, 4 Asian and 3 Afro-Caribbean in ethnicity. The median duration of disease was 7 years (range 3 months −39 years); majority had ileo-colonic distribution with stricturing disease; 16 patients were on thiopurines, 19 on steroids & 4 on biologics. The histological grading showed a variable predominant feature in each layer of the bowel wall (Details in Table 1). In the mucosa, chronic inflammation was more prominent whereas fibrosis was predominant in the submucosa; volume expansion (graded by comparing thickness of the layer with relatively normal regions of the same intestinal tract at the margins) was prominent in the muscularis propria and fibrosis was prominent in the subserosa. Muscular hyperplasia (MPH) was consistently seen to be a prominent feature across all layers of strictured bowel and a statistically significant correlation between MPH and fibrosis noted ($r = 0.648$, $p < 0.001$). Interestingly, adipose hyperplasia was seen to be a feature in submucosal layer.
[Table 1-Results of histological scoring(mean PMTS & standard error of mean)]
Conclusion: Our results suggest that pure fibrostenotic disease is uncommon and chronic inflammation is a prominent feature of this phenotype. In addition to fibrosis, muscle hyperplasia is an important component. Other components such as volume expansion, neuronal hypertrophy and adipose hyperplasia are likely to be important in different layers of the bowel. This suggests that inflammation driven tissue remodelling leading to stricture formation is a complex process resulting in a multitude of changes and not simply characterised by excess deposition of fibrotic tissue.
Disclosure: This abstract presents independent research funded by the NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Abstract No: P0274

	Active Inflammation	Chronic inflammation	Fibrosis	Muscular hyperplasia	Neuronal hypertrophy	Adipocyte proliferation	Space volume expansion
	Mean and SEM	Mean and SEM	Mean and SEM	Mean and SEM	Mean and SEM	Mean and SEM	Mean and SEM
Mucosa	22.92 2.37	52.95 2.56	40.28 5.15	46.88 3.32	- -	- -	24.31 3.81
Submucosa	12.50 2.60	48.38 2.86	70.83 4.40	45.14 3.99	31.94 5.87	33.33 4.09	39.58 4.05
Muscularis propria	6.02 2.04	28.24 2.96	31.25 3.77	30.90 2.86	22.92 4.46	4.86 1.72	38.89 3.34
Subserosa	4.02 1.19	38.06 2.94	53.19 5.13	21.99 4.09	26.24 5.06	- -	36.88 4.45

Reference

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P0275 B CELL-MEDIATED ILEOCECAL IMMUNE RESPONSE IN AN EXPERIMENTAL COLITIS MODEL ANALYZED VIA INTRAVITAL IMAGING

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Introduction: Inflammatory bowel diseases (IBD) often involve the ileocecal region of the intestine. In addition, accumulating epidemiological studies have suggested that appendectomy may reduce the risk of ulcerative colitis. These evidences imply that ileocecal immune response may be considered to affect the development of IBD, but the mechanism is still unclear.
Aims and Methods: The aim of this study is to analyze the ileocecal immune response in the setting of IBD. To this end, oxazolone colitis model was induced in mice under various backgrounds, conditions (including appendectomy), and methods (such as 5-dimensional intravital imaging).
Results: Wild type C57BL6 (WT) mice sensitized with oxazolone revealed lymphocyte infiltration and ulcerations in the colon accompanied by expanding cecal lymphoid follicles (CLF), which became the focus of our study. Mice underwent appendectomy before oxazolone treatment resulted in attenuated colitis with regards to both clinical disease activity and histopathology index with associated decrease of pro-inflammatory cytokine production. Similar clinical and histopathological changes were also observed in mice lacking mature B cells, μMT. Real-time analysis of B cell activity in the CLF was accomplished by using mice with B cell-specific Ca^{2+} biosensor, YC3.60, expression. Utilizing intravital imaging, B cell activation with frequent Ca^{2+} influx was observed in the CLF during the early phase of colitis development. B cells in the CLF expressed higher level of activation markers, such as major histocompatibility complexes, compared to that of the non-colitis control, even though there were no significant changes in the ratios of immunoglobulin (Ig) classes on the B cell surface of the CLF.
Conclusion: Abnormal Ig production induced by Th2 cytokine was previously considered to be the major role of B/plasma cells in the pathogenesis of IBD. Our current studies, however, imply that B cells in the CLF contribute to the induction of immune responses during the early phase of colitis development. These mechanisms revealed by intravital imaging help provide insight to the novel B cell function associated with the pathophysiology of IBD.
Disclosure: Nothing to disclose

P0276 THE CHANGE OF THE ANG, ACE2 AND ANG,1-7,ON TNBS-INDUCED EXPERIMENTAL COLITIS IN MICE AND THE RESEARCH ABOUT PROTECTIVE EFFECT OF MICA

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Introduction: Ulcerative colitis (UC), a chronic intestinal inflammatory condition that affects millions of people worldwide, is characterized by leukocyte infiltration and upregulation of proinflammatory cytokines. Mica is a of silicate mineral drug. Previous studies have shown that mica can promote gastrointestinal mucosal epithelial cell regeneration and anti-inflammatory effect.
Aims and Methods: We aimed to explore the roles of Ang,ACE2 and Ang,1-7, in experimental colitis and investigate the prevention and possible mechanism of mica.
30 male BALB/C mice of clean grade were randomly divided into control group, model group and mica group, 10 mice in each group. Experimental colitis mice were made by TNBS. In first day, the model group and mica group were initiated by intrarectal administration of TNBS (250mg/kg/d) to establish the model, control group was initiated by intrarectal administration of saline water (10ml/kg/d). From the second day,the control group and model group were

intrarectally administrated with (10ml/kg/d), the mica group was intrarectally administrated with Mica (180mg/kg/d), until the fourth day, then all the mice were killed. Macroscopic score and histological score were assessed. Protein expressions of Ang,ACE2 and Ang,1-7, were measured by immunohistochemist. ELISA was used to determine colon tissue inflammatory factor IL-17A and IL-10 level.

Results: 1) Macroscopic total damage: Colonic macroscopic damage index of mice in normal, the model group was much higher than that of the control group (4.00 ± 0.89 vs. 0.00 ± 0.00, $p < 0.01$), the mica group was much lower than the model group (2.00 ± 1.53 vs. 4.00 ± 0.89, $p < 0.01$). **2) Colonic tissues histological score:** The histological score of the model group was much higher than the control group (8.17 ± 2.99 vs. 1.33 ± 1.03, $p < 0.01$). Compared with the model group, the histological score in the mica group decreased statistically significantly (3.83 ± 1.47 vs. 8.17 ± 2.99, $p < 0.01$). **3) The level of Ang, ACE2, Ang1-7 in mice colonic tissues:** The level of Ang, and Ang1-7 in the model group were increased compared with the control group (Ang,:4.83 ± 2.11 vs. 2.16 ± 0.41, $p < 0.01$; Ang1-7:2.0 ± 0.63 vs. 0.13 ± 0.14, $p < 0.05$). But in the mica group the level of Ang, and Ang1-7 were significantly decreased compared with the model group (Ang,:2.33 ± 0.52 vs. 4.83 ± 2.11, $p < 0.01$; Ang1-7:1.04 ± 0.56 vs. 2.0 ± 0.63, $p < 0.01$). Compared with the control group, the expression of ACE2 in colonic tissues from mice in the model group was increased (3.50 ± 0.55 vs. 2.04 ± 0.29, $p < 0.05$), and in the mica group it was significantly increased than in the model group (5.13 ± 1.84 vs. 3.50 ± 0.55, $p < 0.05$). **4) The expression of IL-17A in mice colonic tissues:** The expressions of IL-17A in colonic tissues from mice in the model group and the mica group were significantly increased (6.93 ± 0.44 vs. 0.65 ± 0.03, $p < 0.01$; 2.63 ± 0.64 vs. 0.65 ± 0.03, $p < 0.01$). Meanwhile, the expression of IL-17A in the mica group was lower than in the model group (2.63 ± 0.64 vs. 6.93 ± 0.44, $p < 0.01$). **5) Correlation analysis:** Pearson's correlation analysis show that the expression of Ang, was moderate positive correlation with the mice colonic macroscopic damage index ($r = 0.524$, $p < 0.05$),and was high positive correlation with the mice colonic histological score ($r = 0.909$, $p < 0.01$).

Conclusion: There is an imbalance between Ang, and ACE2, Ang,1-7,in the TNBS-induced experimental colitis mice. And mica can reduce colonic tissues inflammation and damage.

Disclosure: Nothing to disclose

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P0277 TAUROURSODEOXYCHOLIC ACID ATTENUATES COLITIS-ASSOCIATED COLON CANCER BY INHIBITING NUCLEAR FACTOR KAPPAB SIGNALING

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Introduction: Inflammatory bowel diseases (IBD) is associated with an increased risk for the development of colorectal cancer. However, the mechanism of immune signaling pathways linked to colitis-associated cancer (CAC) has not been fully elucidated. Tauroursodeoxycholic acid (TUDCA) exhibits anti-inflammatory and anti-cancer activities. The aim of this study is to investigate the role of TUDCA in the pathogenesis of CAC.

Aims and Methods: CAC was induced in mice using azoxymethane (AOM) and dextran sodium sulfate (DSS) administration, and TUDCA's effect on tumor development was evaluated. HCT 116 and COLO 205 were treated with TUDCA or vehicle and then stimulated with tumor necrosis factor-α (TNF-α). Expression of interleukin (IL)-8 was determined by real-time RT-PCR and ELISA, and IκBα phosphorylation and degradation was evaluated by immunoblot assay. The DNA-binding activity of NF-κB was assessed by electrophoretic mobility shift assay (EMSA). Cell viability assay and real-time RT-PCR of *bcl-xL*, *MCL1*, *c-FLIP-L* and *VEGF* were performed.

Results: TUDCA significantly attenuated the development of CAC in mice. Exposure to TUDCA resulted in extensive epithelial apoptosis and reduced levels of phospho-IκB kinase in the colon. In HCT 116 cells stimulated with TNF-α, TUDCA significantly inhibited IL-8 expression and suppressed TNF-α-induced IκBα phosphorylation/degradation and DNA-binding activity of NF-κB. Furthermore, in both HCT 116 and COLO 205 cells, TUDCA reduced cell viability and downregulated the expression of *bcl-xL*, *MCL1*, *c-FLIP-L* and *VEGF*.

Conclusion: These results demonstrated that TUDCA suppresses NF-κB signaling and ameliorates colitis-associated tumorigenesis, suggesting that TUDCA could be a potential treatment for CAC.

Disclosure: Nothing to disclose

P0278 ANTI-TNF-ALPHA THERAPY INDUCES MICROBIAL AND IMMUNOLOGICAL CHANGES IN DEXTRAN SODIUM SULPHATE ACUTE COLITIS

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Introduction: Anti-TNF alpha represents the best therapeutic option to induce mucosal healing and clinical remission in patients with moderate-severe ulcerative colitis. On the other side, gut microbiota plays a crucial role in pathogenesis of ulcerative colitis but little information exists on how microbiota changes following anti-TNF-alpha therapy and on the role of microbiota in mucosal healing.

Aims and Methods: We aimed to evaluate gut microbiota and adaptive immune system response change following anti TNF-alpha therapy in murine dextransodium sulphate (DSS) colitis. C57BL/6 mice were fed for 5 days with 3% DSS in drinking water. At day 3 of DSS treatment, mice received intravenous administration of 5 mg/Kg of infliximab (IFX), an anti-TNF alpha monoclonal antibody, or placebo. Further 2 groups of mice received IFX or placebo without DSS. Disease severity was scored daily using the 4 points Disease Activity Index (DAI). At day V and XII serum, colon, feces and mesenteric lymph node (MLN) were collected from each animal. Microorganisms belonging to Bacteroides, Clostridiales, Enterobacteriaceae and Fecalibacterium prausnitzii were assessed by qPCR, following bacterial DNA extraction from feces. Th1, Th2, Th17 and Treg cell distribution in the MLN were evaluated by intracellular cytokine staining by flow cytometry.

Results: Anti-inflammatory species (Bacteroides, Clostridiales and Fecalibacterium prausnitzii) decreased during DSS-induced colitis and increased in fecal samples of IFX-treated colitis mice compared to control mice. Conversely, pro-inflammatory microorganisms belonging to Enterococacceae genera increased during colitis and decreased after IFX treatment. Furthermore, in IFX-treated colitic mice, microbial changes are associated to an initial increase (day 5 of the colitis) in Treg cells and a consequent decrease (day 12 of colitis) in Th1, Th2 and Th17 cells. Similarly, healthy mice treated with IFX showed the same histological features, microbial and immune changes of untreated colitic mice.

Conclusion: Anti-TNF alpha treatment in experimental model of colitis improves disease activity trough changes in T cell subsets and in microbiota composition Furthermore, the present study suggests that different components of the microbiota each distinctly influence the differentiation and accumulation of specific populations of immune cells. Further analysis on immune cells within mucosa will be necessary.

Disclosure: Nothing to disclose

P0279 SHORT-TERM ORAL ANTIBIOTICS TREATMENT PROMOTES INFLAMMATORY ACTIVATION OF COLONIC INKT AND CONVENTIONAL CD4$^+$ T CELLS

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Introduction: The gut mucosa is continuously exposed to a vast community of microorganisms, collectively defined as microbiota, establishing a mutualistic relationship with the host and contributing to shape the immune system. Gut microbiota is acquired at birth, and its composition is relatively stable during the entire adult life. Intestinal dysbiosis, defined as a microbial imbalance of gut bacterial communities, can be caused by several factors, including bacterial infections and antibiotic use, and has been associated with an increased risk to develop or exacerbate immune-mediated pathologies, such as allergic reactions, asthma and inflammatory bowel diseases (IBD). Still, the mechanisms by which antibiotic-induced gut dysbiosis may lead to development of mucosal inflammation are still matter of debate.

Aims and Methods: We aimed to evaluate the impact of antibiotic treatment on phenotype and functions of intestinal immune cell populations, including invariant Natural Killer T (iNKT) cells, a subset of lipid specific T cells profoundly influenced by alterations on the commensal microbiota.

A cocktail of broad-spectrum antibiotics was administered for 2 weeks to otherwise healthy mice before re-colonization of the intestinal microbial community with oral gavage of eubiotic or dysbiotic mucosa-associated bacteria and luminal colonic content, followed or not by intestinal inflammation induction.

Results: Short-term antibiotic treatment alters frequency and functions of intestinal iNKT cells, even in the absence of intestinal inflammation. The presence of a dysbiotic microbiota after antibiotic treatment imprints colonic iNKT and

CD4+ T cells towards a pro-inflammatory phenotype that collectively contributes to aggravate intestinal inflammation. Nonetheless, the inflammatory potential of the dysbiotic microbiota decreases over time opening the possibility to temporally intervene on the microbial composition to re-equilibrate dysbiosis thus controlling concomitantly mucosal immune T cell activations.
Conclusion: Antibiotic treatment can induce alterations in the intestinal microbial ecology leading to the activation of colonic pro-inflammatory immune cell responses.
Disclosure: Nothing to disclose

P0280 THERAPEUTIC POTENTIAL OF GLEPAGLUTIDE, A LONG-ACTING GLUCAGON-LIKE PEPTIDE-2 RECEPTOR AGONIST, IN A RAT MODEL OF RECURRENT INDOMETHACIN-INDUCED SMALL INTESTINAL INFLAMMATION

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Introduction: Glepaglutide (ZP1848) is a novel, long-acting GLP-2 receptor agonist that is currently in clinical development for the treatment of short-bowel syndrome. We have previously shown that treatment with glepaglutide in a rat model of indomethacin-induced small intestinal (SI) inflammation enhanced intestinal repair, as measured by increase in intestinal mass and plasma citrulline levels, and decrease in inflammatory markers.
Aims and Methods: The aim was to determine whether pre- and continuous-treatment with glepaglutide would attenuate the SI inflammation response in rats exposed to a second inflammatory episode.
2 cycles of SI inflammation were induced in male Wistar rats by indomethacin administration (7 mg/kg, s.c.) on day 0 and day 1 (primary challenge) and then again on day 18 and day 19 (secondary challenge). Rats were treated with glepaglutide (80 and 400 nmol/kg, s.c.) from day 0 to day 14 (pretreatment), or from day 0 to day 21 (continuous treatment). Groups of rats (n = 8/group) were sacrificed on days 15 and 22. Study endpoints were bodyweight (BW), jejunal and ileal mass/BW, SI length, and SI levels of alpha 1 acid glycoprotein (α-1-AGP; ELISA kit, Life Diagnostics) and myeloperoxidase (MPO; ELISA kit, Hycult Biotechnology).
Results: Pretreatment with glepaglutide (80, 400 nmol/kg) increased jejunal- and ileal mass/BW on day 15 ($p < 0.001$ for both dose levels vs Indomethacin group). The second indomethacin-induced SI inflammation episode was characterized by BW loss, increased jejunal and ileal mass/BW, decreased SI length, and increased SI levels of α-1-AGP and MPO. Pre- (400 nmol/kg) and continuous treatment (80, 400 nmol/kg) with glepaglutide prevented BW loss in animals after the second inflammatory episode ($p < 0.001$ for all comparisons vs Indomethacin group). In addition, both pre- and continuous treatment with glepaglutide (400 nmol/kg) significantly increased ileal mass/BW on day 22, but had no effect on jejunal mass/BW vs Indomethacin group. Both treatment regimens dose-dependently counteracted the shrinking of the SI length, and decreased SI levels of inflammatory markers (α-1-AGP and MPO) during the second phase of inflammation (day 22).
Conclusion: We have demonstrated that pre- and continuous treatment with glepaglutide protected the SI against the recurrent inflammatory episode. In addition, pretreatment with glepaglutide increased SI mass assessed prior to the induction of the second phase of inflammation, suggesting that this increase in SI mass had rendered SI more resistant to the second inflammatory insult. In conclusion, glepaglutide may provide an attractive option for the treatment and/or prevention of the unpredictable course of inflammatory bowel disease.
Disclosure: Jolanta Skarbaliene, Christian Thorkildsen, Mark Berner-Hansen, and Wayne Russell are employes of Zealand Pharma A/S, and hold stock portions in Zealand Pharma A/S.

P0281 CHARACTERISTICS OF MUCOSA-ASSOCIATED GUT MICROBIOTA DURING TREATMENT IN CROHN'S DISEASE

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Introduction: The dysbiosis of gut microbiome seems relevant to the pathogenesis of Crohn's disease (CD), with differences between patients with CD and healthy subjects (HS) in both diversity and composition. However, it is not clear how the gut microbiota changed from active CD to remission after treatment.
Aims and Methods: The aim of this study was to characterize the dynamic alterations of mucosa-associated intestinal microbiota in CD patients after induction of remission. A 16S rRNA sequencing approach was applied to determine the structures of microbial communities in mucosal samples including terminal ileal, ascending colon and descending colon. The composition and function of mucosa-associated gut microbiota were compared between paired samples from CD patients in active and remission stage during treatment.
Results: There were no significant differences in microbial structure among the three anatomical sites within individuals. Compared to active disease, the alpha diversity of CD in remission was increased and approximately up to the level of HS. The principal coordinate analysis revealed that samples of active CD clearly separated from those in remission which clustered close to HS. 42 genera were identified to be differentially abundant between active and quiescent CD with a loss of *Fusobacterium* and a gain of potential beneficial bacteria including *Lactobacillus*, *Akkermansia*, *Roseburia*, *Ruminococcus* and *Lachnospira* after the induction of remission. The combination of these taxa into a microbial dysbiosis index showed a strong positive correlation with clinical disease severity and negative correlation with species richness.
Conclusion: The dysbiosis of mucosa-associated microbiota was associated with disease phenotype, which could be partly restored after the induction of remission. We speculate that the trajectory of early microbiome changes may represent a predictive factor for relapse.
Disclosure: Nothing to disclose

P0282 AUTOPHAGY-RELATED HOST FACTORS ARE INVOLVED IN THE INCAPABILITY OF MACROPHAGES FROM CROHN'S DISEASE PATIENTS TO ELIMINATE ADHERENT-INVASIVE *ESCHERICHIA COLI*

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Introduction: Several experimental data have highlighted the potential role of intestinal macrophages in the pathogenesis of Crohn's Disease (CD). These macrophages present a defect in the control of CD-associated adherent-invasive *E. coli* (AIEC) replication, which could be linked to altered autophagy.
Aims and Methods: We investigated the impact of several CD-associated singer nucleotide polymorphisms (SNPs) including those involved in autophagy on the ability of macrophages from CD patients to eliminate AIEC bacteria. Peripheral blood monocyte-derived macrophages (MDM) were obtained from 95 CD patients, 30 ulcerative colitis (UC) patients and 15 healthy subjects genotyped for CD-associated SNPs related to autophagy, especially *IRGM* (rs10065172) and *ULK1* (rs12303764) and, infected with AIEC LF82 reference strain. Functional assay were performed on MDM after AIEC infection and/or after a short-term silencing of ULK1 gene. The numbers of intracellular bacteria were determined using gentamicin protection assay. IRGM, ULK1 and p62 protein expression was determined by western blot.
Results: AIEC survival was increased within MDM from CD patients compared to those from UC patients or healthy subjects ($p = 0.0019$). MDM from CD patients failed to kill AIEC bacteria especially in patients harboring the CD-associated *IRGM* SNP ($p = 0.045$). In contrast, AIEC survival was decreased in MDM from patients with the CD-associated *ULK1* SNP ($p = 0.046$). ULK1 expression, but not IRGM and p62, was increased in MDM from CD patients infected by AIEC bacteria compared to MDM from UC patients or healthy subjects ($p = 0.0056$) and are significantly correlated with the AIEC survival ($p = 0.0369$). In this line, ULK1 down-regulation within MDM limits the AIEC survival ($p = 0.0018$).
Conclusion: We confirmed that MDM from CD patients failed to eliminate AIEC bacteria compared to those of UC or healthy subjects. Our results highlight a role of CD-associated SNPs, related to autophagy, IRGM and ULK1, on the ability of macrophages from CD patients to mediate AIEC bacterial clearance. At the protein level, our data suggested a role of ULK1, the cornerstone of autophagy initiation, to control AIEC bacteria within macrophages, in patients with CD. This protein could represent a potential new target to alter the interaction between macrophages and AIEC.
Disclosure: Nothing to disclose

P0283 MUCOSAL AND SYSTEMIC IMMUNE PROFILES DIFFER DURING EARLY AND LATE PHASE OF THE DISEASE IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Introduction: Alterations in the immunopathogenesis in ulcerative colitis (UC) due to the natural disease course have been proposed but so far data are lacking. We therefore aimed to determine mucosal and systemic immune profiles at the time of diagnosis (early disease) and after 10 years (late disease) in UC patients.
Aims and Methods: Patients with UC provided serum and mucosal biopsies during a flare at the time of diagnosis and after 10 years of disease. mRNA gene expression in biopsies was analyzed using the Qiagen RT^2 Profiler PCR Arrays Antibacterial response and T Helper Cell Differentiation with 84 genes per array, in total 152 unique genes. Serum samples were analyzed using Olink Proseek Inflammation panel including 92 proteins (normalized protein expression (NPX)), but only the 43 proteins related to digestive tract were included in the analyses. Logarithmic data were analyzed in SIMCA using OPLS-DA to identify parameters discriminating between early and late disease, implementing a Variable Importance for the Projection (VIP) cut-off > 1. Identified parameters were used for univariate analysis and false discovery rate analysis. Data are

presented as fold change of means for mRNA analyses and median (interquartile range) for normalized protein expression.
Results: The study included 15 UC patients (mean age 48 years after 10 years of disease, 60% males) where 8 had extensive, 5 left-sided disease and 2 proctitis. No patient had ongoing treatment with corticosteroids or biologics (2 were previously exposed to Infliximab), 3 patients currently used Azathioprine and 10 oral aminosalicylates. When comparing early and late disease, the mRNA profiles in biopsies discriminated the groups and showed high predictability ($R2 = 0.8$, $Q2 = 0.71$). In total, 37 genes were differently expressed during early and late disease (all $q < 0.05$). In more detail, a fold increase of the Th2 response related genes IL-5 (2.5, $q = 0.01$), IL-13 (2.2, $q = 0.04$) and IL1R1 (2.5, $q = 0.008$) was detected during late compared to early disease. Concomitantly, a fold decrease of the Th1 associated genes TNF (0.66, $q = 0.03$) and SOCS1 (0.66, $q = 0.04$) was recorded during late compared to early disease.
Additionally, the profile of 17 serum proteins discriminated early and late disease ($R2 = 0.63$, $Q2 = 0.40$) and 7 of these were differently expressed between the groups (all $q < 0.03$). The growth factor for dendritic cells, Flt3L (8.7 (8.3–9.0) vs. 7.9 (7.5–8.7) NPX), and the chemokine ligand CCL25 (6.3 (5.8–6.6) vs. 5.5 (5.0–6.0) NPX) involved in intestinal homing of lymphocytes were increased during late as compared to early disease. Further, IL-8 (7.4 (6.9–7.9) vs. 8.9 (7.1–14.5) NPX) and MCP3 (2.2 (1.9–2.6) vs. 2.8 (2.3–8.0) NPX), important for recruitment of neutrophils and monocytes, and TNFSF14 (6.7 (5.4–7.2) vs. 7.6 (6.5–8.3) NPX), CCL20 (4.7 (4.4–5.4) vs. 5.8 (5.5–6.2) NPX) and CCL28 (1.4 (1.2–1.6) vs. 1.6 (1.5–1.9) NPX) associated with lymphocyte homing were decreased during late as compared to early disease.
Conclusion: Mucosal and systemic inflammatory profiles differ between early and late disease in UC patients with active disease, with a change from a T Helper 1 to a T Helper 2 cell driven disease. Improved understanding of the variation in immunopathogenesis due to the natural disease course is important to guide individualized treatment decision-making.
Disclosure: Nothing to disclose

P0284 LOW LEVEL OF KNOWLEDGE OF PREGNANCY-RELATED ISSUES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN POLISH POPULATION

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Introduction: Inflammatory bowel diseases (IBDs) belong to the group of chronic diseases, significantly increase the risk of surgery, colorectal cancer and often impact young people of reproductive age, as they may influence their personal life choices regarding family planning and having children.
Aims and Methods: The aim of the work was to assess the knowledge of female patients with IBD regarding pregnancy and fertility issues in respect of the disease. The goal of the work was also to educate the patients. The examinations were based on validated test CCPKnow (Crohn's and Colitis Pregnancy Knowledge Score). The study included 120 women at the age of 18 to 74, including 86 women at the age up to 45 years old, 59 women with CD (Crohn's disease) and 61 women with UC (ulcerative colitis). All the respondents were treated in Department of Gastroenterology and Hepatology of Wrocław Medical University in years 2014–2017.
Results: The average disease duration of each patient was estimated to 8 years, in case of women of reproductive age (up to 45 years old) was estimated to 6.6 years. Majority of the patients claimed to live in a long-time relationship. In the group of patients up to 45 years old, 63% women did not have any children. All the children born after disease diagnosis were healthy. No congenital abnormality was found. 31% of patients of reproductive age declared that they did not plan to have (more) children in the future, more than half underlined that the decision was made with regard to existing disease. The average amount of points gathered in CCPKnow test was estimated to 6.9 of 17 points possible. Through this research we can state that 40–50% female patients assessed by means of CCPKnow test have low level of knowledge regarding pregnancy and fertility, and only 8–10% display good level of knowledge. Female patients over 45 years gained less points in comparison to younger women (4,85 vs. 7,7; $p = 0.0012$). Significantly higher level of knowledge was stated among women, who gave birth during the disease ($p = 0.0003$), also with higher education and medical education ($p = 0.0157$). It was noticed that, patients with IBD have less children than the general population, which seems to be their conscious choice. The patients of a reproductive age, who declare that they do not want to have (more) children in the future and the ones that chose consciously to be childless, have significantly lower level of knowledge assessed by means of CCPKnow test ($p = 0.0131$), which suggests that education of the patients may have a positive influence on their life choices.
Conclusion: Female patients with IBD have less children in comparison to teh general population. The majority of the patients suffering from IBD have a low level of knowledge regarding pregnancy and fertility, especially women over age of 45. Higher levels of knowledge were observed in the group of female patients who gave birth to children during the disease, also those who had high education and medical education. Lower levels of knowledge were found in the group of women in the reproductive age, who declared consciously to be childless or did not want to have children at all in the future. The lowest level of knowledge was stated among the patients with IBD regarding treatment during pregnancy and when making efforts to get pregnant. Educating patients is very important.
Disclosure: Nothing to disclose

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P0285 ALTERED TUFT CELL POPULATION OF HUMAN COLONIC EPITHELIUM IN INFLAMMATORY BOWEL DISEASES

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Introduction: The gastrointestinal tuft cells (TCs) have recently been revealed as parasite-sensing cells in rodents. TCs play a key role in initiation of a type-2 immune response and lead to parasite expulsion as well as orchestration of the post-inflammatory restoration of the mucosa (1). However, the role of TCs in human pathophysiological conditions is still an open question.
Aims and Methods: The aim of the present retrospective study was to test the hypothesis that the count of colonic TCs in patients with inflammatory bowel disease (IBD) is altered compared to healthy controls (ctrls).
Endoscopic colonic mucosal biopsies from 58 individuals were included in the study; 14 patients with Ulcerative Colitis (UC) in clinical and endoscopic remission (total Mayo score ≤ 2 and no sub score > 1), 9 with clinical and endoscopic active UC (total Mayo score > 2 and Mayo endoscopic sub score > 1), 10 with colonic Crohn's Disease (CD) in endoscopic and histological remission (1 had slight inflammation of the terminal ileum), 8 with endoscopically and histologically active colon CD, and 17 were endoscopically and histologically healthy and served as controls. The TCs were immunohistochemically identified and quantified using a primary antibody raised against cyclooxygenase-1 enzyme and counted by the first authors (TSRJ, SK and URF) independently and blinded to diagnose. Poisson's regression analysis was employed for statistics. Results were adjusted for size of biopsy, gender and age. Values are presented as mean ± SEM. A $p < 0.05$ was considered significant.
Results: On average controls had 104 ± 21 TCs/mm.^{2} Patients with active UC and UC in remission had a 57 % ($38 \pm 6/mm^2$, $p < 0.001$) and a 56 % ($38 \pm 7/mm^2$, $p < 0.001$) decrease in number of TCs compared to controls. Although less pronounced, patients with CD in remission also presented a decrease in TCs of 10 % ($64 \pm 19/mm^2$, $p < 0.001$). Conversely, patients with active CD demonstrated a 28% increase in numbers of TCs ($89 \pm 35/mm^2$, $p < 0.001$).
Patients with CD in remission had lower number of TCs compared to patients with active CD ($p < 0.001$). No difference was observed when comparing active UC to quiescent UC ($p = 0.621$).
Conclusion: To our knowledge, this study is the first to demonstrate that number of colonic mucosal TCs is altered in both UC and CD patients. The concentration of TCs is considerably higher in controls compared to active- and quiescent UC, while just slightly higher compared to quiescent CD. Compared to active CD, ctrls on average have a smaller concentration of TCs. Data suggest that colonic TCs may play a role in disease course and pathogenesis of IBD patients.
Disclosure: Nothing to disclose

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P0286 MICE OVEREXPRESSING MKL1 IN MACROPHAGES EXPERIENCE FULMINANT COLITIS

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Introduction: Mice deficient in the megakaryoblastic leukaemia 1 (*Mkl1*) gene are protected from dextran sulphate sodium (DSS)-induced colitis, implying that *Mkl1* plays a pathological role in inflammatory bowel disease (IBD). However, how *Mkl1* contributes to the development of colitis remains unknown. It was found that the expression of *Mkl1* is higher in the colonic lamina propria macrophages (LPMac) of DSS-treated mice than in those of control mice.
Aims and Methods: In this study, we established a transgenic mouse line that overexpresses human *MKL1* (MKL1-Tg) specifically in cells of the monocyte/

macrophage lineage, in order to investigate the potential role of macrophage *MKL1* in the pathogenesis of colitis.
Results: MKL1-Tg mice displayed spontaneous colon shortening and rectal prolapse. Scattered cryptitis was observed among the colons. Flow cytometric and quantitative RT-PCR analyses revealed that, in MKL1-Tg mice compared to littermate controls, the proportion of LPMac was decreased and had an altered inflammatory phenotype indicative of impaired anti-inflammatory properties. MKL1 also orchestrates macrophage polarization. Of note, overexpression of MKL1 impacts transcriptional activities of NF-κB p65 and PPARγ. Furthermore, MKL1-Tg mice had higher susceptibility to DSS-induced colitis, which was accompanied with prominent B cells infiltration and follicle formation.
Conclusion: Together, our observations indicated that MKL1 crucially contributes to the development of colitis via the regulation of the function of macrophages, suggesting that it may be a potential therapeutic target for the prevention of IBD.
Disclosure: Nothing to disclose

P0287 REGULATORY B CELLS CONTRIBUTE TO ALLEVIATE THE ACUTE COLITIS IN CD19$^{-/-}$MICE

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Introduction: Epidemiological studies showed that there was an inverse relationship between *Helicobacter pylori* (*H.pylori*) infection and the incidence of inflammatory Bowel Diseases (IBD). It was confirmed that CD4+CD25+Foxp3+Treg cells could protect mice from colitis. Our previous study showed that *H.pylori* infection induced the expansion of regulatory B cells (Breg) ahead of the Treg cells.
Aims and Methods: In this study, we investigated the effect of Breg cells on acute colitis induced by dextran sulphate sodium (DSS). SPF CD19$^{-/-}$mice were utilized. 1x10^{6}Breg or B cells or equal PBS were adoptive transferred to the CD19$^{-/-}$ mice via the tail vein. Twenty-four hours later, acute colitis was induced by 3% DSS for 7 days and PBS for 3 days.
Results: There was no significant difference in body weight changes between each colitis group. Adoptive transfer of Breg or B cells improved the survival rates effectively (100%, 83%, 50% for Breg+DSS, B+DSS, PBS+DSS, respectively). The colon length shortened significantly in colitis mice (PBS+DSS vs. PBS+PBS = 4.7 ± 0.16 vs. 7.7 ± 0.45, $p = 0.001$). Adoptive transfer of Breg cells recovered the colon length to a large extent when comparing to the B cells or PBS adoptive transfer groups (Breg+DSS vs. B+DSS = 6.4 ± 0.59 vs. 4.9 ± 0.7, $p = 0.004$; Breg+DSS vs. PBS+DSS = 6.4 ± 0.59 vs. 4.7 ± 0.16, $p = 0.005$; B+DSS vs. PBS+DSS = 4.9 ± 0.7 vs. 4.7 ± 0.16, $p = 0.683$). Colonic histopathology stained by HE showed that colonic inflammatory induced by DSS was alleviated by adoptive transfer of Breg and B cells, and Breg cells were more efficient than B cells. Treg cells in spleen expanded significantly in colitis mice (PBS+DSS vs. PBS+PBS = 14.1 ± 0.21 vs. 11.78 ± 0.64, $p = 0.036$), and adoptive transfer of Breg cells induced more Treg cells while B cells reduced Treg cells significantly (Breg+DSS vs. PBS+DSS = 17.43 ± 1.73 vs. 14.1 ± 0.21, $p = 0.008$; B+DSS vs. PBS+DSS = 11.3 ± 0.5 vs. 14.1 ± 0.21, $p = 0.039$; Breg+DSS vs. B+DSS = 17.43 ± 1.73 vs. 11.3 ± 0.5, $p < 0.001$). Foxp3 mRNA relative expression level in colon was higher in Breg cells adoptive transfer group than B cells ($p = 0.017$) or PBS groups ($p < 0.001$).
Conclusion: Rather than B cells, adoptive transfer of Breg cells induced CD4+CD25+Foxp3+Treg cells expansion and alleviated acute colitis induced by DSS significantly in CD19$^{-/-}$mice.
Disclosure: Nothing to disclose

P0288 IMPAIRED BUTYRATE INDUCED ANTI-INFLAMMATORY IMMUNE REGULATION IN LAMINA PROPRIA CELLS FROM PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Introduction: Modulation of the gut microbiota has emerged as a therapeutic option for patients with ulcerative colitis (UC), yet with modest effects. Microbial dysbiosis and reduced levels of short-chain fatty acids such as butyrate have been identified as key components of the disease and butyrate is known to have anti-inflammatory properties.
Aims and Methods: Here we aimed to determine and compare immunological effects of butyrate on lamina propria (LP) cells from UC patients with active disease and non-inflamed control (CTR) patients.
Duplicate sigmoidal biopsies were cultivated without (none) or with 1.6 mM butyrate (but) for 6h after which biopsies were collected for RNA purification. mRNA gene expression was analyzed using the Qiagen RT^2 Profiler PCR Arrays Antibacterial response and Innate and Adaptive Immune Responses with 84 genes per array, in total 135 unique genes. Logarithmic data were analyzed using principal component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA) with a cut off for Variable Importance for the Projection >1.2. Identified parameters were subject to univariate analysis and false discovery rate analysis and evaluated using Ingenuity Pathway Analysis (IPA). Gene expression data are presented as fold change (FC) of means on a $\log_2$ scale where $\log_2 FC = 1$ and -1 define a 2-fold increase and decrease, respectively.
Results: The study included 8 CTR patients (4 males, age 54 (24–84), median (range)) and 8 patients with UC (6 males, age 38 (32–74)) with a disease duration of 7 (<1–47) years. All UC patients had active disease with endoscopic Mayo score 2 (n = 7) or 1 (n = 1) and all CTR patients had Mayo score 0. Current treatment for UC patients was 5ASA (n = 5), 5ASA and thiopurines (n = 1), corticosteroids (n = 1) and no treatment (n = 1).
PCA analysis of mRNA expression without and with butyrate for UC and CTR revealed differential clustering. UC-none and UC-but were located at the lower and upper right quadrant, respectively, while CTR-none and CTR-but were located at the lower and upper left quadrant, respectively, with only minor overlap between the 4 groups. Highly discriminant and predictive OPLS-DA plots identified 29 genes for UC ($R2 = 0.94$, $Q2 = 0.86$) and 23 genes for CTR ($R2 = 0.90$, $Q2 = 0.71$) that were most regulated by butyrate. Of these genes, 11 were overlapping resulting in a combination of 41 genes used for pathway analysis. The top canonical pathway identified by IPA was "Neuroinflammation Signaling Pathway" (-log(p-value) 39, 27 associated genes) and z-scores of -2.117 and - 0.962 for CTR and UC, respectively, indicated a down regulation in the presence of butyrate for CTR but not for UC. Based on 23 of the 41 genes, IPA mapped 'Inflammatory response' as the top disease function ($p = 2.1 \times 10^{-28}$) and predicted that butyrate decreased the inflammatory response for CTR (z-score = -2.649) but not for UC (z-score = -1.308).
Using univariate analysis, for CTR patients 8 genes were down regulated ($\log_2 FC < -1$, $q < 0.05$; IL2, CXCL10, IL6, IL1a, CD40L, IL1R1, CCL2, FOXP3) and 1 was up regulated ($\log_2 FC > 1$, $q < 0.05$; BIRC3) by butyrate while, for UC patients, 2 genes were downregulated (IL2, XIAP) and 4 were upregulated (TLR5, NLRP3, STAT1, ICAM1) by butyrate.
Conclusion: Butyrate rapidly down regulates pro-inflammatory genes in LP cells from healthy controls but not from UC patients with active inflammation. These discrepancies may at least partly explain why anticipated anti-inflammatory effects of fecal transplantation or local butyrate induction are not always obtained.
Disclosure: Nothing to disclose

P0289 *IN VITRO* ASSESSMENT OF THE EFFECT OF MESENCHYMAL STEM CELL ORIGIN AND QUALITY ON MACROPHAGE POLARIZATION

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Introduction: Mesenchymal stem cell (MSC) have the potential to treat many autoimmune diseases including inflammatory bowel disease. Therapeutic benefit of MSC is due to inhibition of T cell proliferation and polarization of macrophage towards M2 phenotype. MSC derived from different tissues, donors and passages display different immune properties. Although most of MSC research are conducted on MSC derived from bone marrow, MSC of the best quality and greatest benefit have not been defined yet.
Aims and Methods: Our aim is to characterize the effect of MSCs -derived from different origins and passages- on macrophage. Here, we compared the ability of MSC derived from 2 origins [bone marrow (BM-MSC) and adipose tissue (AD-MSC)] and 2 qualities [early-passaged (p1) and late-passaged (p6) BM-MSC] to polarize macrophage towards M1 or M2 phenotype.
Method: We isolated adipose MSC from 10-week-old male C57BL/6 mice and expanded early and late passaged MSC. Then, chemokines and cytokines focused array was performed on the 3 types of cell. MSC were co-cultured with splenocytes for 3 days and after that CD206 and CD86 expression was evaluated by immunohistochemistry. The release of IL10, IL6 and TGF-β were evaluated by ELISA assay before and after co-culture.
Results: Pathway focused PCR array showed that the gene expression profiling of immunomodulatory cytokines and chemokines in MSC was largely different depending on the cell origins and cell qualities. There was a 3-fold increase in *Il6* expression, 36-fold increase in colony stimulating factor 2 (*Csf2*) and 21-fold increase in tumour necrosis factor receptor superfamily member 13b (*Tnfsf13b*) in AD-MSC versus BM-MSC. Late passaged cell decreased the expression of many immune regulatory gene like *Tgfβ2* and tumour necrosis factor receptor superfamily member 11B (*Tnfrsf11b)*. By co-culturing with splenocytes for 3 days, MSC of different qualities showed significantly different properties on regulating the expression of CD206 and CD86 on macrophage. Macrophages were polarized toward M2 phenotype with early-whether derived from adipose tissue or bone marrow- but not with late passaged cells. Cytokines assay showed that only AD-MSC secreted IL10 and that late passaged cell secreted lower level of both IL-6 and TGF-β.
Conclusion: Our data suggests that macrophage polarization by MSC is affected by the cell quality and that passaging of cell could impair its immunomodulatory function.
Disclosure: Nothing to disclose

P0290 DOES ASTHMA INCREASE THE RISK OF INFLAMMATORY BOWEL DISEASE? A META-ANALYSIS OF CASE-CONTROL AND COHORT STUDIES

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Introduction: There have been several studies that assessed the association between asthma and inflammatory bowel disease (IBD) including Crohn's disease (CD) and ulcerative colitis (UC). The positive association may be explained through the hygiene hypothesis, which postulates that a reduction in the frequency of infections contributes directly to the increase in the frequency of autoimmune and allergic diseases.
To provide a quantitative assessment of the association of asthma with subsequent IBD risk, we conducted a meta-analysis of observational studies.
Aims and Methods: We identified studies by searching the PubMed databases through February 2018 and by searching bibliographies of relevant articles. Included studies reported IBD as the primary outcome and evaluated asthma before diagnosed with IBD. We included case - control studies or cohort studies published as original articles; cross-sectional, ecological, and prevalence studies were excluded.
Results: A total of 7 observational studies were included in our meta-analysis. Asthma was associated with an increased risk of CD (summary OR 1.45, 95% CI: 1.30–1.61) and UC (summary OR 1.29, 95% CI: 1.02–1.64).
Conclusion: This meta-analysis demonstrates that asthma is associated with an increased risk of developing both CD and UC. Further prospective studies are required to confirm the validity of these observations.
Disclosure: Nothing to disclose

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P0291 THE PREVALENCE OF GASTROINTESTINAL CANCERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE - A DANISH NATIONWIDE COHORT STUDY

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Introduction: Inflammatory Bowel Disease (IBD), mainly represented by Crohn's Disease (CD) and Ulcerative Colitis (UC), is known to be associated with an elevated risk of gastrointestinal (GI) cancer. The pathogenesis is poorly understood, but risk factors seem to be longstanding disease as well as extensive disease and high degree of inflammation. However, the reported magnitude of the risk in IBD patients is still inconsistent and the long-term effects of newer treatment options on the development of cancer have not been investigated thoroughly.
Aims and Methods: To estimate the prevalence of GI cancer development in a cohort of adult IBD, we included all incident patients in the Danish National Patient Register (NPR) between 1997 and 2015, using International Classification of Disease (ICD) codes representing IBD. Minimum 2 diagnostic listings of UC or CD on separate dates were used to improve accuracy and stability of the IBD diagnosis. Patients with a mix of codes for UC and CD during the follow up period were identified as IBD-Unclassified (IBDU). All incident cancer, based on ICD codes, occurring after the index date were included from the national cancer register. Each IBD patient was matched for sex, age and place of residence to reference individuals of the Danish population. P-values for significance between the IBD cohort and reference individuals were calculated by chi-square test.
Results: We identified 35,910 IBD patients (UC = 24,103 (67.1%), CD = 9,740(27.1%) and IBDU = 2,067 (5.8%)) and 1,747,002 reference individuals in the NPR between 1997 and 2015. The median age at IBD diagnosis was 43 (IQR: 30–60). Overall, 4,295 (12.0%) of IBD patients were diagnosed with at least 1 cancer and 487 were diagnosed with 1 or more cancers. Among reference individuals, 174,251 (10.0%) were identified with 1 diagnostic listing of cancer and 20,724 with 2 or more. The overall prevalence of cancer was significantly higher in the IBD population ($p < 0.001$) compared to reference individuals. Characteristics of the study population are shown in table 1.
While colorectal cancer (CRC) was more frequently observed in IBDU (n = 31 (1.5%)) and UC patients (n = 235 (1.0%)) compared to CD (n = 85 (0.9%)), upper GI cancer (including small bowel cancer) was more common in CD patients (n = 72 (0.7%)) compared to UC (n = 111 (0.4%)) and IBDU patients (n = 10 (0.5%). In reference individuals, prevalence of upper GI cancer and CRC was 6,039 (0.4%) and 15,648 (0.9%), respectively and therefore similar to that of the overall IBD population ($p > 0.05$ for both comparisons). However, prevalence of CRC was significantly lower compared to IBDU patients ($p < 0.05$).
Conclusion: In a Danish nationwide cohort of IBD patients, overall cancer as well as neoplasms located to the small bowel, anus/anal canal, liver, bile ducts and pancreas were more prevalent compared to the reference individuals. There was a significant difference in the prevalence of colorectal cancer between reference individuals and IBDU patients, but not compared to the overall IBD cohort.
*[Table 1. Characteristics of study population. N (%) if not otherwise stated. * $p < 0.05$, † $p < 0.001$ compared to the reference population]*
Disclosure: This study was financed by a grant from Tillotts pharma.

P0292 NATURAL HISTORY OF ACUTE SEVERE ULCERATIVE COLITIS IN ELDERLY: A POPULATION-BASED STUDY

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Introduction: Acute severe attack of ulcerative colitis (ASUC) can occur in 12 to 25% of UC patients. This is a challenging and life threatening in elderly patients. Evolution of ASUC in late onset UC diagnosed after the age of 60 years is unknown.
Aims and Methods: The aim of this study was to describe clinical presentation, treatment and prognosis of ASUC in a cohort of late onset UC.
Patients and methods In a Northern France population-based cohort, we identified 472 patients aged >60 years at UC diagnosis ulcerative colitis (UC). These patients were followed for a median time of 6.2 years. Among these patients, those hospitalized with an ASUC according to the Truelove's criteria were analyzed. Clinical presentation, comorbidities (Charlson index), treatment and surgery needs as well as postoperative complication and mortality were recorded.
Results: 23 patients (5%) including 14 men were included. ASUC occurred at diagnosis in 12 patients (52%) and during the first year of follow-up in 19 patients (83%). The Charlson comorbidities score was ≥ 3 in 96% (n = 22) and ≥ 5 in 52% (n = 12) of the cases. First-line treatment was intravenous corticosteroid (64%, n = 14), colectomy (22%, n = 4) or exclusive artificial nutrition (24%, n = 5). No patient received second line medical treatment ciclosporin or infliximab. Among the 18 operated patients, median time between admission for severe acute colitis and intervention was 15 days (Q1 = 7, Q3 = 39). Surgery was a subtotal colectomy with double stomy in 13 cases, a partial colectomy in 3 cases, total colectomy in 1 case and a stomy alone in 1 case. Stoma were definitive in 69% (n = 9) of cases. 1 or more postoperative complications occurred in 6 patients (26%) i.e. renal insufficiency (n = 4), thromboembolic event (n = 4),

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	IBD	UC	CD	IBDU	Controls
Total	35,910	24,103 (67.1)	9,740 (27.1)	2,067 (5.8)	1,747,002
Sex, men	16,658 (46.4)	11,554 (47.9)	4,221 (43.3)	883 (42.7)	808,835 (46.3)
Median age at first IBD diagnosis (IQR)	43 (30–60)	46 (32–62)	38 (26–55)	39 (27–56)	–
Median age at first cancer diagnosis (IQR)	64 (48–74)	66 (52–75)	59 (40–70)	59 (40–71)	66 (52–76)
Any cancer	4,782 (13.3)†	3,177 (13.2) †	1,285 (13.2)†	320 (15.5)†	194,975 (11.2)
Upper GI cancer (excluding small bowel cancer)	116 (0.3)	65 (0.3)*	43 (0.4)	8 (0.4)	6039 (0.3)
Small bowel cancer	77 (0.2)†	46 (0.2) †	29 (0.3) †	2 (0.1)	367 (<0.0)
Colorectal cancer (CRC)	351 (1.0)	235 (1.0)	85 (0.9)	31 (1.5)*	15,648 (0.9)
Anal cancer	17 (<0.0)*	8 (<0.0)	9 (0.1)†	–	401 (<0.0)
Liver, bile ducts pancreatic cancers	161 (0.4)†	118 (0.5) †	31 (0.3)	12 (0.6)*	4567 (0.3)

septic shock (n = 2). 5 patients (22%) died, of which 4 after surgery, leading to a 3-month survival rate of 75% (IC95% [58–97]) (Figure 1).
Conclusion: In this population-based study conducted in the prebiotherapy era ASUC in elderly onset UC patient was rare but particularly severe requiring surgery in 74% of patients and life-threatening with a mortality rate close to 25% at 3 months. Management of these severe patients in referral centers is mandatory.
Disclosure: Nothing to disclose

P0294 SMOKING REMAINS A MAJOR CONTRIBUTOR TO THE BURDEN OF CROHN'S DISEASE IN IRELAND AND WARRANTS THE DEVELOPMENT OF A SPECIFIC TARGETED SMOKING CESSATION INTERVENTION

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Introduction: Approximately 15,000 people in Ireland have Crohn's disease (CD) and the incidence is increasing. Previous data suggest smokers are twice as likely to develop CD and active CD smokers have a higher risk of relapse, hospital admissions, steroid therapy and surgery. Despite this, many Irish CD patients continue to smoke perhaps due to lack of knowledge and awareness.
Aims and Methods: To determine current smoking rates and the impact of smoking on CD severity and to assess patient knowledge and awareness of the risks associated with smoking. Following ethical approval, a prospective case control study of Irish CD patients' and age and sex matched non IBD GI patient controls was undertaken. A self-assessment questionnaire was employed to assess smoking habits, basic demographics and education status overall as well as disease characteristics and awareness of the impact of smoking in the CD cohort. Groups were compared using a Chi^2-test, p of less than 0.05 were considered statistically significant and odd ratios were calculated where appropriate.
Results: To date 139 questionnaires have been returned, 56 from CD patients and 83 from Controls. The mean age was 47 years (range 19–80) and 62 (47%) were males. Disappointingly, 52% (n = 72) overall reported having ever smoked with similar rates in CD and Control patients, 57% (n = 32) and 48% (n = 40). Both duration (12.3 and 9.0 yrs) and pack quantity per day (0.6 and 0.5) were similar for CD and Controls. There was no difference in education level achieved with 22/70 (31%) vs. 17/66 (26%) having completed primary education only in smokers compared to non-smokers. However, CD patients were 1.8 times more likely to report being a current smoker compared to Controls, p = 0.3.
Within the CD cohort 52% (n = 30) had previous surgery. Smokers were 1.5 times more likely to have had IBD-related surgery although this did not reach statistical significance; 13/32 (41%) CD vs. 6/24 (25%) controls. HBI results were available for 35 (63%) CD patients. Current smokers reported higher HBIs 13 vs. 5, p = 0.01 (95% CI = 1.91–13.6). In fact, active smokers were twice as likely (80% vs. 37%) to have an elevated HBI > 7, RR = 2.2, p = 0.02. There was no difference in biologic use between the groups.
Only 41% (13/32) of our CD cohort thought smoking was a significant risk factor for IBD. While only 28% (9/32) thought smoking was a risk factor for surgery while just 25% (8/32) thought smoking cessation could significantly decrease the severity of their disease.
Conclusion: Disturbingly, smoking rates remain high in our Irish CD population, with a negative impact on disease severity and need for surgery. Surprisingly few CD patients were aware of the negative impacts of smoking and the potential benefit of cessation. Emphasizing an urgent need for a specific targeted smoking cessation intervention.
Disclosure: Nothing to disclose

P0295 OCULAR MANIFESTATIONS IN A TERTIARY IBD CENTER: BETTER TO KEEP AN EYE ON

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Introduction: Extra-intestinal manifestations (EIM) are common in inflammatory bowel disease (IBD) occurring in up to 50% of patients, while ocular manifestations are reported in 0.3% to 13.0% of the cases. Reported data, however, mostly rely on not recent population based studies. In fact, the few available prospective studies, suggest a much higher occurrence of ocular diseases, ranging from 29% to 71%.
Aims and Methods: The aim of the study was to assess the prevalence of ocular disease in a cohort of IBD patients followed in tertiary referral Italian center.
IBD patients followed at our center were consecutively enrolled in the study. Enrolled patients underwent ocular evaluation including assessment of visual acuity, examination of fundus oculi and anterior ocular segment as well as a measure of intraocular pressure, Schirmer's test and break up time test, when appropriate.
Results: A total of 193 IBD patients were enrolled in the study, 54.9% females and 45.1% males, 47.7% CD, 43.5% UC, and 8.8% indeterminate colitis, 35.7% of patients had a moderate-severe activity of disease, 39.4% were under active steroid therapy, 35.8% were under anti-TNFalpha and 64.3% were taking mesalamine.
Overall, any ocular disease was identified in 46.1% of enrolled patients, 17.1% CD and 23.8% UC and 5.2% IC. The most common ocular disease was dry eye (12.4%). At multivariate analysis use of mesalamine (OR 2.3, 95% CI 1.1–5.0), steroids (OR 3.6, 95% CI 1.1–11.8) and moderate-severe activity of disease (OR 5.1, 95% CI 2.3–11.1) were all correlated with an increased risk of ocular disease.
Conclusion: Ocular manifestations in IBD patients are more frequent than reported especially in referral center. Patients under treatment with mesalamine or steroids and with a moderate-severe disease activity might benefit of an ophthalmological evaluation.
Disclosure: Nothing to disclose

P0296 INTESTINAL AND EXTRA-INTESTINAL CANCER IN IBD PATIENTS ADMITTED TO AN ITALIAN TERTIARY CENTRE

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Introduction: Inflammatory bowel disease (IBD) patients are at higher risk to develop colon cancer. While the association between colorectal cancer and ulcerative colitis (UC) is well known, the risk for Crohn's disease (CD) is less defined. Similarly, little information exists on extra-intestinal tumors in different settings of patients.
Aims and Methods: The aim of the study was to assess occurrence of malignancies in IBD patients admitted to the hospital. All patients admitted for CD or UC to Policlinico "A. Gemelli" between 2000 and 2013 were identified using ICD-9-CM codes for IBD.
Occurrence of gastrointestinal or extra-intestinal cancer was assessed for every patient analyzing ICD9-CM codes. Demographic characteristics of admitted patients were also recorded.
Results: A total of 3467 patients were admitted for an IBD between 2000–2013, in particular 42.8% CD and 57.2% UC, 51.8% male and 48.2% female patients, with a median age at admission of 45.7 years. Repeated admissions for the same patient were excluded.
Occurrence of any type of cancer was 5.3%, without significant difference between intestinal and extra-intestinal location (2.8% versus 2.5%, respectively). Malignant tumors, at any site, were more frequent in UC than in CD (7.3% versus 2.7%, respectively; p < 0.01). Cancer occurrence was higher in men in comparison to women (6.1% versus 4.4%, respectively, p < 0.05).
Median age at admission was 44.0 years for patients without a diagnosis of tumor and 63.8 years for those with a diagnosis of cancer.
The occurrence of colon and rectal cancer was 1.7%, with 81% cases affecting UC patients.
The most frequent extra-intestinal malignancies were prostate cancer and myeloproliferative disorders. Colon and rectal cancer accounted for 59.8% of all gastrointestinal cancer.
Conclusion: About 5% of admitted IBD patients presented a cancer diagnosis. Higher cancer occurrence was observed in UC and in older patients, with a median age of about 60 years and more frequently in men. Colorectal cancer occurrence in UC was about 2%.
Disclosure: Nothing to disclose

P0297 LONG-TERM STABILITY OF SEROLOGICAL ANTIBODIES IN A POPULATION-BASED INCEPTION COHORT OF INFLAMMATORY BOWEL DISEASE - THE IBSEN STUDY

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Introduction: Serological biomarkers in inflammatory bowel disease (IBD) predicting complicated disease are warranted. Several microbial antibodies and auto-antibodies have been associated with IBD and especially ASCA and pANCA have been proposed as potential biomarkers. Studies have shown that their presence might vary over time thus their clinical impact is still discussed. Long term studies of ASCA and pANCA stability have not been performed in population-based cohorts.

Aims and Methods: The aim of the present study was to investigate potential change in antibody status over time by analysing a panel of relevant serum antibodies at 10 and 20 years after disease onset in a population-based inception cohort of IBD patients (the IBSEN cohort).

The IBSEN cohort is an inception cohort of patients diagnosed with IBD between 1990 and 1994. The patients have been followed prospectively for 20 years. At the 10 and 20 year follow-up visits, the following panel of antibodies was analyzed in serum: pANCA, ASCA IgA and ASCA IgG. All analyses were performed at Prometheus Laboratories Inc. (San Diego, CA). Changes in antibody status within individuals from 10 to 20 years were assessed using Wilcoxon signed ranks test.

Results: Sera were available from 342 and 272 UC patients and 159 and 135 CD patients at the 10 and 20 year follow-up, respectively. The proportions of patients positive for the analyzed antibodies at the 10 and 20 year follow-up are presented in table 1. As previously shown, ASCA was more prevalent in CD than UC and in complicated CD behavior vs. inflammatory CD behavior at the 10 year follow-up (1). On group level, this distribution was similar at the 20 year follow-up. For 228 UC patients and 113 CD patients, sera were available at both time points. The antibody status within individuals changed significantly for ASCA IgG for patients with both UC ($p<0.001$) and CD ($p<0.001$).

Conclusion: In a population-based inception cohort the status of pANCA and ASCA IgA remained stable from 10 to 20 year follow-up. The status of ASCA IgG on the other hand, changed significantly. These findings indicate that pANCA and ASCA IgA might be more useful biomarkers of disease phenotype and potential complications during follw-up.

[Proportions of patients testing positive for each antibody at 10 and 20 year follow-up (% of n 10 y/ % of n 20 y)]

	pANCA	ASCA IgA	ASCA IgG
UC whole group	54.7/ 54.0	9.9/8.8	9.1/ 8.5
Proctitis	42.9/ 44.0	5.4/ 8.0	7.1/ 8.0
Left sided colitis	58.6/ 56.3	3.0/ 4.6	6.1/ 6.9
Extensive colitis	57.9/ 56.3	15.0/ 11.9	9.0/ 9.6
CD whole group	33.3/ 42.2	38.4/ 35.6	37.1/ 34.1
Location			
Ileal	30/ 28.6	35.0/ 33.3	40.0/ 38.7
Colonic	45.7/ 52.8	14.3/ 19.4	17.1/ 19.4
Ileocolonic	32.5/ 41.0	49.4/ 43.6	42.9/ 39.7
Upper GI	42.9/ 33.3	28.6/ 50.0	42.9/ 16.7
Behavior			
Inflammatory	45.8/ 42.0	10.4/ 16.0	12.5/ 14.0
Stricturing	33.3/ 43.3	47.6/ 43.2	42.9/ 45.5
Penetrating	26.8/ 41.5	58.5/ 51.2	53.7/ 46.3
Perianal	16.7/ 31.3	66.7/ 62.5	61.1/ 62.5

Disclosure: Sera were analysed by Prometheus laboratories free of charge.

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P0298 INCIDENT CANCER IN INFLAMMATORY BOWEL DISEASE; CHARACTERIZATION AND RISK FACTORS IN A PROSPECTIVE MULTICENTER NESTED CASE-CONTROL IG-IBD STUDY AT 6 YEARS

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Introduction: Cancer risk in Inflammatory Bowel Disease (IBD) is still debated.

Aims and Methods: Primary end point was to characterize, in a prospective, multicenter, nested case-control study at 6 years (yrs), incident cases of cancer in IBD. Secondary end point was to evaluate risk factors for cancer overall, including clinical characteristics of IBD versus the use of thiopurines (IS) and/or anti-TNFs.From December 31st, 2011 to December 31st, 2017, all incident cases of cancer in IBD patients (pts) referring to 16 IG-IBD Units (≥2 visits/yr) were recorded. Each IBD pt with incident cancer was matched with 2 IBD pts with no cancer for: IBD type (Crohn's Disase, CD; Ulcerative Colitis, UC), gender, age (±5yrs). Statistical analysis: Data expressed as median (range). Wilcoxon, Chi-squared, Fisher's exact test, multivariate logistic regression analysis (OR [95%CI]).

Results: Incident cancer occurred in 403 IBD pts: 204 CD (CD-K), 199 UC (UC-K). The frequency of cancer was comparable between CD and UC (50.6% vs. 49.4%; $p>0.05$). In IBD, cancer ($n=403$) involved/included (n[%]) digestive system (129 [32%]), skin (60 [14.9%]: 27 NMSC, 31 melanoma, 2 others), urinary tract (39 [9.7%]), lung (28 [6.9%]), breast (22 [5.5%]), genital tract (26 [6.5%]), thyroid (8 [1.98%]), lymphoma (11 [2.72%] all in CD), small bowel cancers (SBC) (16 [3.9%]; 15 CD [7.3%], 1 UC ileal pouch [0.5%]), others (64 [15.9%]). The frequency of cancer was comparable between CD and UC considering (n[%]): digestive system (61 [30%] vs. 6 [34%]); skin (33 [16%] vs. 27 [13.5%]) lung (14 [6.8%] vs. 14 [7.0%]); breast (22 [10.7%] vs. 24 [12.1%]);genital tract (15 [7.3%] vs. 11 [5.5%]; $p>0.05$). Colorectal and urinary tract cancers were more frequent in UC vs CD (58 [29%] vs. 35 [17%]; $p<0.005$; 26 [13%] vs. 13 [6.3%]; $p=0.039$). Extracolonic cancers were more frequent in CD vs. UC (35/204 [17%] vs. 58/199 [29%]; $p<0.005$). Risk factors for any cancer considered in multivariate analysis: age (<40 vs. ≥40 yrs), IBD duration (<10 vs. ≥10 yrs), smoking (Yes/No;Y/N), ISS and/or anti-TNFs (Y/N), IBD-related surgery, UC extent (extensive vs distal; subtotal vs distal), CD pattern (B3 vs B1;B2 vs B1) perianal CD. Significant risk factors for any cancer in UC: UC-related surgery (4.63 [2.62–8.42]), extensive vs distal UC (1.73 [1.10–2.75]). No other risk factors identified in UC (OR 1.30 [0.74–2.39]; 0.92 [0.63–1.35]; 0.92 [0.55–1.52]; 0.84 [0.51–1.38]; 1.54 [0.95–2.51], respectively). In CD, perforating pattern was the only significant risk factor for cancer overall (OR 2.33 [1.33–4.11]), as no other risk factors were identified (OR 0.93 [0.59–1.48]; 0.98 [0.67–1,43]; 0.74 [0.51–1.07]; 1.31 [0.90–1.92]; 0.97 [0.62–1.51]; 1.25 [0.79–2.01]; 1.02 [0.65–1.60], respectively). The percentage of pts with penetrating CD was higher in CD-K vs CD-C (26% [54/204] vs 15% [63/408]; $p=0.0033$), when considering also inflammatory (34% [71/204] vs. 43% [178/ 408]) or fibrostricturing CD (39% [79/204] vs. 41% [167/408]). The percentage of pts with extensive UC was higher in UC-K vs. UC-C (51% [101/199] vs. 38% [152/398]; $p=0.0045$), when considering also distal (21% [43/199] vs. 33% [131/398]) or subtotal UC (28% [55/199] vs. 29% [114/398]). Second ($n=11$) or third incident cancer ($n=2$) occurred in 11 IBD pts.

Conclusion: In a prospective, multicenter, nested-case control study at 6 years, penetrating CD, extensive UC and UC-related surgery were significant risk factors for any incident cancer. Clinical characteristics of severity of IBD may increase the overall cancer risk. Lymphoma and SBC were associated with CD.The high frequency of second and third cancers further supports a higher cancer risk in subgroups of patients.

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Pharma, Zambon; S Renna. Lecture fees/Advisory Board: Abbvie,MSD, Takeda; A Orlando:. Lecture fees/consultant: Abbvie, Chiesi, MSD, Otsuka, Takeda, Sofar, Mundipharma, Consultant to: Abbvie, MSD, Takeda, Biogen, Hospira-Pfizer; Lecture fees: Abbvie, Pallone F: Lecture Fees: Zambon, Takeda. Alvisi P, Neri B, Ruffa A, Gesuale C, De Cristofari E, Romeo S, Calabrese E, Rossi A, Spina L, Rogai F: Notihing to disclose.

P0299 WHAT FACTORS CAN IMPROVE THE EXPERIENCE OF PATIENTS WITH CHRONIC HEALTH CARE? A SURVEY OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The experience of patients with health care has been related to important outcomes (1).

Aims and Methods: In this work we describe the perception of inflammatory bowel disease (IBD) patients on their experience with chronic health care in Spain through IEXPAC, a validated questionnaire, and the influence of demographic and health care-related factors.

The IEXPAC scale *("Instrument to Evaluate the EXperience of PAtients with Chronic diseases")* was developed and validated in Spain by health care professional and social organizations, experts in quality of health care and chronic patients (2,3). It is structured in 12 items with Likert responses from 'always' to 'never', yields an overall score from 0 (worst) to 10 (best experience), and allows identifying health care areas needing improvement. 3 sub-scores derive from the scale: A) productive interactions (items on patient-health care professionals relationship), B) self-care (on patients' ability to self-care) and C) new relational model (on the use of new technologies and contact with other patients). Consecutive IBD patients from 25 Spanish clinics completed the IEXPAC scale by pre-paid mail. Bivariate comparisons and a multivariate analysis were made to explore the association between scores and demographic and health care-related characteristics.

Results: 575 patients received the survey, 341 (59.3%) returned it (mean age 47 years, 48% women). Mean overall score was 5.9 (SD 2.0), sub-scores were: productive interactions: 7.7 (2.3); self-care: 6.9 (2.4); new relational model: 2.2 (2.3). Scores did not differ by age, sex or degree of education (except new relational model, better in younger and in those with higher education level). Experience score was better in patients followed-up by the same physicians (score 6.0 [1.9]) vs different physicians (5.0 [2.1], $p = 0.002$), if there was follow-up by a nurse (score 6.2 [2.1]) vs no follow-up by nurse (5.6 [1.8], $p < 0.001$) and in those with lower number of medicines ($p = 0.010$). Patients treated with subcutaneous/intravenous (SC/IV) drugs scored higher in the 'productive interactions' sub-score ($p = 0.052$). Multiple linear regression models (table) showed that being followed up by the same physician or by a nurse, and being treated with lower number of medicines or with SC/IV drugs were independently associated to better overall experience scores.

[Multivariate analysis. Variables associated to IEXPAC experience scores. Positive coefficients mean better experience (higher IEXPAC score)]

Conclusion: Through IEXPAC, IBD patients identified important factors that can improve their experience with health care, like having the same physician as reference in the clinic and being followed-up by a nurse. Lower number of treatments was also associated to better experience and treatment with SC/IV drugs to higher 'productive interactions' sub-score, maybe in relation to a more personalized care.

Disclosure: This study was funded by Merck Sharp & Dohme of Spain and endorsed by the Spanish association of patients with Crohn's disease and ulcerative colitis (ACCU). We thank the participant patients for providing this valuable information by completing the survey. Marta Mosquera, Nadia Soto, Berta Juliá and Luis Cea-Calvo are employees at Medical Affairs, Merck Sharp & Dohme of Spain

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P0300 PATIENT-REPORTED COMPLEMENTARY AND ALTERNATIVE MEDICINE USE IN IBD: 10 YEARS OF OBSERVATION AMONG PATIENTS INCLUDED IN A NATIONAL COHORT

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Introduction: Complementary and alternative medicines (CAM) may be defined as treatments that fall outside of conventional healthcare. Patients with IBD often turn to CAM, mainly without discussing it with their physician. We repetitively collect information on patient-reported CAM use between 2007 and 2016.

Aims and Methods: 1) to assess main categories of patient-reported CAM used by year, 2) to assess factors associated with CAM use in 2016.

The Swiss IBD cohort started in November 2006. At enrollment and on a yearly basis, patients were asked to complete self-reported questionnaires. CAM were collected using a list of previously identified CAM[1,2] and a free text option. Additional clinical and patient-reported data collected within the framework of the cohort was used to characterize CAM users. For descriptive purposes, we classified CAM using recommendations of the US National Center for Complementary and Integrative Health (NCCIH). Changes in life habits (e.g. diet and sportive activities) was taken as an additional category. Dietary and nutritional supplements were not assessed here. Multivariate logistic regressions were performed to search for factors associated with CAM use (i.e. $>= 1$ CAM reported from 2007–2016).

Results: 3334 patients were included since Nov 2006. Overall, CAM were used by 21.7% to 29.3% of patients over years. Types of CAM were natural products and biologically based therapies (range: 6.9% to 11.9%), change in life habits (6.2% to 11.2%), whole medical systems and traditional medicines (5.8% to 9.6%), mind-body interventions (3.2% to 7.7%), body-based interventions (3.5% to 6.9%) and energy therapies (1.9% to 4.6%). When looking to the history of CAM use by patients in 2016, we found that 41.9%/44.4% of CD/UC patients used $>= 1$ CAM. The most frequent CAM used by CD/UC patients were "change in life habits" (20.6%/18.7%), homeopathy (12.5%/14.5%) and acupuncture (9.2%/10.5%). No significant differences were observed regarding CAM use and type of diseases, except for bio-electromagnetic therapies (3.5% for UC, 1.9% for CD; $p = 0.010$). CAM use in CD was significantly higher among women ($OR = 1.9$; $p < 0.001$), French-speakers ($OR = 1.5$; $p = 0.002$) and patients with arthritis complications ($OR = 1.5$; $p = 0.001$) and lower among smokers, higher SF-36 mental scores, higher age at diagnostic and B1p disease behavior profiles. CAM use in UC was significantly higher among women ($OR = 2.3$; $p < 0.001$), patients with arthritis complications ($OR = 1.4$; $p = 0.017$) and aged 36 to 45, and lower with increased IBD QoL score.

Conclusion: CAM were assessed through patients self-report over time. CAM use varied between a fifth and a fourth of IBD patients during 10 years of data collection, without many changes among types of CAM. On average, 43% of patients reported a history of CAM use in 2016. Factors associated with CAM use differed between UC and CD. Some of them seemed to be linked to relieving articular and musculoskeletal pain or improving IBD-specific or mental QoL.

Abstract No: P0299

	Overall score		Productive interactions		Self-care		New relational model	
	Beta coefficient	p	Beta coefficient	p	Beta coefficient	p	Beta coefficient	p
Sex (women vs. men)	−0.250	0.322	−0.306	0.311	−0.253	0.415	−0.218	0.434
Age (per year of increment)	−0.002	0.852	−0.011	0.451	0.012	0.392	−0.012	0.374
Follow−up in a region different from home region (vs same region)	0.072	0.890	−0.341	0.578	0.103	0.872	0.382	0.508
Being affiliated to patients association (vs No)	−0.091	0.826	0.845	0.090	−0.166	0.744	−1.229	0.008
Number of specialists visited the last year (per unit of increment)	−0.100	0.151	−0.088	0.291	−0.096	0.260	−0.111	0.151
Being followed by the same physicians (vs different)	0.956	<0.001	1.216	<0.001	1.059	0.001	0.418	0.151
Being followed by a nurse (vs no nurse follow up)	0.876	0.001	0.893	0.006	0.691	0.037	1.135	<0.001
Having help from others for care (vs only self−care)	0.504	0.070	0.269	0.426	0.529	0.123	0.607	0.049
Number of different medicines (per unit of increment)	−0.175	0.008	−0.164	0.041	−0.179	0.028	−0.156	0.031
Being treated with SC/IV drugs (vs no SC/IV treatment)	0.272	0.304	0.751	0.018	0.204	0.531	−0.238	0.413
Educational level achieved (university or further)	0.087	0.625	−0.063	0.768	0.013	0.952	0.524	0.008

Disclosure: Nothing to disclose

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P0301 FECAL CALPROTECTIN MAY BE A SENSITIVE BIOMARKER IN ASSESMENT OF HISTOLOGIC DISEASE ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: In patients with ulcerative colitis (UC) histological remission leads to better outcome, whereas presence of histological inflammation in quiescent disease is risk factor of future relaps. Fecal calprotectin (FCP) turned to be good biomarker in assesment of endoscopic and clinical disease activity.

Aims and Methods: The aim was to explore the association of FCP with histologic disease activity

82 patients with UC from a single tertiary IBD Centre were enrolled in this prospective, observational study. Mayo endoscopic sub-score was used to evaluate an endoscopic activity. For the assessment of histological activity, Geboes's, Nancy's and Robart's score were used. Active (structural changes, the presence of polymorphonuclear leucocytes with cryptitis and crypt abscesses, and erosions or mucosal ulcers) and chronic inflammations were estimated. Histologic remission was defined by Geboes score < 3.1 or Nancy's index ≤ 1 or Robart's index < 6. Basal plasmocytosis, as a predictor of relapse, was described as well. Buhlmann rapid test was used to determine FCP using cut off level of 100 μg/g. Statistical analysis was carried out using SPSS 20.0 (Chicago, IL).

Results: 38% (31/82) of patients were in endoscopic remission while 33% (27/82) achieved histological remission. Statistically significant association was observed between FCP and histological indicators of active inflammation: a. structural changes $p = 0.001$, CI ± 8.58; b. presence of the presence of polymorphonuclear leucocytes with cryptitis and crypt abscesses $p < 0.001$, CI ± 10.61; c. presence of erosion and mucosal ulcers $p < 0.001$, CI ± 6.72, as well as with basal plasmocytosis ($p < 0.001$, CI ± 6.42). The association with chronic inflammation was not observed ($p = 0.002$, CI ± 9.37). The correlation was found between FCP and all 3 scores with the strongest for Nancy index ($p < 0.001$, $r = 0.538$- Spearman correlation). The correlation with Robarts score ($p < 0.001$, $r = 0.505$- Spearman correlation) or Geboes ($p < 0.001$, $r = 0.382$- Spearman correlation) were slightly lower.

Conclusion: Fecal calprotecin may be a good, sensitive, noninvasive biomarker in the assesment of histological disease activity and point out a forthcoming relaps. This association with validated histologic score may even enhance the significance of FCP in clinical practice in the future.

Disclosure: Nothing to disclose

P0303 THE EFFECT OF ARYLESTERASE AND PARAOXONASE-1 LEVELS ON ULCERATIVE COLITIS: A RANDOMISED CONTROLLED STUDY

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Introduction: This study aimed to investigate the relationship between ARE(Arylesterase) and PON-1(Paraoxonase-1) levels in ulcerative colitis (UC) patients and the difference in these levels in UC patients in comparison to the control group.

Aims and Methods: The study population consisted of 66 (73.3%) UC patients and 24 (26.7%) healthy individuals as the control group. The UC patients and the control group were compared in terms of PON-1 and ARE levels as oxidative stress markers. The UC patients were also grouped according to Mayo UC activity scores and the differences in their PON-1 and ARE levels were assessed.

Results: 37 (56.1%) of 66 UC patients included in the study were male and 29 (43.9%) were female. The mean age in the control group was 42.2 ± 12.8 years (age range: 17–66 years). Most of the patients in the ulcerative colitis (UC) group used a combination of oral and rectal mesalamine treatments (20 patients, 33.3%). Most of the patients in the UC group had left-sided colon involvement (30 patients 45.5%). The mean arylesterase (ARE) level in the UC group was 786.32 U/L; the mean ARE level in the control group was 919.56 U/L. The ARE level was higher in the control group than the UC group, and this difference was statistically significant ($p = 0.017$). The mean paraoxonase-1(PON-1) value in the UC group was 264.14 U/L; the mean PON-1 value in the control group was 316.64 U/L. This difference was not statistically significant ($p = 0.33$).

When analysed based on gender, there was no difference in PON-1 levels ($p = 0.23$) and ARE levels ($p = 0.98$) between males and females in the UC group When the Hb value was lower (equal and less than 10 mg/dl) and higher (higher than 10 mg/dl), the ARE value was statistically higher in the group with a high Hb value ($p = 0.016$). When assessed in terms of the Mayo Disease Activity Index (DAI) and Rachmilewitz Colonoscopic Activity (Group A:≤6 and 7≥ Group B) scores, no statistical difference was found between the ARE and PON-1 values for UC patients in Group A and Group B.

The ARE values of 66 UC patients were found to be negatively correlated with their white blood cell counts (r-29; $p = 0.03$). In our study, ARE and PON-1 values were positively correlated in the UC group ($r = 0.27$; $p = 0.026$). Correlations between ARE and albumin ($r = 0.27$; $p = 0.041$) and ferritin ($r = -0.302$, $p = 0.037$) were determined based on our data. There were no correlations between PON-1 and hs-CRP (High sensitive C reactive protein), sedimentation, Hb, B12 and ferritin in the UC group. In the linear regression model, the leukocyte levels ($p = 0.025$) and Mayo UC Scores ($p = 0.004$) were found to have an effect on the ARE levels. In addition, it was found that in linear regression model the hs- CRP ($p = 0.009$) levels were found to have an effect on PON-1 levels.

Conclusion: In conclusion, ARE values that denote oxidative capacity were found to be significantly lower in patients with UC than in healthy patients. The efficacy of PON-1, an antioxidative enzyme, in UC patients is unclear. The results of our analyses suggest that there may be a correlation between ARE and PON-1 values in UC patients. Thus, it might be possible to use ARE levels as indicators of oxidative stress in UC patients. There is a need for larger studies to demonstrate the correlation between UC activity and ARE and PON-1 levels. No correlation between PON-1 and ARE levels and the activity of UC patients was detected in our study.

[Table 1 ulcerative colitis and control groups in terms of paraoxonase-1, arylesterase, high sensitive CRP, hematolog]

	Ulcerative Colitis N:66	Control N:24	P
Paroxonase-1 ± (SD)	264.14 ± 193.39	316.64 ± 231.07	0.33
Arylesterase ± (SD)	786.33 ± 270.33	919.56 ± 208.5	0.017

Disclosure: Nothing to disclose

P0304 WHITE CELL COUNT (WCC) AND MEAN CORPUSCULAR VOLUME (MCV) AS SURROGATE MARKERS FOR THIOPURINE MONITORING IN INFLAMMATORY BOWEL DISEASE TREATMENT: A SINGLE CENTRE EXPERIENCE

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Introduction: Thiopurines (TPs) are commonly used in treatment of Inflammatory Bowel Disease (IBD). For Azathiopurine (AZA), optimal dosing is determined by patients' weight and commonly titrated to achieve target range of 2–2.5mg/kg. Levels of 6-thioguanine nucleotide (6-TGN), an active metabolite breakdown of thiopurines and 6-Methylmercaptopurine (6-MMP), an inactive metabolite, can be measured to check for efficacy and toxicity respectively, but this is not widely available due to cost and accessibility.
White cell count (WCC), lymphocyte count (LC) and mean corpuscular volume (MCV) have emerged as surrogate markers to monitor TP efficacy. Previous studies have suggested WCC $< 4x10^9$/L and MCV > 100fl correlate with 6-TGN level and with reduced risk of disease relapse.
Aims and Methods: The aim of our study is to assess these surrogate parameters in our patients on TPs. 200 IBD patients being treated with AZA were included in this retrospective, observational study. Data were obtained from our IBD database and review of medical notes. Recent WCC, LC and MCV were recorded, along with body weight, AZA dose and concomitant treatment with biologic therapy (mainly anti-TNF agents).
Disease activity index was assessed using the Harvey Bradshaw index (HBI) for Crohn's disease (CD) and partial Mayo score for ulcerative colitis (UC) at time of blood testing.
Results: There were 108 (54%) females and 92 (46%) males. Of the 200 patients, 144 (72%) were diagnosed with CD, 55 (27.5%) UC and 1 (0.5%) indeterminate colitis. 117 patients (58.5%) were on AZA monotherapy with 83 patients (41.5 %) on combination therapy with a biologic including anti-TNFs' (Infliximab, Adalimumab, Certrolizumab pegol, Golimumab) or Ustekinumab. The mean age for our study population was 49 (19 - 81). The mean WCC count was $6.81x10^9$/L (range 2.8–14.2). Mean LC was $2.86\ x10^9$/L (0.5 to 8.8) with mean MCV of 91.1 fl (78.4 to 104.3).
7/200 (3.5 %) patients had WCC $< 4x10^9$/L and 7/200 (3.5%) also had a MCV > 100fl. In the IBD AZA monotherapy group, 4/117 patients (3.4%) had leucopenia and the same number 4/117 (3.4%) had macrocytosis and only 1 patient (0.9%) had both leucopenia and macrocytosis. In patients on combination therapy, 3/83 (3.6%) had leucopenia and the same number of patients, 3/83 (3.6%), demonstrated macrocytosis. None in this group had both leucopenia and macrocytosis (***Table 1***).
The mean AZA dose to body weight in our study population was 1.7mg/kg. The mean HBI score was 2.9 and for partial MAYO score was 1.7.
Conclusion: A very small percentage of our study population had leucopenia, lymphopenia or macrocytosis suggesting that many may be sub-therapeutic. Notwithstanding this, the majority of patients were in clinical remission. There was no significant difference in these measured parameters between the AZA monotherapy or combination therapy groups. It is not clear how assiduous we should be in escalating TP dose to target MCV and WCC/ LC in order to maximise efficacy in IBD patients. Work is underway to correlate these surrogate markers with TP metabolites levels and disease activity indices.
[Table 1: Comparison *breakdown patients demonstrating leucopenia & macrocytosis blood picture in monotherapy & combination therapy treatment groups]*

	Total patients (n = 200)	Monotherapy (AZA) (n = 117)	Combination therapy (n = 83)
Leucopenia (WCC < 4 x 10^9/L)	7/200 (3.5%)	4/117 (3.4%)	3/83 (3.6%)
Macrocytosis (MCV > 100 fl)	7/200 (3.5%)	4/117 (3.4%)	3/83 (3.6%)
Both leucopenia and macrocytosis	1/200 (0.5%)	1/117 (0.9%)	0

Disclosure: Nothing to disclose

P0305 PLASMA REG3α CAN BE A USEFUL NON-INVASIVE BIOMARKER FOR DISEASE ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Current biomarkers including CRP and fecal calprotectin have limitations in disease activity monitoring of inflammatory bowel disease. Regenerating Family Member 3α (REG3α) is an antimicrobial C-type lectin protein which is excreted from Paneth cell to promote tissue regeneration and a promising biomarker for lower gut GVHD. We evaluate whether REG3α can be a useful blood-based biomarker for differential diagnosis and disease activity in patients with ulcerative colitis (UC).
Aims and Methods: The study group consisted of 32 patients with ulcerative colitis and 18 healthy controls. Patients with UC were further categorized according to clinical disease activity (Mayo Score) and endoscopic activity (Mayo Endoscopic Subscore, MES). Peripheral blood was collected on the day of sigmoidoscopy or colonoscopy. Plasma REG3α levels were measured using ELISA.
Results: Clinical activity of UC patients was remission (n = 12, 38%), mild (n = 11, 34%), and moderate-to-severe (n = 9, 28%), respectively. MES was 0 (n = 10, 31%), 1 (n = 9, 28%), 2 (n = 10, 31%), and 3 (n = 3, 9%), respectively. REG3α level of healthy controls and patients with UC was 7.06 ng/mL and 7.92 ng/mL, respectively, and the difference was not significant ($p = 0.120$). However, REG3α level was significantly correlated with MES ($p = 0.031$, Spearman coefficient 0.382), and clinical activity was not ($p = 0.066$, Spearman coefficient 0.329). When the cut-off level of plasma REG3α was 7.33 ng/mL, diagnostic accuracy for moderate-to-severe disease and MES ≥ 2 was (sensitivity 88.9%, specificity 47.8%) and (sensitivity 84.6%, specificity 52.6%), respectively. 2 patients were followed up, and it was observed that the REG3α also decreases when the clinical activity decreases.
Conclusion: Plasma REG3α is a useful blood-based biomarker for monitoring endoscopic activity in patients with ulcerative colitis. It can also be applied to inflammatory conditions of the intestine like Crohn's disease and celiac disease.
Disclosure: Nothing to disclose

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P0306 REAL-TIME BIOLOGIC DRUG MONITORING USING BREATH IN INFLAMMATORY BOWEL DISEASE (IBD) - EARLY RESULTS

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Introduction: In recent years, biological drug infusions have had a significant impact on the management of inflammatory bowel disease (IBD); covering Crohńs disease (CD) and ulcerative colitis (UC). These treatments have led to improved quality of life, fewer hospital visits and fewer side-effects from prolonged corticosteroids use. Nonetheless, due to the nature of biological treatment, there is the risk of infusion-related (type 1) allergic reaction, which can be unpredictable. Therapeutic drug monitoring (TDM) traditionally involves the measurement of drug concentrations in blood. Where there is a defined relationship between drug concentration and clinical effect, TDM can be used to predict patient response and to titrate the biologics to maximise therapeutic benefit. However, blood tests are invasive and not available immediately, thereby delaying clinical decision-making. This study investigates whether breath analysis, using gas chromatography ion-mobility spectrometry (GC-IMS), has the potential to provide a rapid, real-time and non-invasive method of TDM for IBD drug monitoring.
Aims and Methods: The aim of this pilot study is to identify changes in exhaled volatile organic compounds (VOCs) that relate directly to the infusion of biologics. 26 established IBD subjects (13 CD, 13 UC) were recruited at University Hospitals Coventry and Warwickshire (UHCW). Patients received either Vedolizumab or Infliximab, administered as an intravenous (IV) infusion. 4 exhaled breath samples were collected, per patient, at different time intervals throughout the infusion: baseline (t = 0); 15 minutes after starting the infusion (t = 15), 30 minutes after starting the infusion (t = 30); and 20 minutes after finishing the infusion (t = 50/80), depending on the duration of the treatment. Tidal breath samples were captured directly and analysed by GC-IMS (G.A.S. BreathSpec, Dortmund, Germany). Only 4 seconds of exhaled breath are required per sample and measurement results are available in less than 10 minutes.
Results: Mean SCAI and HBI scores were 2.6 and 3.2 for UC and CD patients, respectively. This suggests patients were in remission and that the changes in compound intensities do not relate to disease activity. Data analysis was conducted using G.A.S. processing tools to analyse intensity peaks from subjects with CD and UC, receiving Infliximab or Vedolizumab. 10 peaks of interest were identified, based on intensity changes between the baseline (t = 0) and t = 15 or t = 30 measurements. Using G.A.S. library search software, we were able to identify some of the compounds associated with these peaks, by referencing gas chromatographic retention times and ion mobility drift times in a NIST database. VOC analysis indicates that a compound, identified as dimethyl

sulphide, increased above baseline in both Infliximab and Vedolizumab subjects by 110% and 63%, respectively. For those receiving Vedolizumab (UC subjects), there was an increase of pentanoic acid by 24%. Similarly for those receiving Infliximab (CD subjects), an additional compound (butanoic acid) increased by 39%.

Conclusion: The abundance of certain compounds were observed to increase within the first 15 minutes of a biologic infusion; dimethyl sulphide seems to be a common compound to both Infliximab and Vedoluzimab. The recognised trends are expected to become more pronounced by increasing the number of recruited subjects. Next steps would be to correlate with serum levels at similar times. Based on these early findings, BreathSpec GC-IMS offers the potential of a rapid, real-time method of TDM for IBD patients receiving biological therapy.

Disclosure: Nothing to disclose

P0307 INCIDENCE AND NATURAL HISTORY OF INFLAMMATORY BOWEL DISEASE DIAGNOSED IN COLORECTAL CANCER SCREENING

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Introduction: Inflammatory bowel diseases (IBD) are chronic illness with relevant social impact. Since the great part of data are published by tertiary centers, the real burden of IBD could be not completely defined, both in terms of epidemiology and natural history. We describe the data of a subpopulation of patients with IBD, unaware of it and asymptomatic, incidentally diagnosed in a colorectal cancer (CRC) screening program.

Aims and Methods: We have prospectically evaluated a court of people aged 50–74 undergoing screening colonoscopy after a positive faecal immunological (FIT) test, from November 2011 to March 2018. The screening program is still ongoing, and is focused to early diagnosis and prevention of colorectal cancer. Since then, 4490 patient out of 4714 FIT positive have been evaluated with colonoscopy, while 224 (4.75%) refused further examinations. Patients with known CRC or IBD are excluded. Data are prospectically collected, regarding to CRC, advanced adenoma, polyps and IBD incidence. Patients identified as IBD were then followed in our tertiary center.

Results: Out of 4,490 patients evaluated with colonoscopy, 257 (5.72%) needed virtual colonoscopy to complete the examination. Colorectal cancer has been diagnosed in 186 patients (4.14%), 1 or more adenoma in 1532 patients (34.12%). 21 patients (0.46%) had a diagnosis of IBD (7 F, 14 M, mean age 64.6 years, range: 53–76), namely one Crohn's disease (CD) and 20 Ulcerative colitis (UC).

All patients are currently followed in our tertiary center, with a mean follow-up of 22 months. All UC patients are satisfactory treated with mesalazine. The only patient with CD is treated with azathioprine. Up to now, no patient had extra-intestinal manifestations, nor need for surgery.

Conclusion: There is a consistent percentage of persons with IBD that are not known as affected. There is space for improvement in diagnosis and treatment. Further studies are needed to better understand the real incidence of this condition, and the subsequent evolution of the disease in this group of patients.

Disclosure: Nothing to disclose

P0308 THE IMPACT OF TOTAL AND FREE ANTI-DRUG ANTIBODIES ON THE LONG-TERM CLINICAL RESPONSE TO INFLIXIMAB THERAPY

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Introduction: When performed, the monitoring of ADA is generally restricted to the detection of free ADA (fADA) at the trough, using drug-sensitive ADA assays that do not allow the detection of ADA in complex with the drug (IC). Free ADA may underestimate the frequency of ADA-positive patients. Drug-tolerant ADA assays, based on IC dissociation, are available for routine detection of total ADA (tADA), free and in complex with the drug. The relevance of measuring tADA in daily clinical practice remains unclear.

Aims and Methods: The aim of this study is to evaluate the impact of fADA and tADA on the long-term clinical response to infliximab (IFX) therapy. We conducted a prospective observational study of adult IBD patients on IFX maintenance therapy recruited in 2012–2013 and followed until November 2017. IFX levels, fADA and tADA titters were assessed at trough by an enzyme linked immunosorbent assay (ELISA) (fADA and tADA at baseline and fADA at least at every 6 months). Disease activity (symptoms, laboratory markers, endoscopy and imaging), infusion reactions (IR) and therapy adjustments were recorded. The protocol was approved by the local ethics committee.

Results: 20 patients were included (15 Crohn's disease; 5 ulcerative colitis) who were receiving the standard (n = 16) or an intensified (n = 4) IFX regimen, for a median (IQR) duration of 3.4 (3.8) years. Median (IQR) age at inclusion was 40 (15) years. Patients were followed for a median (IQR) of 3.6 (2.3) years.

At baseline, 35% (n = 7) of patients tested ADA+ in both ADA assays (tADA+/fADA+), 30% (n = 6) although negatives in the drug sensitive ADA assay, tested positive in the drug tolerant assay (tADA+/fADA-), and 35% (n = 7) tested negative in both ADA assays (tADA-/fADA-). Clinical remission (CR) rates and median IFX trough levels were higher in fADA-/tADA- group (CR 100%; median IFX 4.5 ug/ml) compared to the tADA+/fADA- group (CR 17%; IFX 1 ug/ml) and to the tADA+/fADA+ (CR 29%, median IFX 0 ug/mL). Drug dose regimens at baseline were similar between the 3 ADA groups. A higher proportion of patients were receiving concomitant immunosuppression in fADA-/tADA- group (100%) compared to tADA+/fADA- (83%) and fADA+/tADA+ (29%) groups.

During follow-up, all patients in the fADA-/tADA- group remained in CR and none became fADA+. IFX dosing was reduced in 5 of the 7 cases. Conversely, in tADA+/fADA+ group, 2 patients underwent IFX intensification without response and IFX was switched or stopped in all cases. In the tADA+/fADA- group only one patient remained in CR without therapy adjustments, 3 patients switched to adalimumab and 2 patients had IFX intensification with increase in drug levels. Only 1 of the 6 tADA+/fADA- became fADA+ over time. IR occurred exclusively in patients with ADA, being more frequent in the tADA+/fADA+ group when compared with tADA+/fADA- group (57% vs. 17%).

Conclusion: Drug-tolerant ADA assays allow us to identify an additional proportion of ADA+ patients. Compared to tADA-/fADA-, tADA+/fADA- patients had lower IFX levels, lower CR rates and more frequently needed switch or IFX intensification. Responses to IFX intensification were overall more favourable in this group than in the tADA+/fADA+ group. Only a minority of tADA+/fADA- patients became fADA+. Larger studies are warranted to confirm these results and determine the clinical benefit of including tADA assessments, to help guide therapeutic decisions, in routine clinical practice.

Disclosure: The present study has been presented as best poster oral presentation in the 2018 national meeting of the Portuguese inflammatory bowel disease study group. This project also received the 2012 research grant of the District Hospitals Gastroenterology Nucleus. The authors disclose no other conflict of interest.

P0309 CHROMOENDOSCOPY IS SUPERIOR TO WHITE LIGHT ENDOSCOPY FOR THE DETECTION OF ADVANCED COLONIC NEOPLASIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Although recent guidelines recommend chromoendoscopy (CE) as a method of choice for neoplasia surveillance in inflammatory bowel disease (IBD), there is still controversy regarding the utility of this technique in clinical practice.

Aims and Methods: The aims of this study were to compare the accuracy of CE and white light endoscopy (WLE) for the detection of overall neoplasia and advanced neoplasia in patients with IBD. Patients who underwent surveillance colonoscopy were identified from a single institution IBD database from 1999 to 2017. Patients with prior history of colon cancer or total colectomy were excluded. CE procedures were compared with their respective WLE controls in a paired comparison and the frequency of all neoplasia, advanced neoplasia and serrated neoplasia was assessed for both targeted and random biopsies. Demographic and clinical data was obtained from review of medical records.

Results: Total 315 procedure performed in 106 individuals were identified over a median follow up 3 years (median 3 colonoscopy/ patients). Among them, 290 procedures performed in 98 individuals were finally included in the analysis. The median age was 56 years (20–87), 55.1% were male, 69.4% had UC and 11.2% had PSC. CE and WLE were performed in 159 and 131 episodes, respectively. CE detected neoplasia in 40.9% of colonoscopies vs. 23.7% with WLE ($p = 0.02$). In addition, CE detected more advanced neoplasia (18.2% vs. 6.1%, $p = 0.002$) and more serrated lesions (14.5% vs. 6.1%, $p = 0.02$). Significantly fewer samples were obtained per procedure with CE (14.9 ± 9.7 vs. 20.9 ± 11.1, $p < 0.01$). Cancer was diagnosed in 2 cases, 1 detected by CE and the other 1 after colectomy.

Conclusion: CE has a higher detection rate than WLE for conventional neoplasia, advanced neoplasia and serrated neoplasia in patients with IBD under surveillance. Considering that significantly fewer biopsies are required, CE may be both more accurate and more cost-effective compared with WLE.

[Table 1. Characteristics of neoplastic lesions detected by chromoendoscopy and whitelight endoscopy]

	Chromoendoscopy (n = 159)	White light Endoscopy (n = 131)	p
Neoplasia per procedure	65 (40.9%)	31 (23.6%)	0.020
Advanced neoplasia per procedure	29 (18.2%)	8 (6.1%)	0.002
Serrated neoplasia per procedure	23 (14.5%)	8 (6.1%)	0.022
Targeted biopsy (mean ± SD)	213 (1.3 ± 1.2)	89 (0.7 ± 1.0)	< 0.001
Neoplasia per targeted biopsy	88	38	0.819
Random biopsy (mean ± SD)	2143 (13.7 ± 9.3)	2630 (20.2 ± 10.6)	< 0.001
Neoplasia per random biopsy	4	5	0.490

Disclosure: Nothing to disclose

P0310 A CLEAR LOOK INTO THE BOWEL WITHOUT CLEANING IT - SIMULTANEOUS PET/MRI ENTEROGRAPHY (18F-FDG) FOR MONITORING INFLAMMATORY ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS - A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: The combination of positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) with magnetic resonance imaging (MRI) as integrated PET/MR enterography in one examination is a new cutting-edge technology for the non-invasive assessment of the inflammatory activity in ulcerative colitis (UC). Regarding the diagnostic goldstandard procedure ileocolonoscopy beside the risk of injury especially the bowel purgation is rated most bothersome.
Aims and Methods: This study's aim was to evaluate whether the inflammatory activity in patients with UC can be detected and accurately quantified by PET/MRI with and without bowel purgation. Patients were randomized to simultaneous PET/MRI (index test) with or without bowel purgation 24h before ileocolonoscopy (reference standard). In every patient the maximum standardized uptake value ratio gut/liver (SUVQuot), an MRI index and an endoscopy index (EI; rated by 2 independent gastroenterologists) were calculated for every segment (ileum, caecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum). Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. Furthermore, receiver operating characteristic (ROC) curves for each colon segment were calculated to determine diagnostic accuracy of PET/MRI for the 2 modes of bowel purgation.
Results: $N = 53$ patients were included in the study. Ten patients were included for protocol optimization and 43 were randomized. Three patients were dropouts (two due to activity of disease other than UC, one refused endoscopy). Therefore, 19 patients (mean age = 42.4 years (SD = 11.71), 11 female (57.9%), mean time since diagnosis = 13.42 years) were randomized to PET/MRI with bowel purgation and 21 patients (mean age = 43.2 years (SD = 12.7), 14 female (66.7%), mean time since diagnosis 12 years) to PET/MRI without bowel purgation. Sociodemographic and clinical characteristics did not differ between the groups. SUVQuot and EI correlated significantly for patients without bowel purgation (r = .53, p = .015) but not for those with bowel purgation (r = .46, p = .063). Overall sensitivity, specificity, positive predictive value, negative predictive value, and accuracy using ileocolonoscopy as reference standard are shown in table 1. ROC analyses for each bowel segment show that the diagnostic accuracy of PET was better for patients without bowel purgation (AUC rectum = .87, p = .03; AUC sigmoid colon = .91, $p < .01$; AUC descending colon = .93, $p < .01$; AUC transverse colon = 1, $p < .001$; AUC ascending colon = .85, $p < .01$; AUC caecum = .77, *n.s.*) than for patients with bowel purgation (AUC rectum = .90, p = .03; AUC sigmoid colon = .76, *n.s.*; AUC descending colon = .74, *n.s.*; AUC transverse colon = .82, p = .02; AUC ascending colon = .63, *n.s.*; AUC caecum = .47, *n.s.*).
Conclusion: The inflammatory activity of UC can be detected and quantified by PET/MRI in patients who did not undergo bowel purgation prior to examination. PET/MRI might serve as a valuable complement for goldstandard ileocolonoscopy to extend the variety of non-invasive diagnostic tools in UC especially when bowel purgation is not applicable.
[Table 1. Testing overall sensitivity, specificity, PPV, NPV, and accuracy using ileocolonoscopy as reference standard]

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
PET with bowel purgation (n = 131 evaluated segments in 19 patients)	87.70	59.46	62.50	86.27	71.76
	81.03	89.89	83.93	87.91	86.39
PET without bowel purgation (n = 147 evaluated segments in 21 patients)					
MRI with bowel purgation (n = 131 evaluated segments in 19 patients)	87.72	87.84	84.75	90.28	87.79
MRI without bowel purgation (n = 147 evaluated segments in 21 patients)	89.67	82.00	76.47	92.41	85.03

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P0311 FECAL BIOMARKERS COMPARED TO MAGNETIC RESONANCE IMAGING USING THE MARIA AND CLERMONT SCORES FOR MONITORING INFLAMMATORY ACTIVITY IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Magnetic resonance imaging (MRI) with the Magnetic Resonance Index of Activity (MaRIA) and the Clermont score as validated MRI activity indices is the gold standard to diagnose and monitor small bowel Crohn's disease (CD). However, noninvasive fecal biomarkers like calprotectin (CAL) and lactoferrin (LF) are increasingly popular and used in all-day patient care and have been evaluated regarding their capacity to differentiate and monitor disease activity in inflammatory bowel disease (IBD).
Aims and Methods: This study's aim was to compare the performance of fecal biomarkers and MRI for monitoring inflammatory activity in patients with CD. Fecal samples were collected to determine LF, CAL, PMN-elastasis (PMN-e), S100 calcium-binding protein A12 (S100A12), and Eosinophil-derived Neurotoxin (EDN) by enzyme immunoassay (EIA). In every patient a MRI was performed, MaRIA and the Clermont score were calculated, and standard cut-offs were applied by two independent experienced radiologists. Receiver operating characteristic (ROC) curves for each fecal biomarker using MaRIA and Clermont score as reference standard were calculated to determine sensitivity, specificity, and accuracy using optimized cut-offs.
Results: $N = 50$ patients with CD (mean age = 43.1 years ($SD = 13.42$), 32 female (64%), mean time since diagnosis = 13.8 years) were included in the study. According the MaRia score n = 41 patients and according to the Clermont score n = 42 patients showed signs of active inflammation. Mean levels for patients with active/inactive inflammation were 12.43/1.90(μg/g) in LF, 224.86/151.17(μg/g) in CAL, 0.17/0.09(μg/g) in PMN-e, 64.91/79.09(μg/g) in S100A12 and 1.4/0.47(μg/g) in EDN. Fecal LF, CAL and EDN were significantly

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	MaRIA				Clermont			
	AUC (p)	Optimized cut-off	Sensitivity	Specificity	AUC (p)	Optimized cut-off	Sensitivity	Specificity
EDN	76 (n.s.)	–	–		81 (0.043)	.27	78.6	75
LF	83 (.016)	5.49	58.5	1	82 (0.035)	5.49	59.5	1
PMN-e	70 (n.s.)	–	–		71 (n.s.)	–	–	–
S100A12	43 (n.s.)	–	–		53 (n.s.)	–	–	–
CAL	71 (n.s.)	–	–		86 (0.017)	195.04	79.4	1

correlated to the Clermont score, however, only LF was correlated to the MaRIA score. Using optimized cut-offs, EDN, LF, and CAL were able to distinguish between active and inactive CD (see table 1).

[Table 1. Testing sensitivity, specificity, and accuracy using optimized cut-offs for MaRIA and Clermont score as reference standard]

Conclusion: These results support the utility of fecal biomarkers for detecting active inflammation in patients with CD.

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P0312 ENDOSCOPIC FOLLOW-UP ALLOWS GOOD CONTROL OF COLORECTAL CANCER INCIDENCE IN IBD PATIENTS WITH LOW AND HIGH-GRADE DYSPLASIA: A FRENCH MULTI-CENTRIC PROSPECTIVE COHORT

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Introduction: Patients with inflammatory bowel disease (IBD) are at high risk of colorectal cancer (CRC). Today American and European guidelines recommend surveillance colonoscopy rather than colectomy after complete removal of endoscopically resectable dysplastic lesions using chromoendoscopy.[1,2] However very few prospective data exist to evaluate the application of these recommendations and patient outcome. Moreover, the endoscopic technics that should be used for lesion resection is not well defined.

Aims and Methods: Describe within a multi-centric prospective cohort the management and follow-up of dysplasia in IBD patients.

Were included all patients with an Ulcerative Colitis (UC) or a Crohn's Disease (CD) with endoscopical remission (Mayo score < 2 for UC and the absence of visible ulceration for CD) that were eligible to prospective endoscopic follow-up with a diagnosis of dysplasia histologically proven within the previously diseased colonic part in 14 French departments of Gastroenterology since 2004. Other CRC risk factors, IBD treatment, relapse of dysplasia, surgery, endoscopic procedure and histological results were assessed all along the study.

Results: From September 2013 to November 2017, 60 patients were included among 14 centers. 43 patients had UC (71.7%), and 17 patients had CD (28.3%). The median follow-up time from the first diagnosis of dysplasia was of 10 years. The median follow-up time with prospective evaluation was of 1.6 year. The mean disease duration at diagnosis of the first dysplasia was 18.3 years +/- 9.9.

52 patients were initially diagnosed with an adenomatous lesion with low-grade dysplasia (LGD; 86.7%), 6 with an adenomatous lesion with high-grade dysplasia (HGD; 0.1%) and 1 CD patient had a serrated polyp with low-grade dysplasia.

18 patients (30%) presented a new area of dysplasia during the follow-up, 15/52 patients with LGD (28.8%) and 3/6 patients with HGD (50%). 2 patients (3.3%) developed a localized colorectal cancer.

19 patients underwent a colorectal surgery (31.7%), with 6 partial colectomies (10%), 8 total colectomies with ileorectal anastomosis (13.3%) and 5 total colectomies with ileoanal anastomosis (8.3%). The absence of surgery was not associated with a higher risk of relapse (HR:1.03; IC95% {0.2618–4.059}). A history of primary sclerosing cholangitis was the only risk factor associated with the decision to have surgery (OR: 6.96; IC95 {1.21; 40.09}). 8 patients presented a polyp associated with dysplastic adjacent mucosa. Among them 4 patients underwent surgery (50%). The 4 endoscopically-treated patients did not present any CRC after a minimum of 7 months of follow-up (median of follow-up: 8.5 months and 5 to 12 endoscopies).

Chromoendoscopy was used in 66.7% of patient (40/60). Regarding endoscopic treatment, the most frequent technic of resection was piecemeal resection (41/60; 68.3%) vs. mucosal resection (16/60; 26.7%) and submucosal resection (3/60; 5%). Resections were assessed macroscopically as complete in 76.7% of the case (46/60). 42% (6/14) with a macroscopically partial resection presented a newly diagnosed dysplasia at a different site (13 LGD, 1 HGD), vs. 28.3% of patient with a complete resection (13/46).

Conclusion: In accordance with the latest guidelines, endoscopic treatment and follow-up is the main modality of management of dysplastic lesions in IBD patient in this cohort both for HGD and LGD with reassuring results regarding cancer occurrence. The use of chromoendoscopy in the follow-up of IBD is insufficient.

Disclosure: The study was supported by Abbvie.

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P0313 QUESTIONING CONSENSUS IN CROHN'S DISEASE: CT AND MR PERIANAL EXTENSION HAS MINIMAL DIAGNOSTIC YIELD AND INCURS ADDITIONAL RADIATION EXPOSURE

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Introduction: To assess the relevance of including perianal region in routine CT/MR enterography for detection of subclinical perianal disease in Crohn's disease (CD), according to recent consensus recommendations.

Aims and Methods: Identification of patients undergoing enterography. Selection of examinations performed with perianal extension in patients with CD. Montreal classification with identification of perianal disease. Evaluation of enterographies for signs of perianal disease, blinded to Montreal classification. Statistics: Kappa concordance test ($p < 0.05$). Radiation increase estimation due to perianal extension, in a Siemens Somaton® 16 CT equipment with filtered back projection (FBP) reconstruction.

Results: 259 patients underwent 325 enterographies, 135 having CD (161 CT, 39 MR, mean 2 examinations/patient). Among CD patients, 24 had clinically apparent perianal disease at the time of first imaging examination. Extended enterographies showed perianal disease in 26 patients with CD, with an additional diagnosis of only 2 cases. The agreement between clinical and radiological detection of perianal disease was $24/26 = 92.3\%$ (Kappa 0.9, $p = 0.000$). The *number-needed-to-detect* perianal disease in the population with CD was 62.5 examinations. The estimated additional radiation associated with perianal extension in CT enterography was 15–18% (dose length product (DLP)).

Conclusion: The extension of enterography to the perianal region has not shown to be superior to clinical evaluation for detection of perianal disease in CD. The consensus recommendation may be prudent only for MR enterography, since CT enterography incurs a non-negligible added radiation and exposure of radiosensitive organs, that otherwise would not be covered.

Disclosure: Nothing to disclose

P0314 PHOTOPROTECTIVE IBD EDUCATIONAL VIDEO ANIMATION ("TAGG SUNCARE VIDEO") IS PREFERRED BY PATIENTS AND IS AN EFFECTIVE WAY OF IMPROVING PATIENT KNOWLEDGE AND AWARENESS

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Introduction: Inflammatory Bowel Disease (IBD) patients are at risk of Malignant Melanoma (MM) and non-melanoma skin cancer (NMSC). Simple photo protective measures and early detection through increased vigilance can reduce the incidence and the burden of disease. Traditional educational methodologies have had limited impact and newer valided educational tools are needed.

Aims and Methods: To assess the impact and validate a novel IBD educational video animation on skin cancer awareness in a cohort of Irish IBD subjects.

Prospective non-randomised educational interventional study using our novel, recently trialled IBD tailored educational animation video based on the Irish Cancer Society 'Sunsmart Guidelines'.

Self assessment questionnaires were employed to collect patient demographics and assess sun smart behaviour awareness at 2 sequential IBD clinics, one where the video was played in the outpatient waiting area (exposed group) and another without any video (control group). The questionnaire included sections on what factor suncream to wear and how often to re-apply it, when to stay in the shade, and how to perform a self skin check including what suspicious changes to look for in a suspicious mole. Results were compared among groups using a Chi Squared test ($p < 0.05$ was considered significant) and an odds ratio (OR) calculated where appropriate.

Results: In all, 84 completed questionnaires were returned, 40 and 44 from the exposed and control groups respectively. Mean age 44 years (Range 16–79), 50 (60%) were women, 46 (55%) had Crohn's disease, 54 (64%) never smoked, 38 (45%) were on biologics.
Not surprisingly this Irish cohort were a high-risk phenotype for the development of skin cancer with 62% (n = 53) having light coloured eyes, 56% (n = 48) had fair skin, 53% (n = 46) had freckles and 30% (n = 26) had red or blonde hair. Shockingly 36% (n = 31) used sunbeds and 57% (n = 49) had blistering sunburn, while 29% (n = 25) worked outdoors. In addition, 13% (n = 11) had a family history and 7% (n = 6) a personal history of skin cancer.
The proportion of correct responses was higher for all questions in the exposed group. The exposed group did statistically significantly better on factor protection, 34/40 (85%) vs. 22/44 (50%), p = 0.001, OR 5.6 and on skin screening techniques 23/40 (58%) vs. 10/44 (23%), p < 0.001, OR 4.6.
In addition, 93% (n = 37) of the exposed cohort found the video useful and 90% (n = 36) felt it was a better medium than traditional patient leaflets. Furthermore, 90% (n = 36) would like more of their education delivered in this format.
Conclusion: The 'TAGG SunCare Video' performed well in this study and following its successful validation it can be rolled out for regular use with a view to reduce skin cancer burden in our cohort.
Disclosure: Nothing to disclose

P0315 IBD PATIENTS ARE FOUR TIMES MORE LIKELY TO DEVELOP ALL TYPES OF SKIN CANCER POSSIBLY RELATED TO HIGH RATES OF IMMUNOSUPPRESSION; WITH YOUNG PATIENTS PARTICULARLY AT RISK OF MELANOMA

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Introduction: Increased rates of non-melanoma skin cancer (NMSC) is a recognised complication of immunosuppression therapy for inflammatory bowel disease (IBD), while little is known of malignant melanoma (MM) risk. Newer therapies, including biologics, their early age of introduction and longer duration may further increase skin cancer risk.
Aims and Methods: To compare the incidence of both NMSC and MM in an Irish IBD cohort compared to controls.
Retrospective single centre case-control study from 2012–2017. Known IBD patients and age and sex matched controls were identified from an IBD and polyp database respectively. Both cohorts were cross-referenced with our hospital's pathology database for NMSC and MM. Patients otherwise at risk of skin cancer including transplant recipients or other indications for long-term immunosuppression and skin cancer genetic syndromes were excluded following review of patient electronic records.
The rates of NMSC and MM were compared among groups using a Chi-squared test ($p < 0.05$ was considered significant), and the impact of age, gender and immunosuppression was examined. Relative risk (RR) and numbers needed to treat (NNT) were calculated where appropriate.
Results: In all, 931 IBD and 1090 age and sex matched controls were identified. The incidence of NMSC was significantly higher in IBD vs controls, 1.18% (n = 11/931) vs. 0.28% (3/1090), p < 0.03 with a RR of 1.7 (p = 0.0001, 95% CI 1.29–2.26) and a NNT of 3.
Melanoma was also more frequent in IBD patients although not reaching statistical significance; 0.43% (n = 4/931) vs. 0.09% (n = 1/1090) p = 0.18, with a similar RR as NMSC, 1.7 (p = 0.01, 95% CI 1.1196- 2.70) and a NNT of 2.94.
MM patients were younger 51.4 years vs. 72.3 years in NMSC (p < 0.004, 95% CI 1.21–40.65)
Immunosuppression use was frequent with 70% (n = 3/4) of MM and 75% (n = 7/11) of NMSC occurring while on immunosuppression.
Conclusion: In addition to all IBD patients being at risk of NMSC, our study has shown for the first time that younger IBD patients also appear to be at a higher risk of malignant melanoma, RR 1.7 and supports a further nested case control study to identify modifiable risk factors, as well as supporting the establishment of a specific IBD skin cancer awareness campaign.
Disclosure: Nothing to disclose

P0316 HEPCIDIN LEVELS IN DIAGNOSING IRON DEFICIENCY ANEMIA IN IBD PATIENTS

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Introduction: Iron metabolism is regulated by hepcidin, polypeptide synthetized primarily by hepatocytes. Hepcidin synthesis may be altered due to hypoxia, inflammation, erythropoiesis and other multiple factors that have an influence on total iron body storage.
Aims and Methods: Our aim was to determine serum hepcidin levels in patients inflammatory bowel disease (IBD) as well to investigate whether there is correlation of hepcidin levels with disease acitivity.
A case-control study was performed among 30 newly diagnosed IBD patients (18 UC, 12 CD) and the same number age, sex-matched healthy controls. All patients underwent a total colonoscopy with ileoscopy. Complete blood count was obtained in addition to inflammatory markers (CRP, erythrocyte sedimentation rate-ESR). Serum levels of hepcidin were determined with commercially available enzyme-linked immunosorbent assay (DRG Instruments, Marburg, Germany). Serum iron, TIBC, UIBC were assesed with an electrochemiluminesence immunoassay and sTfR was assessed using an immunoturbidimetric method. Mayo score and CDAI respectively were calculated for each patient. Statistical analyses were performed using SPSS software version 20.0 for Windows.
Results: There was high statistically significant difference between IBD patients and controls in levels of hepcidin (p < 0.01). Serum hepcidin levels were significantly higher in control group (9.77 ± 2.71 vs. 6.40 ± 2.42 ng/ml, p = 0.00). Serum ferritin (394 ± 515 vs. 119 ± 124 ng/ml, p = 0.00) as well serum hepcidin to ferritin ratio (0.34 ± 0.17 vs. 0.22 ± 0.09, p = 0.02) were significantly higher in control group. There was no statistically significant correlation of serum hepcidin with CRP, Mayo score or CDAI respectively (p > 0.05). However we have found statisticaly significant negative correlation of sTfR, TIBC with hepcidin (p < 0.01).
Conclusion: Serum hepcidin is a very important novel marker in patients with iron deificinecy anemia (IDA), and it shoud be used in IBD patients considering difficulties in establishing IDA diagnosis due to inflammation.
Disclosure: Nothing to disclose

P0317 MONITORING HISTOLOGICAL ACTIVITY IN ULCERATIVE COLITIS - CORRELATION OF FECAL BIOMARKERS WITH THE RILEY SCORE AND THE NANCY INDEX

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Introduction: Histological healing in ulcerative colitis (UC) may be a better predictor than macroscopic appearance or clinical criteria for time to relapse. Histological assessment revealed that indicators of acute mucosal inflammation, including crypt abscesses, mucin depletion or an acute inflammatory cell infiltrate which are used in the Riley Score or the Nancy index were associated with a 2- to 3-fold increase in the risk of UC relapse during 12 months' follow-up. However histologic assessment requires invasive endoscopy and gaining of biopsy. Non-invasive surrogates of mucosal healing like fecal biomarkers would help to lower risks, costs and might increase patient acceptance.
Aims and Methods: The study aimed to investigate the performance of non-invasive fecal biomarkers compared to the Riley Score and Nancy index in patients with UC. Colonoscopy was performed in every patient and a fecal sample was harvested within 72 hours. 3 biopsies were taken from the macroscopically most inflamed location or random from each colonic segment and the Riley Score and Nancy index were calculated. For each patient the highest calculated score was compared to the fecal biomarkers Lactoferrin (LF), Calprotectin (CALPREST - CalP), PMN elastase (PMN-E), S100 calcium-binding protein A12 (S100A12) and Eosinophil-derived Neurotoxin (EDN). In addition, a Kruskal-Wallis test was performed to evaluate if the median levels of the fecal markers differ significantly between the grades 0–4 of the Nancy index.
Results: 50 patients (32 female), mean age 42.9 ± 12.3 years (range 23–67) with diagnosed UC were included in the study. The Riley score and the Nancy index were correlated significantly with EDN (r (49) = 0.561; p = 0.001/ r (49) = 0.445; p = 0.001), S100A12 (r (49) = 0.327; p = 0.022/ r (49) = 0.346; p = 0.015), PMN-e (r (49) = 0.314; p = 0.028/ r (49) = 0.289; p = 0.044) and LF (r (49) = 0.452; p = 0.001/ r (49) = 0.345; p = 0.015), but not with CalP (p > 0.05). The median levels of the fecal markers according to the grades 0–4 of the Nancy index and the results of the Kruskal-Wallis test are presented in table 1. Only LF, EDN and S100A12 differed significantly between the grades. Subsequent post-hoc tests showed that LF differed significantly between the grades 2 and 3 (z = −3.125, p = 0.011), EDN between the grades 2 and 4 (z = −3.006, p = 0.016) and S100A12 between the grades 2 and 3 (z = −3.968, p = 0.000) and 2 and 4 (z = −3.067, p = 0.013).
Conclusion: The fecal biomarkers LF, EDN, S100A12 and PMN-e were correlated significantly with the Riley and Nancy index, LF, EDN and S100A12 differed significantly between the grades of the Nancy index. The results support the utility of fecal biomarkers for detecting active histologic inflammation in patients with ulcerative colitis.
[Table 1. Median levels (range) of the fecal markers PMN-e, LF, EDN, CalP and S100A12]

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Five grades of the Nancy histological index

	0/1 (n = 2)	2 (n = 9)	3 (n = 19)	4 (n = 19)	p
PMN-e (μg/g	0.075 (0.06–0.09)	0.06 (0.03–0.54)	0.27 (0.04–10.28)	0.21 (0.05–0.45)	0.051
LF (μg/g)	1.21 (0.10–2.21)	2.32 (0.38–47.67)	51.90 (1.47–462.82)	32.97 (1.91–465.72)	0.002
EDN (μg/g)	0.97 (0.31–1.63)	0.47 (0.09–4.69)	1.74 (0.14–5.28)	3.18 (0.47–6.32)	0.016
CalP (μg/g)	246.29 (101.07–391.50)	430.10 (86.51–727.01)	712.81 (197.93–551.45)	389.10 (251.63–745.31)	0.076
S100A12 (μg/g)	18.82 (15.02–22.62)	5.62 (1.41–63.52)	91.32 (6.82–233.87)	87.77 (2.47–164.67)	0.001

PMN-e = Polymorphonuclear elastase, LF = Lactoferrin, EDN = Eosinophil-derived Neurotoxin, CalP = CalprotectinCALPREST, S100A12 = S100 calcium-binding protein A12

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P0318 AZATHIOPRINE METABOLITE (6-TGN) LEVELS WITHIN A DEFINED THERAPEUTIC RANGE ARE ASSOCIATED WITH LOWER FECAL CALPROTECTIN IN CROHN'S DISEASE - A RETROSPECTIVE ANALYSIS

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Introduction: Azathioprine/6-mercaptopurine (AZA/6-MP) are first-line immunosuppressants for the treatment of Crohn's disease. While recent meta-analyses have reported a positive association of their active metabolite 6-thioguanine (6-TGN) with clinical outcomes, 6-TGN levels have not been correlated with surrogate markers of mucosal healing, which is an increasingly recognised therapeutic goal.

Aims and Methods: We therefore investigated whether 6-TGN levels are inversely associated with fecal calprotectin (FC) in Crohn's disease patients on azathioprine monotherapy. 6-TGN and FC levels of 96 Crohn's disease patients on AZA/6-MP monotherapy visiting the IBD outpatient clinic between 2009 and 2016 were retrospectively analysed. In a small sub-cohort with serial 6-TGN measurements, longitudinal FC measurements were assessed.

Results: In patients with 6-TGN levels within a defined range (250–450 pmol/8×10^8RBCs), FC levels were significantly lower (median FC 149 vs. 346 mg/kg, $p = 0.007$), and hemoglobin concentrations as well as transferrin saturation levels were significantly higher than in patients with lower or higher metabolites. CRP and protein levels were not different. In the small cohort that was followed longitudinally, all patients achieved an increase in 6-TGN levels upon dose escalation, and fecal calprotectin levels decreased in 54%.

Conclusion: In our retrospective analysis on Crohn's disease patients receiving AZA/6-MP monotherapy, 6-TGN levels within a defined range (250–450 pmol/8×10^8red blood cells) were associated with significantly lower fecal calprotectin levels. A treat-to target concept directed by 6-TGN levels to reach mucosal healing appears promising, but requires prospective studies (DRKS00013246).

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P0319 DEVELOPMENT AND VALIDATION OF A SIMPLIFIED MAGNETIC RESONANCE INDEX OF ACTIVITY (SMARIA) FOR CROHŃS DISEASE

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Introduction: The MaRIA index is the best-characterized Magnetic Resonance Enterography (MRE)
index for the assessment of luminal Crohn's disease (CD) activity. However, a number of limitations had been recognized.

Aims and Methods: The aim of this study was to develop and to validate a simplified and accurate Magnetic Resonance Index of Activity (sMaRIA) for assessing disease activity and therapeutic response of luminal CD.
MRE data from 98 patients, including active and inactive segments (colon and terminal ileum), from 2 prospective studies were re-analyzed to develop the sMaRIA using endoscopy (CDEIS) as gold standard. Further analysis of responsiveness and reliability, in an independent cohort of 37 patients who underwent MRE and endoscopy before and after a therapeutic intervention was performed. Comparison of the diagnostic performance between the original MaRIA and sMARIA for detecting active/severe lesions was performed.

Results: Logistic regression analysis showed that wall thickness >3 mm, presence of mural edema, ulcers and perienteric fat stranding were independent predictors of disease activity and were used therefore as descriptors of sMaRIA. The sensitivity and specificity of sMaRIA at segment level for detecting active disease using a cutoff point ≥1 were 90% and 81% (AUC 0.91, 95% CI 0.88–0.94), and for detecting severe lesions (ulcers) using a cutoff point ≥2 were 85% and 92% (AUC 0.94, 95% CI 0.91–0.96), respectively. Correlation between sMaRIA and CDEIS/MaRIA was excellent ($r = 0.82$ and $r = 0.91$, respectively; $p < 0.001$). There were no differences with regard to diagnostic performance between the sMaRIA and the original MaRIA for detecting active ($p = 0.7$) and severe disease ($p = 0.5$). The sMaRIA accurately detected changes in lesion severity in response to a therapeutic intervention and was as reliable as endoscopy for the assessment of mucosal healing.

Conclusion: Simplified MaRIA index allows a faster and easier assessment of inflammation in CD by keeping high accuracy for both diagnosis and therapeutic response. Main advantages over MaRIA include a less time-consuming calculation and that is not confounded by missing segments.

Disclosure: Nothing to disclose

P0320 VALIDATION AND INVESTIGATION OF THE OPERATING CHARACTERISTICS OF THE ULCERATIVE COLITIS ENDOSCOPIC INDEX OF SEVERITY

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Introduction: The ulcerative colitis endoscopic index of severity (UCEIS) is a novel, validated instrument to evaluate endoscopic disease activity in ulcerative colitis (UC) (1). Recent studies have demonstrated that the UCEIS outperforms the more widely used Mayo endoscopic score (MES) in predicting long-term prognosis (2,3), including the need for colectomy (4). It also has precise item definitions and is likely to be more responsive than the MES score by virtue of its greater number of stratifications (scores range between 0–8, as opposed to 0–3). However, despite these potential benefits many gastroenterologists still prefer to use MES, because its operating characteristics are better defined and its grades are more readily applicable to clinical decision making; a MES ≥ 2 is generally accepted as the cut-off for treatment escalation (5). The equivalent for the UCEIS cut-off is not yet defined, which limits its clinical utility.

Aims and Methods: Our aims were to determine a UCEIS threshold most closely associated with the need for treatment escalation as well as to perform a validation exercise using clinical, biochemical and histological measures of disease activity. Colonoscopies and sigmoidoscopies performed in UC patients between Nov 2016-Jan 2018 at Guy's and St Thomas' Hospital were retrospectively reviewed. Data regarding demographics, UC phenotype and medication, Simple Clinical Colitis Activity Index (SCCAI), UCEIS, MES, CRP and Nancy Histological Index (NHI) were collected as well as treatment alteration decisions based on endoscopic findings.

The measure of agreement between the UCEIS and the Mayo score was examined using Kappa (κ) statistics. A UCEIS cut-off for the perceived need for treatment escalation was calculated using a Chi square test, receiver operating characteristic (ROC) curve and area under the curve (AUC) analyses. Pearson correlation coefficient was used to compare the linear relationship between the UCEIS and SCCAI, CRP and NHI.

Results: 363 endoscopic procedures were carried out in 295 patients during the data collection period. 201 of the 363 procedures (56%) documented both the UCEIS and MES. These scores demonstrated a substantial agreement between the indices ($\kappa = 0.713$, $p < 0.001$).

Overall, treatment escalation was considered necessary following 199 (56%) procedures, but was not in the remaining 156 (44%). ROC analysis of the perceived need for treatment escalation showed the highest sensitivity and specificity (0.80 and 0.93, respectively) for UCEIS ≥ 4 with an AUC of 0.93. Of 170 patients with a UCEIS ≥ 4, treatment escalation was considered necessary for 159 (94%), but not for 11 (6%). Of 185 patients with a UCEIS ≤ 3, treatment escalation was considered necessary in 40 (22%), cases but was not in 145 (78%) cases ($p < 0.001$).

UCEIS values demonstrated moderate correlation with SCCAI (0.671, $p < 0.001$) scores and strong correlation with NHI values (0.723, $p < 0.001$), but only weak correlation with CRP measurements (0.279, $p < 0.001$).

Conclusion: Our data demonstrate that a UCEIS score ≥ 4 was significantly associated with the perceived need for treatment escalation. This cut-off could/should therefore be used to support clinical decision-making based on endoscopic findings. Our study also showed that UCEIS has strong correlation with histological disease activity, moderate correlation with a clinical activity index, but only weak correlation with CRP.

Disclosure: Nothing to disclose

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P0321 FATIGUE AS A POSSIBLE MARKER OF SARCOPENIA IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Recently, there is growing interest in the assessment of muscular mass in inflammatory bowel disease (IBD) as sarcopenia is associated with important outcomes.

Aim of the study was to evaluate prevalence of reduced muscular mass in IBD patients and assess its correlation with fatigue.

Aims and Methods: A first cohort underwent Dual Energy X-ray Absorptiometry (DEXA), a second cohort underwent Bio-Impendensometric Analysis (BIA). For DEXA, skeletal muscular mass index (ASMI), was calculated. Reduced muscular mass was defined for values of ASMI < 7.23 Kg/m^2 for men and ASMI < 5.67 Kg/m^2 for women. For BIA, skeletal muscle mass index (SMI) was calculated. Reduced muscular mass was defined for values of SMI < 10.75 Kg/m^2 for men and SMI < 6.75 Kg/m^2 for women. For comparison we also enrolled a control group for every cohort. Fatigue was assessed by means of visual analogue scale (VAS) evaluating patient reported 'current strenght'. Fatigue was defined for a VAS score < 70.

Results: For the first cohort, 42 IBD patients, 53% Crohn's Disease (CD), 47% ulcerative colitis (UC), and 45 healthy controls were enrolled and evaluated by DEXA. For the second cohort 68 IBD patients, 58% CD and 42% UC, and 35 healthy controls were enrolled and evaluated by BIA.

Reduced muscular mass was more frequent in IBD patients in comparison to controls both for DEXA (50% versus 9%, respectively, $p < 0.01$) and for BIA (29% versus 9%, respectively, $p < 0.05$).

Reduced muscular mass was found in 57% of underweight, 55% of normal weight, 17% of overweight and 0% of obese patients ($p < 0.001$). Fatigue was present in 62% of patients compared to 44% of controls ($p < 0.05$, ODD ratio $= 2.07$, 95% CI $= 1.06$ to 4.09).

Concomitant reduction in muscular mass and fatigue was present in 27% of patients compared to 1% of controls. This difference is statistically significant, with an increased risk for patients to meet both criteria in comparison to controls ($p < 0.001$; ODD $= 204.27$; 95% CI $= 32.54$–8049.00).

Conclusion: Reduced muscular mass indicating sarcopenia is common in IBD patients and can be evaluated with either DEXA or BIA. Assessing fatigue by means of VAS scale might help to identify patients requiring nutritional assessment.

Disclosure: Nothing to disclose

P0322 USE OF SYNTHETIC AND BIOLOGICAL BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS) IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH ENTEROPATHIC SPONDYLOARTHRITIS: A COMBINED GASTRO-RHEUMATOLOGICAL APPROACH IN PROSPECTIVE STUDY AT 2 YEARS

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Introduction: Enteropathic spondyloarthritis (eSpA) is a chronic inflammatory disease associated with inflammatory bowel disease (IBD).

Aims and Methods: In a prospective study at 2 years, we aimed to assess the diagnosis and outcome of IBD patients with musculoskeletal pain assessed by a combined gastro-rheumatological approach. At this purpose, IBD patients referring arthralgias to IBD-dedicated gastroenterologists were evaluated in a multidisciplinary gastro-rheumatological assessment. At baseline and at 3,6,12,24 months, the following parameters were recorded in a database: diagnosis, scores, biochemical, SpA and IBD activity scores, treatments, bDMARDs (biological disease-modifying anti-rheumatic drugs), csDMARDs (conventional synthetic DMARDs). Associations between treatments and IBD characteristics were evaluated by logistic regression (Adjusted Odds Ratio, AOR [95% CI]).

Results: Overall, 229 IBD patients were referred to rheumatologists, including 141 (61.6%) with CD, 88 (38.4%) with UC. Among these 229 patients, eSpA was diagnosed in 147 (64.2%), while in the remaining 82 (35.8%) patients arthralgias were not related to IBD (No-eSpA). The median age was higher in patients without vs with eSpA (52.5 [41–62] vs 46 [37–56]; $p = 0.022$). Among the 147 patients with eSpA, 96 (65.3%) showed peripheral and 51 (34.7%) axial

involvement (age: 46 [37–56]; females: 99 (67.3%); IBD duration: 14.6±9.7). bDMARD treatments increased over the follow-up (baseline to 24 months: 32.6–60%; AOR 3.45 [1.93–6.2]; $p < 0.001$). bDMARD use was less frequent in elderly patients (AOR 0.73 [0.56–0.96], $p = 0.023$), in UC (AOR 0.43 [0.2–0.94]; $p = 0.034$) and in patients with peripheral involvement (AOR 0.53 [0.3–1.04]; $p = 0.067$). csDMARD use was increased in patients with peripheral involvement (AOR 4.65 [2.09–10.33]; $p < 0.001$) and with UC (AOR 2.30 [1.13–4.67]; $p = 0.021$). CRP, ESR, ASDAS-ESR (Ankylosing Spondylitis Disease Activity Score) and BASFI (Bath Ankylosing Spondylitis Functional Index) significantly decreased over the follow up ($p \leq 0.022$; $p \leq 0.033$; $p = 0.05$; $p = 0.03$, respectively). The same was not observed for UC activity score (pMayo), Ankylosing Spondylitis Disease Activity Index (BASDAI) and Health Assessment Questionnaire for SpA (HAQ-S).

Conclusion: In a prospective study at 2 years, a multidisciplinary gastro-reumathological approach showed to optimize the diagnosis, therapeutic management and outcome of IBD patients referring arthralgias. In patients with eSpA, bDMARD use paralleled an improvement in disease activity scores and confirmed a good safety profile.

Disclosure: Biancone L: Lecture fees or Advisory Board: Zambon, MS&D, Takeda, Abbvie, Sofar, Ferring, Wassermann;

P0323 EVALUATION OF CROHN'S DISEASE BY USING A NOVEL CAPSULE ENDOSCOPY SCORING METHOD: CROHN'S DISEASE ACTIVITY IN CAPSULE ENDOSCOPY (CDACE)

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Introduction: Small bowel capsule endoscopy (SBCE) for Crohn's disease (CD) with small bowel lesions is a low-invasive method that enables visualization of the small bowel mucosa. 2 scoring methods are used to evaluate the images obtained: the Lewis score (LS) and the capsule endoscopy Crohn's disease activity index (CECDAI). However, CD shows varied pathology, including inflammation and stenosis; it is difficult to assess the disease state, including the range of lesions, and presence/absence of stenosis solely on the basis of sum scores obtained by either one of the scoring methods.

Aims and Methods: To develop and evaluate a novel scoring method with which pathology can readily be assessed from sum scores by using SBCE data of CD patients with small bowel lesions. The subjects included 93 CD patients with small bowel lesions who underwent SBCE between June 2010 and May 2017. SBCE was carried out a total of 162 times in these patients, including 104 times in men, 49 times for small bowel CD, and 113 times for small-and-large bowel CD. The novel scoring method was established as Crohn's disease activity in capsule endoscopy (CDACE), and its correlations with the scoring methods in current use, LS and CECDAI, and also with the clinical disease activity index (CDAI) and biomarkers, were analyzed. In CDACE, the small bowel was divided into four zones according to Rapid software analysis, and for each zone, the inflammation was scored on a scale of 0 to 4, giving a total score of 0 to 16 (inflammation score: A). In addition, inflammation present was scored on a scale of 0 to 4 (zone score: B) and the severity of stenosis was scored on a scale of 0 to 3 (stenosis score: C). CDACE was calculated as the sum of $A \times 100 + B \times 10 + C$.

Results: The correlations between CDACE and the existing scoring methods were as follows: CDACE and the LS: $r = 0.44$ ($p < 0.0001$) and CDACE and the CECDAI: $r = 0.83$ ($p < 0.0001$). Thus, the correlation with the CECDAI was higher. With respect to CDACE, the LS, and the CECDAI, respectively, the correlations of each with the CDAI and biomarkers were as follows: CDAI: $r = 0.39$ ($p < 0.0001$), $r = 0.19$ ($p = 0.0119$), and $r = 0.37$ ($p < 0.0001$) and C-reactive protein (CRP): $r = 0.23$ ($p = 0.0027$), $r = 0.05$ ($p = 0.5201$), and $r = 0.24$ ($p = 0.0018$). Therefore, CDACE and the CECDAI showed approximately the same correlations with the CDAI and CRP.

Conclusion: With CDACE, it is possible to interpret the inflammation morphology (the second / third / forth digit) and the severity and presence/absence of stenosis (the first digit) in the small bowel on the basis of the sum scores obtained. In addition, the correlation with the CECDAI has been clearly demonstrated. Therefore, CDACE represents a novel, useful scoring method in clinical practice for patients who underwent SBCE for CD with small bowel lesions.

Disclosure: Nothing to disclose

P0324 LONG-TERM OBSERVATION REGISTRY -CEDUR - IN GERMAN IBD PATIENTS

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Introduction: Inflammatory bowel disease (IBD) is diagnosed in approximately 350000 patients in Germany with increasing incidence and prevalence. Although on-going inflammation can result in irreversible damage to the GI tract, undertreatment and reluctance to use immunmodulatory therapies earlier in the course of disease are present. On the other hand, costs for therapies, surgeries and hospitalization are high, once damage has occurred. In 2015 we therefore implemented an independent national IBD registry (CEDUR) to methodically collect real-life data of IBD patients with regard to the usefulness and comparability of immunmodulatory strategies.

Aims and Methods: CEDUR is a web-based, descriptive registry of large tertiary IBD centers throughout Germany, using time sparing documentation in an adapted medical charts-software via GDT interface. Patients with IBD who are willing to participate have visits every 3 months and fill in questionnaires that are later-on completed and controlled by their physicians. Since 2015 and for at least 10 years, data on phenotypes, therapeutic effects including efficacy, safety and economy as well as hospitalizations, surgeries, comorbidities, day-off-work and quality of life are continuously collected in patients with Crohn's disease (CD) and ulcerative colitis (UC).

Results: So far, 1856 IBD patients (UC: 859, CD: 992, indeterminate colitis 5) were enrolled, of whom 47% are men and 53% are women.

In CD and UC, 24.3% were younger than 21 years, 38.6 between 21 and 30, 19.0% between 31 and 40, 10.5% between 41 and 50 and 7.5% older than 50 years. In CD, age at first diagnosis was younger than 21 in 29.8% and older than 50 years in 6.5%. In UC, age at first diagnosis was younger than 21 years in 17.6% and older than 50 years in 28.8%. In CD, biologics were used in 73.9% of patients, of those anti-integrins in 6.0% and IL-12/23 blockers in 5.6%. 31.4% of patients with TNF-blockers were treated for more than 4 years. 54.2 % of patients under infliximab received infusions every 7 to 9 weeks, 31.6% every 4 to 6 weeks. 49.5 % of patients under adalimumab received injections of 40mg every 2 weeks, and 38.4 % at least 80mg every 2 weeks.

In UC, TNF-blockers or other biologics were used in 59.0% of patients, of those anti-integrins in 12.05% and IL-12/23 blockers in 0.2%. 24.8% of patients with TNF-blockers were treated longer than 4 years. 47.1 % of patients under infliximab received infusions every 7 to 9 weeks, 36.9% every 4 to 6 weeks. 52.7 % of patients under adalimumab received injections of 40mg every 2 weeks, and 37.9% at least 80mg every 2 weeks.

Conclusion: We successfully implemented a large national IBD registry for the collection of real-life data by a contribution of patients and physicians from tertiary IBD centers throughout Germany.

As a first result we can present the data on the use of biologic therapy in more than 1800 Crohn's disease and ulcerative colitis patients. IBD significantly affect patients in their young ages, biologic therapies seem to be necessary in much more patients than commonly assumed and standard treatment has to be adapted to higher doses in TNF-blockers in UC more than CD and in adalimumab more than infliximab.

Our registry can serve as database for a wide range of efficacy, safety and economy issues in IBD patients.

Disclosure: AbbVie, Biogen, Boehringer, r-Biopharm, Janssen, MSD, Pfizer, Shield, Takeda

P0325 A RETROSPECTIVE ANALYSIS OF THE MULTIGENE ANALYSIS TEST DIBICOL® TO DIFFERENTIATE BETWEEN ULCERATIVE COLITIS, CROHN'S DISEASE AND NON-IBD

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Introduction: DiBiCol® is a diagnostic test that can differentiate between ulcerative colitis (UC), Crohn's disease (CD) and non-inflammatory bowel disease (Non-IBD). DiBiCol® is a PCR-based method that monitors 7 proprietary biomarkers from a single colonic biopsy. By applying a specially designed algorithm, a diagnosis of UC, CD and Non-IBD can be made with a high degree of certainty. The algorithm was established in 3 clinical studies. Since 2009 the DiBiCol® test has been used in Sweden in clinical routine practice at a large number of clinics and colonic biopsies from more than 1200 patients have been analysed.

Aims and Methods: The aim of the study is to retrospectively evaluate the clinical application and the outcome of the multigene analysis test DiBiCol® in differentiating between UC, CD and Non-IBD.

In this retrospective analysis the clinical application and the outcome of the DiBiCol® test was studied in 1110 patients. The consistency of the DiBiCol test result from duplicate colonic biopsy samples were compared in 300 patients. In a subset of 79 patients, DiBiCol® test results were compared to clinical diagnosis and histopathology diagnosis retrospectively.

Results: Based on the data compiled from over 30 IBD units in Sweden over 2 years the causes for requesting the DiBiCol® test were in 52% cases of unclassified IBD, in 16% patients representing IBD like symptoms for the first time, in 13% cases of indeterminate colitis, in 8% cases before surgery to confirm diagnosis, in 6% cases of changing symptoms and in 5% other reasons.

In 994 out of 1110 samples a conclusive diagnosis with more than 70% probability could be made, UC in 492 cases, CD in 431 cases and 71 cases of Non-IBD, while in 116 cases the test result was inconclusive for different reasons. Duplicate colonic biopsy samples taken at the same time were available in 300 patients and provided the same test results in 83% of the cases. In 52/300 patients the test result was different between the 2 biopsies but only in 24 patients a different diagnosis with $\geq$ 90% probability was evident meaning a clearly different test results only in 8% of cases (24/300). In 34 patients DiBiCol® was tested at 2 time points 4 weeks apart and in 94% of cases the test results were in alignment with each other.

In a subset of 79 patients the clinical and histological diagnosis were compared to the DiBiCol® test results and the data showed that 93% of these cases, in which the clinical diagnosis matched with histopathology, were correctly diagnosed by DiBiCol® with $\geq$ 70% probability. The sensitivity / specificity of the DiBiCol®

test was calculated to be 97% / 92% for UC diagnosis and 78% / 88% for CD diagnosis. There was a better correlation between the DiBiCol® result and the histopathology evaluation than the clinical diagnosis in this subset.
Conclusion: Real-world data on the use of DiBiCol® demonstrate that this multigene analysis test is a useful diagnostic tool and can support physicians to diagnose IBD and to differentiate CD from UC.
Disclosure: Disclosure of Interest: T. Knittel Consultancy for: InDex Pharmaceuticals, Shareholder of: InDex Pharmaceuticals. R. Löfberg Consultancy for: InDex Pharmaceuticals, Shareholder of: InDex Pharmaceuticals. C. Admyre employee at: InDex Pharmaceuticals, Shareholder of: InDex Pharmaceuticals. A. Zargari employee at: InDex Pharmaceuticals, Shareholder of: InDex Pharmaceuticals. Å. Öst Consultancy for: InDex Pharmaceuticals.

P0326 FAECAL CALPROTECTIN DISCRIMINATES CRYPTOGLANDULAR FROM CROHN'S DISEASE PERIANAL FISTULAE

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Introduction: Faecal calprotectin (FC) is a surrogate marker of mucosal inflammation. Our aims were to determine the diagnostic accuracy of FC for (i) the differentiation between cryptoglandular (CG) perianal fistulae and perianal fistulising Crohn's disease (pCD) and (ii) the detection of intestinal ulcers in pCD patients with an active perianal fistula.
Aims and Methods: This was a retrospective single-center study. Patients with a perianal fistula between 2009 and 2017 were identified by an institutional database search. Adult patients with an active perianal fistula, an available FC concentration and a complete ileocolonoscopy within a time window of 10 weeks were included. Active fistulae were defined by spontaneous drainage or upon gentle finger compression as reported by patient or physician. Patients with an abscess or GI infection were excluded. Endoscopy images and reports were independently reviewed for the presence of ulcers.
Results: 56 patients were included (pCD, $n = 37$; CG perianal fistula, $n = 19$). Intestinal ulcers were present in 19 of the pCD patients (51.4%). FC was significantly higher in patients with pCD compared to CG perianal fistulae (median [interquartile range]) (708.0 [207.0–1705.0] vs. 32.0 [23.0–77.0] µg/g, $p < 0.001$). Area-under-the-curve (AUC) value for FC receiver operating characteristic (ROC) statistics was 0.900, 95% confidence interval (CI) [0.818–0.982]. Optimal FC cut-off was achieved for a value of ≥150 µg/g (sensitivity 0.81, specificity 0.89, positive predictive value 93.8%, negative predictive value 70.8% and overall accuracy 83.9%). When the analysis was limited to patients without intestinal ulcers, FC could still accurately discriminate active CG perianal fistulae from pCD with the same optimal cut-off value of 150 µg/g (AUC 0.857 [0.733–0.980]; sensitivity 0.67, specificity 0.90, positive predictive value 85.7%, negative predictive value 73.9% and overall accuracy 78.4%). In the pCD population, FC was significantly increased in the presence of ulcers (1672.0 [403.0–1800.0] vs. 238.0 [75.8–795.0], $p = 0.004$). AUC value was 0.776, 95%CI [0.622–0.931]. Optimal FC cut-off was achieved for a value of ≥250µg/g (sensitivity 0.89, specificity 0.56, positive predictive value 68.0%, negative predictive value 83.0% and overall accuracy 73.0%). Of the pCD patients with a FC above the determined optimal cut-off value of 250 ($n = 25$), 32% had a false positive result and in fact had endoscopically quiescent disease.
Conclusion: FC is an accurate and clinically useful tool to distinguish between active CG perianal fistulae and active Crohn's disease perianal fistulae, even in the absence of intestinal ulcers. In pCD patients with an active fistula, an elevated FC does not accurately predict the presence of intestinal ulcers and should be interpreted with caution.
Disclosure: Nothing to disclose

P0327 QUALITY OF LIFE IS ASSOCIATED WITH WEARABLE-BASED PHYSICAL ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE, OBSERVATIONAL STUDY

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Introduction: Patient-reported outcomes such as quality of life are gaining in importance in the assessment of patients suffering from inflammatory bowel disease (IBD). The association of objectively measured physical activity and quality of life in IBD patients has not been studied in depth.
Aims and Methods: To investigate the association of disease-specific quality of life and physical activity as well as clinical and biochemical disease activity in IBD patients, 91 IBD patients were stratified into 4 groups (Crohn's disease - CD and ulcerative colitis - UC, in remission and with moderate-severe activity, respectively), and evaluated with respect to disease-specific quality of life (IBDQ), physical activity (accelerometry), body composition (bioelectrical impedance analysis, BIA), as well as clinical (HBI, SCCAI) and biochemical (CRP, fecal calprotectin) parameters of disease activity.
Results: In patients with moderate-severe disease activity, IBDQ was significantly lower as compared to patients in remission (Mann-Whitney-U test and Kruskal-Wallis test, $p < 0.001$). The physical activity level (PAL) was higher in remission than in active disease (Mann-Whitney-U test, $p < 0.05$). IBDQ was significantly correlated with the duration of strenuous physical activity per day ($p = 0.029178$, $r = 0.235$), skeletal muscle mass ($p = 0.033829$, $r = 0.229$), and biomarkers of inflammation (CRP: $p < 0.005$, $r = -0.335$, fecal calprotectin: $p < 0.005$, $r = -0.385$, Spearman's rank correlation).
Conclusion: In this prospective, cross-sectional study, disease-specific quality of life was significantly associated with accelerometrically determined physical activity in patients with inflammatory bowel disease. This may be related to a reciprocal impact of both factors (DRKS00011370).
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P0328 ABNORMAL MENTAL HEALTH IS DIFFERENT AND MORE SEVERE IN CROHN'S DISEASE COMPARED WITH ULCERATIVE COLITIS

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Introduction: Abnormal mental health symptomatology in Crohn's disease (CD) and ulcerative colitis (UC) occurs commonly. However, the nature of these symptoms and the identity of their predictors at different levels of disease activity remain incompletely understood.
Aims and Methods: Consecutive unselected consenting adult patients (age ≥ 18 years) with CD and UC, with psychiatric illness and medication excluded, were recruited at out-patient clinics and via the CD and UC Patients' Association, and provided demographic and economic information. Disease activity was self-scored by the Patient Harvey-Bradshaw Index (P-HBI) in CD, or the Patient Simple Clinical Colitis Activity Index (P-SCCAI) for UC. Active disease was defined by a score of P-HBI ≥5 or P-SCCAI ≥ 3. Mental health was measured by the self-report Brief Symptom Inventory (BSI) of 53 symptoms grouped in nine 'categories': depression, somatization, obsession-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The BSI yields three 'summary' scores: (1) General Severity Index (GSI, mean of category scores, range 0–4), (2) Positive Symptom Total (PST, sum of recorded symptoms, range 0–53); (3) Positive Symptom Distress Index (PSDI, summation of the item values divided by PST, range 0–4). Higher scores indicate more mental ill-health.
Results: There were 289 CD patients with active and 390 with remittent disease; in UC, 110 and 106 patients, respectively. CD patients were aged 37.7 ± 14.0 years, UC patients 48.9 ± 16.2 years ($p < 0.001$). In CD 58.3% were females; in UC 54.4% females. In univariate analysis, GSI, PST, PSDI, depression, somatization, obsession-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism were all scored higher (were worse) in active versus remittent CD ($p < 0.001$). All summary and category scores except paranoid ideation were higher in active versus remittent UC ($p < 0.01$-0.001). All summary and category scores were higher in active CD versus active UC ($p < 0.03$-0.001). Scores in remittent disease were lower than in active disease, yet CD demonstrated higher scores than UC ($p < 0.02$-0.001) in all categories except interpersonal sensitivity ($p = 0.07$). Based on these findings, a linear regression analysis comparing CD and UC was performed, controlling for patients' age, gender and economic status (Table). Somatization, anxiety and paranoid ideation were significantly higher in active CD versus UC. Somatization and anxiety were significantly higher in remittent CD versus UC. GSI, PST and PSDI were significantly higher in active CD versus active UC, whereas in remittent CD versus remittent UC the summary scores were not statistically different.
Conclusion: Mental health is significantly worse in patients with CD compared with UC, and in the active disease state. However, differences of mental health between CD and UC in the remittent state largely disappeared when controlling for age, gender and economic status, whereas active CD patients remained more severely affected mentally compared with active UC patients in the categories of somatization, anxiety and paranoid ideation. Awareness of possible mental aberrations will lead to prompt treatment.

Variable	Active CD	Active UC	β	p	Remittent CD	Remittent UC	β	p
Somatization	1.6±.9	1.2±.9	−0.164	0.002	.9±.8	.5±.5	−0.136	0.007
Anxiety	1.4±.9	1.1±.9	−0.112	0.032	1.0±.8	.6±.5	−0.098	0.046
Paranoid ideation	1.0±1.0	.7±.8	−0.123	0.017	.7±.8	.5±.6	−0.051	ns
GSI	1.2±.8	.9±.8	−0.117	0.022	.8±.7	.5±.4	−0.081	0.098
PST	30±13	26±14	−0.121	0.019	22±14	17±12	−0.062	0.215
PSDI	2.0±.6	1.7±.6	−0.134	0.010	1.7±.5	1.4±.5	−0.079	0.122

[Mental health in active and remittent disease.]
Disclosure: Nothing to disclose

P0329 THE ASSOCIATION BETWEEN DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH MODERATE-TO-SEVERE ULCERATIVE COLITIS IN EUROPE

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Introduction: Patients with ulcerative colitis (UC) experience periods of recurring and episodic clinical signs and symptoms. This study sought to establish the association between disease activity and health-related quality of life and other patient-reported outcomes.
Aims and Methods: Data from the 2015 and 2017 Adelphi Inflammatory Bowel Disease Specific Programmes (IBD-DSP) were used. The IBD-DSP is a database of patient chart information abstracted by selected gastroenterologists across the European Union Five ([EU5]; i.e., France, Germany, Italy, Spain, and the United Kingdom [UK]). Eligible gastroenterologists who agreed to participate were asked to complete patient record forms for their next 7 consecutive eligible adult patients with UC. Using available chart information (including endoscopy results based on Mayo scoring), physicians classified their patients into 1 of the following categories: remission with an endoscopic score = 0 (''deep remission''), remission without an endoscopic score = 0 (''remission''), or active disease. Patients were then invited to complete a survey including various patient-reported outcomes: EuroQoL-5D (EQ-5D), Short Quality of Life in Inflammatory Bowel Disease Questionnaire (SIBDQ), and Work Productivity and Activity Impairment-Ulcerative Colitis (WPAI-UC) questionnaire. Only patients with moderate-to-severe UC were included in the analysis (defined as those who had used either an immunomodulator [IM] or a biologic). Differences among disease activity categories with respect to patient-reported outcomes were analyzed using generalized linear models, controlling for demographic (age, sex, country) and clinical factors (body mass index, smoking history, years diagnosed, and the Charlson comorbidity index) as confounders.
Results: A total of N = 1037 patient charts with linked surveys were included (France: N = 347 Germany: N = 379, Italy: N = 55, Spain: N = 171, UK: N = 85; 55.6% male, mean age = 39.2 SD = 13.8). Patients had been diagnosed for a mean of 5.3 years (SD = 5.9). 33.6% had active disease, 53.0% were in remission, and 13.3% were in deep remission. Patients with active disease reported significantly lower levels of EQ-5D health state utilities (Adjusted Mean [AdjM] = 0.78) compared with remission (AdjM = 0.91) and deep remission (AdjM = 0.91) (both $p < 0.05$). Similar findings were observed with the total score of the SIBDQ (AdjMs = 4.2, 5.6, and 5.7, respectively; both $p < 0.05$ compared with active disease). Both overall work impairment and activity impairment (from the WPAI-UC) were also highest among patients with active disease (AdjMs = 54.4% and 47.6% impairment, respectively) followed by remission (AdjMs = 19.4%, 18.9%) and deep remission (AdjMs = 13.8%, 15.7%) (both $p < 0.05$ compared with active disease).
Conclusion: Among patients with moderate-to-severe UC in EU5, active disease was associated with significant impairments in health-related quality of life and impairments in work and leisure activities.
Disclosure: A Armuzzi has received research support from MSD, lecture fees from AbbVie, AstraZeneca, Chiesi, Ferring, Hospira, MSD, Mundipharma, Nikkiso, Otsuka, Pfizer Inc, Takeda, TiGenix, Zambon, and consultancy fees from AbbVie, Allergan, Biogen Idec, Celltrion, Eli Lilly, Ferring, Hospira, Janssen, MSD, Mundipharma, Pfizer Inc, Samsung Bioepis, Sofar, Takeda; M Tarallo, M DiBonaventura, D Bargo, L Salese, J Cappelleri, G Gigante are employees and shareholders of Pfizer Inc; J Lucas, D Bluff and B Hoskin are employees of Adelphi Real World.

P0330 A PILOT [^{11}C]PBR28 TSPO PET IMAGING STUDY TO EVALUATE INFLAMMATION IN CROHN'S DISEASE

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Introduction: Crohn's Disease (CD) features segmental inflammation, which can affect any part of the gastrointestinal tract, with lesions extending across all tissue layers. Although endoscopy and histology can be used to monitor mucosal disease, in vivo assessment of progression and regression of transmural lesions, especially in the small bowel remains challenging. The 18 kDa translocator protein (TSPO), located on the mitochondrial outer membrane, is overexpressed in activated macrophages, and has been used as a marker of inflammation. PET imaging with TSPO selective radioligands allows for the quantification of inflammation, and has been used extensively in both brain and peripheral inflammatory diseases.
Aims and Methods: Here we aim to evaluate the utility of TSPO PET, using radioligand [^{11}C]PBR28, for assessing the inflammation in the gastrointestinal tract in subjects with CD compared to healthy subjects. Subjects were recruited by Hammersmith Medicines Research. For subjects with CD, inclusion criteria included CD confirmed by endoscopy, and them being naïve to biologics. 4 CD patients (2 males and 2 females) and 5 healthy volunteers (3 males and 2 females) have been recruited to date and undergone 2 dynamic [^{11}C]PBR28 PET-CT scans: baseline and 2 hours post a 90 mg oral dose of XBD173 on the same day. XBD173 is a TSPO selective compound and is thereby used to confirm the specificity of the signal in this particular application. Patient Crohn's Disease Activity Index (CDAI), C-reactive protein (CRP), Faecal Calprotectin (FC) as well as TSPO rs6971 genotype (a common polymorphism in the TSPO gene which affects ligand binding affinity[1]) were measured at screening. Regions of interest (ROIs) were manually delineated on the terminal ileum, small bowel, descending colon, sigmoid colon, and skeletal muscle in each subject based on PET and CT co-registered images. The mean and max standard uptake value (SUV, radioactivity concentration normalized by total injected activity and body weight) were estimated in these ROIs.
Results: The CDAI of the CD patients range from 116 to 172, with CRP ranges from 0.2 to 3.8 mg/L, and FC from 49 to 510 mg/kg. Among the 4 CD patients, 3 are high affinity binders (HABs) and 1 is a mixed affinity binder (MAB). There are 2 HABs and 3 MABs in the control group. Compared to healthy controls, CD patients showed a trend of higher heterogeneous ligand uptake in the GI tract, especially in the small bowel. The mean SUVs in different ROIs are listed in the table below.
Conclusion: Preliminary data suggest that the observed PET signal in the small bowel of CD patients can be attributed to TSPO, and by inference inflammatory activity. Should these results to be confirmed, TSPO PET may allow the identification of inflammatory foci in the GI tract of Crohn's patients even with mild disease activities, providing a non-invasive method to assess and quantify inflammatory activity not captured by endoscopy. Recruitment into this pilot study continues.

	Terminal ileum	Small bowel	Descending colon	Sigmoid colon	Muscle
Healthy controls	1.33±0.30	2.01±0.55	1.40±0.74	1.15±0.31	1.25±0.83
CD patients	1.95±0.47	2.68±0.45	1.23±0.43	1.46±0.30	1.32±0.65

[Regional mean SUVs (30–60 min) in healthy and Crohn's patients (mean ± sd).]
Disclosure: Qi Guo, Just Genius, Yanping Luo, and Robert Comley are employees of AbbVie. Gaia Rizzo, Eugenii Rabiner and Azeem Saleem are employees of Invicro. Mavi Walther and Matilde Luce are employees of Hammersmith Medicines Research.

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P0331 DEPENDENCE OF THE LEVEL OF INFLAMMATION MARKERS ON THE PRESENCE OF CLOSTRIDIAL INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: In patients with inflammatory bowel disease (IBD), there was a more frequent development of clostridial infection (CI) and much higher morbidity and mortality rates compared with patients without IBD. Immunosuppressive therapy is a risk factor.
Aims and Methods: We aimed to determine the frequency of clostridial infection (CI) in patients with inflammatory bowel disease undergoing treatment in the Department of treatment of IBD Moscow Clinical Research Center.
Of the 1224 patients with IBD, 764 were found to have toxins A and B in *Clostridium difficile* in feces by enzyme immunoassay. Comparative analysis

between the groups was performed by the method of 4-field tables using non-parametric statistical criteria.
Results: CI was found in 132 (17.3%) patients of IBD, patients without CI - 632 (82.7%). Among IBD patients with CI men - 61 (46.2%), without CI men - 313 (49.5%). Extraintestinal manifestations were present in 37 (28.1%) patients with IBD with CI, in 174 (27.5%) - without CI ($p > 0.05$). The mean albumin level in patients with CI was 28.4±2.83 g/l, in the group without CI - 35.6±3.79 g/l ($p = 0.128376$). The mean level of C-RP among patients with CI was 65.9±4.8 mg/l, in the group without CI - 37.8±3.7 mg/l ($p = 0.000004$). The mean level of ESR in patients with CI was 43.5±6.5 mm/h, in the group without CI - 19.4±3.3 mm/h ($p = 0.000991$). The mean level of fecal calprotectin among patients with CI was 1680±120 mg/g, in the group without CI - 480±95 mg/g ($p = 0.00000$).
Conclusion: The activity of the inflammatory process is higher in patients with inflammatory bowel diseases with associated clostridial infection.
Disclosure: Nothing to disclose

P0332 MICROBIOTA PROFILE AND DYSBIOSIS ASSESSMENT IN CLINICAL PRACTICE: A PILOT STUDY ON IBD PATIENTS

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Introduction: A growing body of evidence suggests that dysbiosis plays a key role in the pathogenesis of inflammatory bowel disease (IBD). However, due to intrinsic limitations in current diagnostic methods and lack of agreement on the appropriate test to use, in clinical practice the characterization of dysbiosis in IBD patients remains challenging.
Aims and Methods: We compared a commercially available dysbiosis test and a stool standard analysis test to profile the microbiota at phylum level in IBD patients and healthy control subjects.
Human fecal samples from 13 IBD patients and 4 healthy control subjects were examined by the GA-map™ Dysbiosis Test (Oslo, Norway) and Illumina Mi-Seq test by BMR-genomics (Padova, Italy). GA-Map is a 16S rRNA test that utilize 54 DNA probes based on 7 variable regions (V3-V9) and recognizing gut bacteria profiles for identification and characterization of dysbiosis. The BMR-genomic test applies the universal primer based on the V3-V4 hypervariable region of 16S rRNA using an Illumina Mi-Seq next-generation sequencer. The correlation between variation of microbiota expressed as the Dysbiosis Index (DI) and fecal calprotectin (FC) levels in IBD patients was also investigated.
Results: BMR-genomics reports on the relative abundance (*ra*) of the major *phyla* on IBDs microbiota. So far, we compared the trend of *ra* with normalized signal for fluorescent probes of DI between the 2 techniques. From descriptive analysis, the 2 methods show a similar trend for *Actinobacteria, Bacteroidetes* and *Proteobacteria,* especially on CD disease (Figure 1). However, there was a substantial difference in the trend on *Firmicutes*. FC levels were correlated with the DI in CD but not in UC patients ($r = 0.74$ vs $r = 0.2$, respectively). Indeed, 100% of CD patients and 75% of UC patients with dysbiosis (DI 3–5) showed an increased FC (>50μg/g). Finally, only by BMR-genomics analysis we found a significant variation on *Faecalbacterium prausnitzii* between IBD and controls ($p < 0.05$).
Conclusion: We observed that GA-Map™ Dysbiosis Test and the BMR-genomic test produce comparable results in terms of degree of variation of microbiota in IBD patients and thus both can be used to identify and characterize dysbiosis in IBD patients. Furthermore, dysbiosis as assessed by these methods seems to well correlate with biochemical activity in CD patients and thus could be considered a potential target for treatment.
Disclosure: Nothing to disclose

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P0333 VALIDATION OF THE RIDA®QUICK ADM MONITORING: A RAPID TEST FOR ADALIMUMAB DRUG CONCENTRATION MONITORING WHICH SUPPORTS TIMELY DOSE ADJUSTMENTS IN CLINICAL PRACTICE

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Introduction: Therapeutic drug monitoring of adalimumab (ADM) is increasingly implemented in clinical practice to improve clinical decision-making and maximize treatment outcomes in patients with inflammatory bowel disease (IBD). However, classical assays (e.g. ELISA) are time-consuming and require simultaneous assessment of multiple samples. Hence, timely dose adjustments and tight disease control are delayed. Here, we would like to present the validation of the RIDA®QUICK ADM Monitoring, a rapid test for adalimumab drug concentration monitoring.
Aims and Methods: The aim of our study was to validate a rapid test for the quantitative measurement of ADM drug concentrations. In the RIDA®QUICK ADM Monitoring (R-Biopharm AG, Darmstadt, Germany), serum samples are diluted 1:50 and incubated with a mixture of reagent A and B (final dilution 1:500) for 5 minutes. Next, 100 μL of the 1:500 dilution is applied to the sample pad of a lateral flow test strip and read after 15 minutes using the RIDA®QUICK SCAN II. The limit of quantification and precision were determined based on CLSI guideline EP17-A2 and EP05-A3, respectively. The recovery was determined by spiking 3 reference samples with varying concentrations of ADM and was analyzed using 2 different lots. Method comparison was performed with 212 serum samples of patients with IBD, which were withdrawn just before the next dose administration at week 0 ($n = 30$), week 4 ($n = 100$) or week 12 ($n = 82$) of ADM therapy, versus the RIDASCREEN® ADM Monitoring (ELISA; R-Biopharm AG). Both assays use the same monoclonal anti-ADM antibody clone 40D8, derived at KU Leuven.[1]
Results: The limit of quantification and measuring range of the RIDA®QUICK ADM Monitoring were 0.5 μg/mL ADM and 0.5–25 μg/mL ADM, respectively. The mean recovery (defined as the % deviation of the observed versus the expected concentration) and imprecision (%CV) were ≤ 10% and ≤ 17%, respectively. An excellent agreement with the RIDASCREEN® ADM Monitoring was observed: Pearson r and intraclass correlation coefficients (ICC) were 0.95;0.92 (Pearson r;ICC) and 0.98;0.97, for patient samples collected at week 4 and week 12, respectively. All 30 week 0 samples were below the limit of quantification in both assays.
Conclusion: The RIDA®QUICK ADM Monitoring allows accurate and precise quantification of adalimumab within the clinically relevant 0.5–25 μg/mL concentration range. The RIDA®QUICK ADM Monitoring shows excellent agreement with the RIDASCREEN® ADM Monitoring, which uses the same highly specific antibody clone to improve assay harmonization. The RIDA®QUICK ADM Monitoring is easily accessible and supports timely dose adjustments of patients receiving adalimumab treatment in routine clinical practice.
Disclosure: Chris Barthel, Karin Wagenhäuser, Daniela Fichtner, Steffen Rameil and Thomas Van Stappen are employees of R-Biopharm AG (Darmstadt, Germany).

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P0334 TARGET GOLIMUMAB LEVELS TO ACHIEVE MUCOSAL HEALING IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Golimumab is approved as a therapy for ulcerative colitis (UC) patients. Recent data also demonstrate efficacy and mucosal healing in Crohn's disease (CD); however, little is known regarding target drug levels. Our aim is to identify trough golimumab levels in IBD associated with endoscopic remission.
Aims and Methods: This was a retrospective analysis of patients on maintenance golimumab for a minimum of 4 months. Concomitant therapies, disease status at the time of levels, endoscopic and clinical response (significant reduction in symptoms and biochemical markers with weaning of steroids) were recorded. Endoscopic and radiology records approximate to the date of the assay were reviewed. Primary outcome was mucosal healing defined as Mayo 0–1 or SES-CD score < 5. Secondary outcomes included clinical remission and endoscopic improvement. Drug levels were measured with Dynacare assay, mean trough levels compared using Kruskal-Wallis test, and used logistic regression to construct a probabilistic model determining sensitivity and specificity of levels predicting mucosal healing.
Results: 55 patients were included ($n = 39$ CD, $n = 16$ UC/IBD-U). Median time on drug was 11 months (range 4–48). 34% ($n = 19$) were co-treated with an immunomodulator, 88% ($n = 49$) of patients were anti-TNF experienced and 14% ($n = 8$) had 3 or more prior biologic therapies. During induction, intravenous golimumab was used in 20% ($n = 11$), and 9% ($n = 5$) received standard induction dose with the remainder receiving higher doses. Maintenance dosing varied, ranging from 50 mg monthly to 400 mg every 2 weeks. The endoscopic response rate was 21% ($n = 9$ CD, $n = 3$ UC/IBD-U), and 45% ($n = 17$ CD, $n = 8$ UC/IBD-U) achieved mucosal healing. The rate of antibody formation was low (3.6%, $n = 2$), although the assay used was drug-sensitive which may have masked the presence of low titre antibodies. In CD, golimumab trough levels were higher in patients with mucosal healing ($n = 17$, mean 9.1 μg/ml) compared with non-response ($n = 11$, mean 4.1 μg/ml, $p = 0.001$) and in patients with endoscopic improvement ($n = 28$, mean 7.8 μg/ml) vs non-response ($n = 11$, mean 4.1 μg/ml, $p = 0.02$). After calculation of an ROC curve for mucosal healing vs non-response, AUC was 0.84 (std error 0.09, 95% CI 0.67–1, $p = 0.003$) and a trough golimumab level > 6.1 μg/ml was associated with mucosal healing with 81.3% sensitivity and 88% specificity and a likelihood ratio of 4.9. In UC/IBD-U, the

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Endpoint, n (%)	Placebo n = 103	Adalimumab n = 102	P value*
Primary Endpoint: Clinical remission (CDAI <150) at Week 4	7 (6.8)	38 (37.3)	< 0.001
Key Secondary Endpoints at Week 4:			
Clinical remission and hs-CRP reduction of 50% from baseline	0	34 (33.3)	< 0.001
Clinical response (decrease in CDAI≥70 from baseline)	28 (27.2)	69 (67.6)	< 0.001
Clinical response and hs-CRP reduction >30% from baseline	12 (11.7)	63 (61.8)	< 0.001
Clinical remission and hs-CRP <3 mg/L	0	28 (27.5)	< 0.001
Clinical remission and hs-CRP <3 mg/L, fecal calprotectin <250 μg/g	0	10 (10.8)	< 0.01
IBDQ remission (IBDQ ≥170)	21 (20.4)	41 (40.2)	< 0.01
Key Secondary Endpoint at Week 26 in Patients with Response at Week 8:	Adalimumab, n = 144		P value**
Clinical remission	93 (64.6)		< 0.001

* Compared to placebo; **Compared with clinically meaningful threshold of 30%.

mean level was higher in patients with mucosal healing (n = 8, mean 5.9 μg/ml) vs non-response (n = 5, mean 2 μg/ml, p = 0.06) although analysis was limited by lower numbers in this cohort.
Conclusion: Treatment with golimumab was associated with mucosal healing in 45% IBD patients. Higher golimumab levels were associated with mucosal healing in CD and trough levels > 6.1 μg/ml were associated with endoscopic remission.
Disclosure: Nothing to disclose

P0335 EFFICACY AND SAFETY OF ADALIMUMAB IN CHINESE PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE

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Introduction: The efficacy and safety of adalimumab induction and maintenance treatment in Chinese patients with moderately and severely active Crohn's disease (CD) were assessed in a 26-week, phase 3, randomized, double-blind, placebo-controlled, multicenter study.
Aims and Methods: Adult patients naïve to anti-TNF therapy (CD Activity Index [CDAI] 220–450, hs-CRP≥3 mg/L) were stratified by CDAI (≤300/>300) and corticosteroid use (yes/no) at baseline and randomized (1:1) to double-blind adalimumab 160/80 mg at weeks 0/2, 40 mg at weeks 4/6 or placebo at weeks 0/2 followed by blinded adalimumab 160/80 mg at weeks 4/6. At week 8, all patients received open label (OL) 40 mg adalimumab every other week for up to 18 weeks. The primary endpoint (clinical remission [CDAI < 150]) and key secondary endpoints (Table) were assessed at week 4 between adalimumab and placebo using the Cochran-Mantel-Haenszel (CMH) test and stratified by the randomization factors. Clinical remission at week 26 was assessed in patients with response (decrease CDAI≥70 points from baseline) at week 8 and compared with a clinically meaningful threshold of 30% using the 1 sample Exact test. Adverse events (AE) were collected throughout the study.
Results: Of 205 randomized patients (65 [31.7%] female, 32.9 [9.9] mean [SD] years of age and 2.7 [3.0] years disease duration), 196 (95.6%) completed the induction period and 159 (77.6%) completed OL treatment to week 26. The primary endpoint and key secondary endpoints were met (Table). Serious AEs and serious infections, respectively, were reported in 2/102 (2.0%) and 0 patients with adalimumab, 1/103 (1.0%) and 0 patients with placebo during double-blind treatment and in 36/200 (18.0%) and 7/200 (3.5%) patients receiving any adalimumab during the trial.
Conclusion: Adalimumab induced and maintained clinical remission and response in Chinese patients with CD who failed conventional therapy. The safety profile of adalimumab was generally comparable with placebo and consistent with the known safety profile of adalimumab.[1]
[Table. Primary and key secondary endpoints.]
Disclosure: B Chen: has nothing to disclose X Gao: has nothing to disclose J Zhong: has nothing to disclose J Ren: has nothing to disclose X Zhu: has nothing to disclose Z Liu: has nothing to disclose K Wu: has nothing to disclose M Chen: has nothing to disclose J Kalabic, B. Huang, T Doan, AM Robinson are AbbVie employee; may own AbbVie stock and/or options

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P0336 IMPROVED PATIENT-REPORTED OUTCOMES WITH UPADACITINIB AS AN INDUCTION THERAPY FOR PATIENTS WITH ULCERATIVE COLITIS: DATA FROM U-ACHIEVE

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Introduction: Upadacitinib (UPA) is an oral selective Janus kinase 1 inhibitor that is being assessed in patients with ulcerative colitis (UC). The effects of UPA on patient-reported outcomes (PRO) were evaluated in the double-blind placebo-controlled dose-ranging 8-week induction portion of the phase 2b/3 study (U-ACHIEVE [NCT02819635]).
Aims and Methods: Adult patients with moderately to severely active UC (Adapted Mayo score [Mayo score without Physician Global Assessment] 5–9 points and centrally-read endoscopy subscore 2–3) who had inadequate response or intolerance to immunosuppressants, corticosteroids, or biologics were randomly assigned in a 1:1:1:1:1 ratio to double-blind induction therapy with placebo (PBO) or the modified-release formulation of UPA at 7.5, 15, 30, or 45mg once daily (QD) for 8 weeks. Patients answered the following PRO questionnaires at baseline, and Weeks 2, 4, and 8: Inflammatory Bowel Disease Questionnaire (IBDQ), EuroQol-5 dimensions (EQ-5D), 36-Item Short Form Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), and Work Productivity and Activity Impairment (WPAI). Mean change from baseline to Week 8 was assessed using analysis of covariance; missing data were reported using last observation carried forward. The percentage of patients with IBDQ response, defined as increase ≥16 points from baseline to Week 8, was determined; comparisons between UPA dosage groups and PBO were based on Cochran-Mantel-Haenszel tests and missing data were reported using non-responder imputation.
Results: A total of 250 patients with mean age 42.3 years, 60% male, and mean UC duration 8 years were analysed. At baseline, mean IBDQ was 125, EQ-5D visual analogue scale (VAS) was 53, SF-36 Physical Component Summary (PCS) was 42, SF-36 Mental Component Summary (MCS) was 41, FACIT-F was 29, WPAI activity impairment was 52%, and overall work impairment was 51%. Significant improvements in all PROs were consistently observed as early as Week 2 in patients receiving 45mg QD ($p < 0.05$). At Week 8, IBDQ response was reported by significantly more patients taking UPA (67%, 62%, and 77% for 15, 30, and 45mg QD, respectively) than PBO (35%) (all $p < 0.05$). For patients treated with UPA compared to PBO, significant improvements from baseline to Week 8 were reported in IBDQ score, EQ-5D VAS, and SF-36 PCS for all UPA doses (all $p < 0.05$; Table). Significant improvements were also shown for FACIT-F and overall work impairment and activity impairment in 15, 30, and 45mg QD (Table).
[Table. IBDQ Response and Mean Change from Baseline to Week 8 in Patient-Reported Outcomes]
Conclusion: Patients with moderately to severely active UC treated with 8-week UPA induction therapy reported significant and clinically meaningful improvements in disease-specific and general health-related quality of life, fatigue, work performance, and ability to perform daily activities. Improvements in all PROs were seen as early as Week 2.
Disclosure: Financial support for the study and medical writing services (Joann Hettasch, Fishawack) was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content. Ghosh: Steering committee: Pfizer, Janssen, AbbVie, BMS, Celgene, Boehringer-Ingelheim; Speaker: AbbVie, Janssen, Takeda, Shield, Ferring, Falk. Colombel: Consultant/advisory board: AbbVie, Amgen, Boehringer-Ingelheim, Celgene, Celltrion, Enterome, Ferring, Genentech, Janssen and Janssen, Medimmune, Merck & Co, Pfizer, Protagonist, Second Genome, Seres, Shire, Takeda, Theradiag; Speaker: AbbVie, Ferring; Speaker's bureau: Amgen; Stock options: Intestinal Biotech Development, Genefit; Research grants: AbbVie, Takeda, Janssen and Janssen. Vermeire: Consulting: AbbVie, MSD, Takeda,

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	PBO n = 46	UPA 7.5mg QD n = 47	UPA 15mg QD n = 49	UPA 30mg QD n = 52	UPA 45mg QD n = 56
IBDQ response (Δ≥16)	34.8%	46.8%	67.3%**	61.5%*	76.8%**
Mean change from baseline					
IBDQ score	11.4 (n = 45)	30.8* (n = 44)	42.0*** (n = 48)	42.8*** (n = 49)	48.9*** (n = 55)
EQ-5D VAS	−1.0 (n = 44)	11.5* (n = 44)	16.4*** (n = 48)	14.3*** (n = 48)	21.5*** (n = 54)
SF-36 PCS	0.5 (n = 44)	5.4* (n = 44)	5.8*** (n = 48)	6.8*** (n = 48)	7.8*** (n = 54)
FACIT-F	3.2 (n = 44)	6.9 (n = 44)	9.2** (n = 48)	10.4*** (n = 48)	10.5*** (n = 53)
WPAI: % activity impairment	−7.7 (n = 44)	−14.8 (n = 44)	−17.1^{+} (n = 48)	−24.2** (n = 48)	−27.2*** (n = 54)
WPAI: % overall work impairment[a]	−0.8 (n = 27)	−10.5 (n = 27)	−22.6** (n = 30)	−19.1* (n = 33)	−23.0** (n = 39)

***, **, *, $^{+}$statistically significant at 0.001, 0.01, 0.05, and 0.1 level for treatment group vs PBO. [a]Only employed subjects.

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P0337 MUCOSAL 5-ASA CONCENTRATION IN THE LEFT HEMICOLON AND RECTUM IN PATIENTS WITH QUIESCENT ULCERATIVE COLITIS

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Introduction: 5-aminosalicylic acid (5-ASA) is the mainstay of treatment of patients with ulcerative colitis (UC). 5-ASA acts locally in the colonic mucosa and mucosal concentrations of 5-ASA are inversely correlated to disease activity(1–4). Previous studies suggest that treatment with Asacol (pH-dependent release formulation) yields higher mucosal 5-ASA concentrations than Pentasa (time-dependent release formulation)(1, 5). However the different 5-ASA formulations are often considered clinically equally efficient (6). After Mezavant (MMX formulation) was marketed, it has not been published studies comparing mucosal 5-ASA concentrations of Mezavant, Asacol and Pentasa.

Aims and Methods: In this cross-sectional non-randomized study, we have measured mucosal concentration of 5-ASA and its inactive metabolite acetyl-5-ASA (Ac-5-ASA) in the left hemicolon and rectum in patients with quiescent UC taking Mezavant, Asacol or Pentasa. Patients with quiescent UC using oral mesalazine monotherapy in the maximal dose recommended by the manufacturers (4.0–4.8g o.d.) were included. 8 hours after ingestion of mesalazine, patients underwent blood sample collection, followed by bowel preparation with enema and sigmoidoscopy. A total of 5 mucosal biopsies were collected 10, 25 and 40 cm from the anal verge. 5-ASA and Ac-5-ASA concentrations were measured in biopsies and serum by high-performance liquid chromatography. Disease activity was assessed by Mayo score (MS), Geboes histological score (GS) and measurement of plasma ESR, CRP, blood leukocytes and fecal calprotectin concentrations. Kruskal-Wallis test and ANOVA analyses were applied to compare demographic and clinical characteristics. Linear mixed model was used to compare the 5-ASA concentrations (log transformed) at different locations and between the different formulations.

Results: 42 patients (23 male) were included, 18 patients using Mezavant, 14 using Asacol and 10 using Pentasa. No significant differences in demographic or clinical characteristics between the groups were found, except for leukocyte concentration ($p = 0.036$) and endoscopic MS ($p = 0.01$). Mean leukocytes (SD) were all within normal ranges; 6.7 (1.4), 8.1 (2), 6.6 (1.1) for Mezavant, Asacol and Pentasa, respectively. Median (IQR) endoscopic Mayo score were 1.0 (2.0) for Mezavant and 0.0 (1.0) for both Asacol and Pentasa. 67% of Mezavant, 79% of Asacol and 70% Pentasa patients were in deep remission (GS < 2.1 and endoscopic MS ≤1), $p = 0.750$. The geometric mean 5-ASA concentrations for Mezavant, Asacol and Pentasa, averaged over locations were 2.39 (CI 1.09–5.28) ng/mg, 1.60 (CI 0.65–3.91) ng/mg and 0.57 (CI 0.20–1.64) ng/mg, respectively ($p = 0.099$, test for overall difference in adjusted mean). When adjusting for remission the results did not change notably. Whereas the inter-individual difference was large, the intra-individual variation was small. The pairwise comparisons revealed a significant difference between Mezavant and Pentasa ($p = 0.033$), but not between Mezavant and Asacol ($p = 0.50$). The mucosal concentration of Ac-5-ASA decreased in oral to anal direction, and did not differ between the formulations. There was no significant differences in serum 5-ASA ($p = 0.202$) or serum Ac-5-ASA ($p = 0.20$) between the formulations.

Conclusion: Patients using Mezavant had significantly higher mucosal 5-ASA concentrations than patients using Pentasa, despite higher endoscopic MS. There was small intra-individual variations, but large inter-individual variations in mucosal 5-ASA concentrations in the left hemicolon of patients with UC using oral mesalazine preparations.

Disclosure: Nothing to disclose

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P0338 EFFICACY OF MIRIKIZUMAB ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ULCERATIVE COLITIS: A RANDOMISED, DOUBLE-BLIND, CONTROLLED, PHASE 2 STUDY

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Introduction: The efficacy and safety of mirikizumab (miri), an IL-23p19 antibody, has been evaluated in moderate-to-severe ulcerative colitis (UC) in a phase 2, randomized, double-blind, placebo (pbo)-controlled trial (AMAC, NCT02589665; presented at DDW 2018). Miri demonstrated efficacy on multiple measures in the 12-week induction treatment.

Aims and Methods: This analysis evaluated the effects of miri on health-related quality of life (HRQoL) in patients with UC. Patients with moderate-to-severe UC (Mayo score 6–12; Endoscopic subscore ≥2) were randomised 1:1:1:1 to receive intravenous miri 50 mg (N = 63) or 200 mg (N = 62), both with possible exposure-based increase (2–12 fold or 1.5–3 fold, respectively, to a maximum 600 mg dose), or fixed dose miri 600 mg (N = 61), or pbo (N = 63) at Weeks 0, 4, and 8. Patients could receive oral 5-ASA, corticosteroids (≤20 mg/d prednisone equivalent), or thiopurines; must have failed ≥1 conventional UC therapy; and were either naïve to or had prior exposure to biologics. HRQoL was measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) and evaluated using a mixed model repeated measures (MMRM) analysis. The percentage of patients at Week 12 with clinical response,[1] endoscopic healing,[2] IBDQ total score ≥170, and IBDQ improvement ≥16 were also assessed.

Results: As early as Week 4, and continuing through Week 12, IBDQ total scores improved versus baseline and versus pbo across all miri groups except miri 50 mg versus pbo at Week 12 (Table). At Week 12, the proportions of patients with IBDQ total score ≥170 were higher with miri 50 mg, 200 mg, and 600 mg than

pbo (44%, 56%, 54% vs. 30%, respectively) and higher proportions of miri- than pbo-treated patients had improvements ≥16 points from baseline in IBDQ total score. At Week 12, clinical response and endoscopic healing rates were greater for miri 50 mg and 200 mg versus pbo (Table).

	Pbo	Miri 50 mg	Miri 200 mg	Miri 600 mg
	N = 63	N = 63	N = 62	N = 61
Baseline IBDQ total score, mean (SD)	124 (30)	123 (29)	133 (35)	126 (34)
IBDQ total score change from baseline, LS mean (SE)				
Week 4	14 (3)	24 (3)[a,c]	29 (3)[b,c]	27 (3)[a,c]
Week 12	22 (4)	33 (5)[c]	42 (4)[b,c]	44 (5)[b,c]
Clinical response at Week 12, n (%) NRI	13 (21)	26 (41)[a]	37 (60)[b]	30 (49)[a]
Endoscopic healing at Week 12, n (%) NRI	4 (6)	15 (24)[a]	19 (31)[b]	8 (13)

Nominal p-value, vs. placebo [a]$p < 0.05$, [b]$p < 0.001$; vs. baseline [c]$p < 0.001$; MMRM includes baseline, geographic region, prior biologic therapy, treatment, time and treatment*time as variables (IBDQ) or logistic regression to compare rates (clinical response, endoscopic healing). NRI: nonresponder imputation, used for missing values.
[1]Clinical response: 9-point Mayo subscore decrease ≥2 points and ≥35% change from baseline, with rectal bleeding = 0,1 or decrease ≥1, excluding PGA. [2]Endoscopic healing: Mayo endoscopic subscore = 0 or 1.
Conclusion: Induction treatment with miri was associated with HRQoL improvement in patients with UC. These are the first data evaluating the effects of an IL-23p19 antibody on the HRQoL of patients with UC.
Disclosure: Drs. Sandborn, Ferrante, Bhandari, D'Haens, Berliba, and Feagan report consulting fees and/or research grants from and/or have participated in speaker's bureau for and/or have participated on a scientific advisory boards for commercial interests including Eli Lilly and Company, and/or are on the board of directors of various organizations. J Laskowski is an employee of Eli Lilly and Company. P Klekotka, M Durante, J Tuttle, and A Naegeli are employees and/or shareholders of Eli Lilly and Company.

P0339 COMPARATIVE FREQUENCY OF CLOSTRIDIAL INFECTION IN PATIENTS WITH ULCERATIVE COLITIS RECEIVING MESENCHYMAL STROMAL CELLS AND BIOLOGICAL PREPARATIONS

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Introduction: Patients with inflammatory bowel disease (IBD) experienced more frequent development of Clostridial infection and much higher rates of morbidity and mortality compared to patients without IBD. Risk factors are immunosuppressive therapy.
Aims and Methods: The aim is to compare the frequency of Clostridial infection (CI) in patients with ulcerative colitis (UC) receiving bone marrow mesenchymal stromal cells (MSC) and biological therapy.
Materials and methods. The patients were divided into 3 groups: the first group (n = 23) received the MSCs culture according to the scheme (0-1-2 weeks, then every 26 weeks); the second group of patients with UC (n = 21) received infliximab (IFX) in combination with azathioprine (AZA) according to the recommended scheme, the third group received only IFX according to the scheme. The toxins A and B of *Clostridium difficile* were determined by the enzyme immunoassay in the stool. The comparative analysis was carried out using the method of 4-field tables using nonparametric statistical criteria.
Results: In patients of the 1st group, toxin A was detected in 1/23 patients (4.3%), in the 2nd group - in 2/21 (9.5%) (RR - 0.45, 95% CI 0.04–4.6, x^2 −0.46, p > 0.05), in the third - in 2/18 (11.1%) (RR-0.4, 95% CI 0.04–3.98, x^2- 0.7, p > 0.05). In patients of the 1st group, toxin B was detected in 2/23 patients (8.6%), in the second group in 3/21 (14.3%) patients (RR −0.6, 95% CI 0, 1–3.3, x^2 −0.3, p > 0.05), in the third - in 2/18 (11.1%) (RR-0.8, 95% CI 0.12–5, 03; x^2 −0.07; p > 0.05). In patients of the 1st group toxins A and B were not detected - 0/23 (0,0%), in the 2nd group toxins A and B were detected in 7/21 (33.3%) patients (x^2 - 9.5, $p < 0.05$), in the third - in 5/18 (27.8%) (x^2 −7.3, $p < 0.05$). Totally in patients of the 1st group, *Clostridium difficile* toxin A and B was detected in 3/23 patients (13.1%), in the second group - in 12/21 (57.1%) patients with UC (RR-0.23, 95 % CI 0.075–0.7, x^2 -9.5, $p < 0.05$), in the third - in 9/18 (50.0%) (RR-0.26, 95% CI 0.08- 0.82, x^2 -6.6, $p < 0.05$).
Conclusion: The frequency of Clostridial infection in patients with ulcerative colitis receiving mesenchymal stromal cells is significantly lower than in patients with ulcerative colitis receiving biological immunosuppressive preparations.
Disclosure: Nothing to disclose

P0340 CORRELATION OF BIOMARKERS OF INFLAMMATION WITH CLINICAL AND ENDOSCOPIC ENDPOINTS IN PATIENTS WITH MODERATE-TO-SEVERE CROHN'S DISEASE: DATA FROM CELEST

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Introduction: Treatment with upadacitinib (UPA) has shown dose-dependent improvements in clinical and endoscopic outcomes and markers of inflammation in a Phase 2b study (CELEST; NCT02365649) in patients with Crohn's disease (CD) (1,2). In this report, the correlation between the markers of inflammation serum C-reactive protein (CRP) and faecal calprotectin (FC), and clinical and endoscopic endpoints is assessed.
Aims and Methods: CELEST enrolled 220 adults with moderately to severely active CD who received induction treatment with placebo or the immediate release formulation of UPA 3 mg, 6 mg, 12 mg, 24 mg twice daily (BID), or 24 mg once daily (QD) for 16 weeks. Patients who completed Week 16 were re-randomised to receive UPA 3 mg, 6 mg, 12 mg BID, or 24 mg QD for 36 weeks. For this analysis, patients who received UPA induction treatment (N = 183, combined) were included in the Week 16 evaluation, and patients who achieved clinical response to UPA at Week 16 (N = 94, combined) were included in the Week 52 evaluation.
The proportion of patients who achieved clinical remission at Week 16 and 52 (stool frequency [SF]≤2.8 and abdominal pain [AP]≤1.0, neither worse than baseline [BL]), and endoscopic improvement at Week 12/16 and 52 (decrease in SES-CD > 50% from BL or endoscopic remission; defined as SES-CD ≤4 and ≥2-point reduction from baseline, with no subscore of > 1) were analysed by high sensitivity (hs)CRP (< 5 or ≥5 mg/L) and FC (< 250 or ≥250 μg/g) levels at Week 16 and 52 using Chi-square test. Correlation between clinical remission and endoscopic improvement (yes/no) with hsCRP (< 5 or ≥5 mg/L) and FC (< 250 or ≥250 μg/g) levels at BL and Week 16 or 52 was assessed with polychoric correlation and 2-sided Wald Chi-square test.
Results: A statistically significant higher proportion of patients with hsCRP levels < 5 mg/L at Week 16 and 52, and FC levels < 250 μg/g at Week 52 achieved clinical remission compared to patients with hsCRP ≥5 mg/L and FC ≥250 μg/g, respectively (Table). Significantly more patients with hsCRP < 5 mg/L and FC < 250 μg/g at both Weeks 12/16 and 52 achieved endoscopic improvement. Moderate to high correlation was observed between hsCRP status (elevated at BL and < 5 mg/L at Week 16) and clinical remission at Week 16 ($\rho = 0.59$, $p < 0.001$), and endoscopic improvement at Week 12/16 ($\rho = 0.50$, $p < 0.001$) or hsCRP status (elevated at BL and < 5 mg/L at Week 52) and clinical remission at Week 52 ($\rho = 0.73$, $p < 0.001$), and endoscopic improvement at Week 52 ($\rho = 0.78$, $p < 0.001$). Moderate to high correlation was observed for FC status (elevated at BL and < 250 mg/L at Week 16 [$\rho = 0.68$, $p < 0.001$] or elevated at BL and < 250 mg/L at Week 52 [$\rho = 0.52$, $p = 0.006$]) and endoscopic improvement at Week 16 and Week 52. A high correlation between clinical remission and FC status was only observed at Week 52 (elevated at BL and < 250 mg/L at Week 52; $\rho = 0.60$, $p < 0.001$).

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		hs-CRP			Faecal calprotectin		
Endpoint	Week	< 5 mg/L	≥5 mg/L	P value	< 250 μg/g	≥250 μg/g	P value
Clinical Remission*, n/N (%)	16	26/68 (38.2)	14/71 (19.7)	0.016	8/32 (25.0)	20/58 (34.5)	0.352
Clinical Remission*, n/N (%)	52	27/37 (73.0)	8/31 (25.8)	< 0.001	21/27 (77.8)	10/24 (41.7)	0.008
Endoscopic improvement^, n/N (%)	12/16	29/73 (39.7)	12/77 (15.6)	< 0.001	17/31 (54.8)	11/62 (17.7)	< 0.001
Endoscopic improvement^, n/N (%)	52	26/39 (66.7)	10/33 (30.3)	0.002	20/28 (71.4)	9/25 (36.0)	0.010

Data are reported as observed * Clinical remission defined as very soft/liquid stool frequency (SF)≤2.8 and abdominal pain (AP) score ≤1.0, both not worse than baseline, among subjects with baseline very soft/liquid SF > 4.0 or AP score > 2.0 ^Endoscopic improvement defined as a decrease in SES-CD > 50% from BL or endoscopic remission (SES-CD ≤4 and ≥2-point reduction from baseline, with no subscore of > 1)

[Proportion of patients meeting clinical and endoscopic endpoints by hsCRP and faecal calprotectin status Week 12/16 and 52.]

Conclusion: In this phase 2b study with upadacitinib, normalization of hsCRP levels was associated with achieving clinical remission and endoscopic improvement, whereas normalization of FC levels was mostly associated with endoscopic improvement.

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P0341 EARLY INFLIXIMAB TROUGH LEVELS PREDICT LATE EFFICACY OF INFLIXIMAB IN A RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH ACTIVE CROHN'S DISEASE COMPARING CT-P13 AND INNOVATOR INFLIXIMAB

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Introduction: We demonstrated similarity of efficacy, safety and pharmacokinetics (PK) between CT-P13 and Innovator Infliximab (INX) in the phase 3 randomized control trial in moderate to severe Crohn's disease (CD) patients (1). Recent studies suggested an association between higher infliximab trough concentrations and better clinical outcomes in the treatment of inflammatory bowel disease (2), which has to be examined in a prospective observation.

Aims and Methods: This *post-hoc* analysis of the CT-P13 3.4 study (NCT02096861) assessed whether early C_{trough} level could be used as a predictor of subsequent clinical efficacy. A total of 198 patients who underwent efficacy analysis at Week 54 and had PK parameters at Week 6 (pre-dose concentration at Week 14) and Week 14 (pre-dose concentration at Week 22) were included in this analysis. All PK parameters were analyzed while the patients received INX or CT-P13 at 5 mg/kg with no dose escalation until week 22. Mann-Whitney U test was used to analyze the difference of C_{trough} level in patients achieving or not achieving clinical response at Week 54, and between CT-P13 and INX treatment groups among responders. Receiver operating characteristic (ROC) curves were constructed for sensitivity (S) and specificity (Sp) analyses of C_{trough} and efficacy at Week 54.

Results: Median Week 6 C_{trough} levels were 3.7 and 3.6 μg/ml, and Week 14 C_{trough} levels were and 2.6 and 2.2 μg/ml in the CT-P13 and INX groups, respectively. C_{trough} levels were significantly higher ($p < 0.01$) in Week 54 responders (CDAI < 150) than in non-responders in both CT-P13 and INX treatment groups. Since overall C_{trough} levels in responders were not significantly different between CT-P13 and INX treatment groups ($p > 0.05$), both groups were pooled for further analysis. In a ROC analysis, Week 14 C_{trough} were much more specific to predict clinical success (specificities > 90%) than Week 6. Suggested diagnostic cut-offs to predict clinical remission were C_{trough} > 4.5 μg/ml at Week 6 (ROC: 0.71 S: 51.2%, Sp: 77.1%), and, 4.0 μg/ml at Week 14 (ROC: 0.71, S: 39.7%, Sp: 93.3%). *[C_{trough} level in the CT-P13 and INX according to clinical response at Week 54]*

Conclusion: Week 6 C_{trough} and Week 14 C_{trough} of CT-P13 and INX have predictive value for late efficacy (Week 54) in terms of CDAI-70, CDAI-100, and remission. There was no difference in C_{trough} levels among responders between CT-P13 and INX. We suggest a critical minimum of C_{trough} level > 4.5 μg/ml at Week 6, and C_{trough} level > 4.0 μg/ml at Week 14 as a predictor of subsequent clinical remission. In addition, Week 14 levels appear to be more specific to predict one year outcome than Week 6 levels.

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P0342 ADDITIONAL POWER OF ELEMENTAL DIET ON MAINTENANCE BIOLOGICS THERAPY IN CROHN'S DISEASE (ADORE STUDY) - A MULTICENTER, PROSPECTIVE, COHORT STUDY

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Introduction: Although concomitant elemental diet (ED) and anti TNF-alfa inhibitor (Anti-TNF) is known to be effective as a maintenance therapy for Crohn's disease (CD), there is no prospective study on this topic. The aim of this study is to clarify an additional power of ED diet on maintenance Anti-TNF.

Aims and Methods: 17 institutions participated this multicenter, prospective, non-randomized cohort study. CD patients who received initial Anti-TNF induction therapy and provided informed consent for this study were enrolled. Patients who achieved clinical response (defined as delta CDAI > 70 and CDAI < 200) at 10–14 weeks after the starting of infliximab (IFX, 5mg/kg at 0, 2, 6 weeks) or adalimumab (ADA, 160mg at 0, 80mg at 2 weeks) were included. Eligible patients took a tolerability examination of ED (900kcal/day) at least for 3 days. Then patients who prefer to ED during Anti-TNF maintenance therapy

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	CT-P13 Median(IQR) (μg/ml)			INX Median(IQR) (μg/ml)		
Week 6 C_{trough}	Responder	Non-responder	p-value	Responder	Non-responder	p-value
CDAI-70	3.90 (2.05–7.07)	2.42 (0.55–5.93)	0.088	3.76 (2.15–6.95)	1.72 (0.76–4.85)	0.026
CDAI-100	3.96 (1.80–7.30)	2.88 (0.55–5.56)	0.083	4.02 (2.15–7.16)	2.17 (0.91–4.20)	0.018
Clinical remission	4.9 (2.32–8.06)	1.72 (0.55–4.39)	0.001	4.45 (2.5–8.49)	2.17 (0.91–3.71)	0.0005
Week 14 C_{trough}	**Responder**	**Non-responder**	**p-value**	**Responder**	**Non-responder**	**p-value**
CDAI-70	2.98 (0.74–6.14)	0.61 (0.55–1.42)	0.020	2.47 (0.88–4.14)	0.55 (0.55–2.35)	0.012
CDAI-100	2.98 (0.74–6.14)	0.61 (0.55–2.13)	0.016	2.85 (0.94–4.6.)	0.61 (0.55–2.11)	0.004
Clinical remission	3.40 (1.14–6.56)	0.68 (0.55–2.54)	0.0002	3.11 (0.94–6.03)	1.17 (0.55–2.68)	0.001

Note. Lower limit of quantitation of serum Infliximab concentration was 0.55 μg/ml

(IFX: 5mg/kg every 8 weeks, ADA: 40mg every other weeks) and confirmed tolerability of ED were allocated to ED group and administered elemental diet 900kcal/day or more. Other patients were allocated to Non-ED group. Primary endpoint was the cumulative remission rate at 2 years after baseline. CDAI was calculated at each visit during 2 years after baseline. Clinical relapse defined as 200 < CDAI and/or need for additional treatment including dose escalation of Anti-TNF and surgery. Adherence of ED was confirmed by clinician's interview to patients at each visit and amount of prescriptions.
Results: 88 patients were enrolled and 16 patients were excluded due to no response of Anti-TNF induction therapy. Of the 72 patients, 37 were allocated to ED group and 35 subjects were allocated to Non-ED group. As for clinical features, previous enteral nutrition was more frequent observed in ED group ($p = 0.03$). The cumulative remission rate at 2 years was no significant difference between two groups (60.9% in ED group, 56.7% in Non-ED group, $p = 0.98$). In a multivariate analysis, intestinal stricture (HR: 5.0, 95% CI: 1.6–15.2), previous steroid therapy (HR: 4.0, 95% CI: 1.1–14.9) and CRP > 5mg/L (HR: 6.5, 95% CI: 1.8–24.4) at baseline were risk factors of clinical relapse. Adherence of ED in ED group was relatively low and only 11 patients had been kept 900kcal /day or more of ED.
Conclusion: Additional power of ED for CD patients who responded to initial Anti-TNF induction therapy could not be confirmed. Efficacy of concomitant ED in other clinical setting such as loss of response need to be clarified in the future. Moreover, improvement of adherence might be important in order to obtain clinical efficacy of ED.
Disclosure: Nothing to disclose

P0343 EARLY OPTIMIZATION OF GOLIMUMAB DOSE INDUCES DELAYED RESPONSE AND LONG-TERM CLINICAL BENEFIT IN ULCERATIVE COLITIS

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Introduction: Data assessing outcomes of SC golimumab (GLM) dose optimization in patients with ulcerative colitis (UC) are lacking. According to the summary of product characteristics by the European Medicines Agency (EMA) patients with body weight less than 80 kg received GLM maintenance doses of 50 mg every 4 weeks (q4wk) starting at week 6 (1). The benefit of GLM dose escalation from 50 mg q4wk to 100 mg q4wk has not been evaluated in clinical practice.
Aims and Methods: The aim of this study was to evaluate outcomes of early optimization of GLM from 50 mg q4wk to 100 mg q4wk in UC patients with inadequate response to GLM induction treatment.
This observational multicentre cohort study included consecutive UC patients without response to GLM induction doses, in which weight-based GLM maintenance doses (according to European labelling) of 50 mg q4wk were optimized to 100 mg q4wk before week 14. At week 14, we assessed outcomes based in partial Mayo score. We defined response as an improvement ≥3 points from week 0 and remission as a final score ≤2. Long-term cumulative probabilities of GLM failure-free survival and colectomy-free survival were calculated during follow-up. GLM failure was defined as discontinuation of the drug due to intolerance or complete loss of response despite dose optimization.
Results: We evaluated 24 UC patients with body weight below 80 kg, 18 (75%) were female, 18 (75%) had extensive colitis and 5 (20%) left-sided colitis. The mean age of the patients was 47 (standard deviation 14), and the median disease duration was 9.5 years (interquartile range [IQR] 4–14). 14 patients (58%) had previous anti-TNF failure (4 infliximab, 2 adalimumab and 8 both). All patients received induction with GLM 200 mg/100 mg at weeks 0 and 2. In all patients GLM 50 mg q4wk was optimized to 100 mg q4wk, starting at week 6 in 10 patients and at week 10 in 14 patients. At week 14, 16 of 24 patients (67%; 12 were corticosteroid-free) recovered clinical response. Of these, 4 patients (17%) achieved corticosteroid-free remission. After a median follow-up of 12 months (IQR 10–22), 13 of 24 patients (54%) avoided GLM failure. 13 of 16 patients (81%; all but 1 were corticosteroid-free) who achieved delayed response at week 14 maintained clinical benefit with GLM 100 mg e4wkat last follow-up. Eleven of 24 patients (46%) had GLM failure. Reasons for GLM discontinuation were nonresponse at week 14 in 8 patients (73%) and secondary loss of response in 3 patients (27%) who had delayed response at week 14. None of the patients experienced adverse events leading to GLM withdrawal. All 24 patients avoided colectomy at last follow-up. None of the patients were dose de-escalated to GLM 50 mg q4wk.
Conclusion: Early optimization of GLM from 50 mg q4wk to 100 mg q4wk induces delayed response (by partial Mayo score) at week 14 in two thirds of UC patients with body weight below 80 kg who were non-responders to GLM induction. Continuing GLM 100mg q4wk in patients who do not demonstrate an early clinical response to GLM induction but achieve a delayed response was safe and leads to long-term clinical benefit.
Disclosure: CT has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, and Gebro Pharma. The remaining authors declare that they have nothing to disclose.

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P0344 BASELINE DEMOGRAPHIC FEATURES OF ULCERATIVE COLITIS PATIENTS AS PREDICTORS OF CLINICAL RESPONSE TO ADSORPTIVE DEPLETION OF MYELOID LINEAGE LEUCOCYTES AS REMISSION INDUCTION THERAPY

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Introduction: Inflammatory bowel disease (IBD) is associated with elevated myeloid lineage leucocytes, which show activation behaviour (1) including the CD14+CD16+DR++ phenotype known as proinflammatory monocytes and a major source of tumour necrosis factor-α (2). Accordingly selective depletion of myeloid leucocytes by granulocyte/monocyte apheresis (GMA) with an Adacolumn is expected to promote remission and enhance drug efficacy. However, hitherto studies in IBD have reported contrasting efficacy outcomes, ranging from an 85% (3) to a statistically insignificant level (4). Patients' demographic features should guide to select responder patients.
Aims and Methods: In a single-centre retrospective setting, we looked at the baseline clinical and endoscopic features of responders and non-responders to adsorptive GMA in 145 consecutive ulcerative colitis patients who had undergone GMA as remission induction therapy. 73 patients were steroid naive, 70 were steroid dependent, and 2 were steroid refractory. Patients had received up to 11 GMA sessions over 10 weeks. At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her or his own control. Clinical activity index (CAI) ≤4 was defined as remission. Biopsies from endoscopically detectable inflamed mucosa were processed to see the impact of GMA on leucocytes within the mucosa.
Results: At entry, the average CAI was 12.8, range 10–17. 93 patients (64.1%) had responded to GMA, 52 of 73 steroid naïve (71.2%), 40 of 70 steroid dependent (57.1%), and 1 of the 2 steroid refractory cases. On average remission was sustained for 8.6 months in steroid naïve patients and for 10.4 months in steroid dependent cohort. Mucosal biopsies revealed that infiltrating leucocytes were mostly neutrophils and monocytes. There was a marked reduction of infiltrating leucocytes in the biopsies from the responder patients. Patients with extensive deep UC lesions together with loss of the mucosal tissue at the lesions were non-responders. Patients with the first UC episode were identified as the best responders (100%), followed by steroid naive patients. Further, a short duration of active UC prior to GMA marked a patient as a likely responder.
Conclusion: Patients who responded well to GMA attained a favourable long-term clinical course. GMA was more effective if applied immediately after a relapse than after a lag time. In general, GMA is favoured by patients for its safety profile and for being a non-drug remission induction option. Patients with extensive deep ulcers, with long duration of UC refractory to multiple pharmacologicals are unlikely to benefit from GMA. In therapeutic settings, knowing baseline features, which may identify responder patients should help to avoid futile use of medical resources.
Disclosure: Nothing to disclose

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P0345 ANTI-TNF INDUCED LUPUS (ATIL) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Anti-tumour necrosis factor alpha (anti-TNF) therapies are effective and widely used in the management of patients with inflammatory bowel disease (IBD). Patients may develop a distinct 'lupus like' syndrome, recently termed anti-TNF induced lupus (ATIL). The widely-accepted diagnostic criteria for this syndrome being (1) a temporal relationship between symptoms and anti-TNF therapy and resolution of symptoms following cessation of the offending medication, (2) at least 1 serologic American College of Rheumatology criteria of systemic lupus erythematosus (SLE), either a positive ANA or anti-dsDNA, and (3) at least 1 non-serological criteria such as arthritis, serositis or rash (1). ATIL is increasingly recognised and described in the rheumatology literature, however, data remains limited in IBD populations due to lack of recognition of the condition as well as difficulty making a diagnosis as there is significant overlap in symptoms with the extraintestinal manifestations of IBD.
Aims and Methods: To evaluate the incidence, clinical and serological markers, as well as risk factors for developing ATIL in an IBD population. A retrospective observational cohort study of all IBD patients that completed induction as well as at least one maintenance dose of anti-TNF therapy (infliximab or adalimumab) at Royal Perth Hospital between January 2008 and December 2017. A diagnosis of ATIL was confirmed based on the criteria outlined above. Demographic, clinical and serological parameters were obtained from electronic and paper records.
Results: 454 patient treatment courses with anti-TNF therapy (300 infliximab and 154 adalimumab) were included. 17 (5.7%) patients that received infliximab and 1 patient (0.6%) on adalimumab developed ATIL. Patients that developed ATIL were more likely to be older at commencement of anti-TNF (46.47 years ± 13.79 years vs. 38.85 years ± 14.75 years, $p = 0.033$) and there was a trend they were more likely to be female (72.2% vs. 47.0%, $p = 0.052$). 5/18 patients were on concurrent immunomodulator therapy at time of ATIL diagnosis. We were unable to establish whether concurrent immunomodulator therapy was a preventative factor, as patients were on varying doses and durations during their anti-TNF course. The mean duration of anti-TNF therapy till development of ATIL was 19.78 months ± 15.76 months. The most common clinical symptom was polyarthritis in 15 patients (83.3%) with rash occurring in 5 patients (27.8%). All patients with a diagnosis of ATIL demonstrated an elevated ANA with results ranging from 7 to 30 IU/ml. In those patients who had a baseline ANA performed prior to commencing anti-TNF therapy (14 patients), the ANA level increased compared with their baseline level. Other serological markers in patients that developed ATIL included anti-dsDNA in 10/15 (67%), anti-histone antibodies (marker for drug induced lupus) 2/15 (13%), anti-Smith antibodies (marker for idiopathic SLE) 0/15 (0%), Rheumatoid Factor (autoimmune arthropathy) 0/8 (0%) and anti-CCP (Rheumatoid arthritis) 0/5 (0%).
Conclusion: Our study suggests, 1 in every 20 patients that commences infliximab will develop ATIL. The incidence of ATIL, 5.7% for infliximab and 0.6% for adalimumab are much higher than post-marketing study reports of 0.22% and 0.10% respectively (2). Older age at commencement of therapy is a risk factor for development. A panel of serological markers is useful to confirm the diagnosis and exclude other autoimmune conditions, which may mimic ATIL. Increasing recognition of the condition and diagnostic criteria among physicians treating patients with IBD is essential.
Disclosure: Nothing to disclose

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P0346 MEDICAL AND SURGICAL MANAGEMENT OF INFLAMMATORY BOWEL DISEASE: AN INTERNATIONAL COMPARISON BETWEEN CHINA, INDIA, AND THE UNITED STATES

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Introduction: Although the prevalence of inflammatory bowel disease (IBD) continues to rise globally, particularly in Asia, there exists limited knowledge regarding the variation in IBD management among different countries.
Aims and Methods: We evaluated the differences in medical and surgical management within 1 year (yr) of diagnosis (dx) of Crohn's disease (CD) and ulcerative colitis (UC) for patients recruited from China, India, and the United States (US). Patients, during a clinic visit or online, completed a questionnaire, which collected demographic and clinical characteristics, medication history (amino-salicylates [ASA], immunomodulators [IMM], biologics, and steroids), and types and dates of IBD-related surgeries. Multivariable logistic regressions examine the differences in medication use and surgical history by country.
Results: Of 746 recruited participants, CD patients were more likely to participate in China (68%) and the US (55%); more UC patients participated in India (74%). Age at dx ranged from 4 to 77 yrs. Duration of disease at the time of questionnaire was greater in the US (13 yrs) compared to China and India (3 yrs). Majority of IBD participants were female (57%) in China and the US; fewer CD (21%) and UC (43%) females were recruited from India. ASAs were commonly used within 1 yr of CD (India 88%, US 49%, China 45%) and UC (India 94%, China 87%, US 57%) dx. Steroids were similarly used within 1 yr of CD (India 71%, US 43%, China 31%) and UC (India 66%, US 38%, China 32%) dx. IMM use within 1 yr varied by country and IBD type, and it was more commonly used for CD (China 30%, US 26%, India 25%) than UC (India 31%, US 15%, China 6%). Among those diagnosed in 2008 and later (when biologics were available in all countries), biologics were most commonly used within 1 yr of dx in the US (28%), followed by China (12%) and India (2%). After adjustment of diagnosis after 2008, participants with CD from the US (Odds Ratio [OR], 95% Confidence Interval [CI]: 23.1, 8.7–61.1) were more likely to report ever use of biologics relative to those in China. UC participants from the US (OR, 95% CI: 14.0, 0.01–4.7) were also more likely to have used biologics relative to China. IBD-related surgery was reported in China (26%), the US (21%), and India (4%). For CD, surgery within 1 yr was common in China (13%), the US (10%), and India (8%). For UC, surgery within 1 yr was more common in China (2%) than the US (1%) and India (0%). After adjustment, CD participants from China (OR, 95% CI: 2.06, 1.03–4.10) were more likely to undergo IBD-related surgery relative to the US; there were no differences among countries in odds of surgery for UC.
Conclusion: IBD patients in India and China, relative to those in the US, were less likely to report the use of biologics within 1 year of disease diagnosis, but were equally likely to utilize ASA and steroids, Additionally, IBD patients in China were more likely to undergo surgery for CD. Our findings may reflect the differential availability of biologics among these countries. Barriers to health-care access, including IBD specialist availability and medication costs, or varying disease activity may play a role in management disparities. Further research to evaluate the underlying reasons for variation in utilization may be integral to globally optimizing pharmacologic therapy and surgery for patients with IBD.
Disclosure: Nothing to disclose

P0347 EXPOSURE-RESPONSE ANALYSES OF UPADACITINIB (ABT-494) EFFICACY IN SUBJECTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS-ANALYSES OF A PHASE 2 DOSE RANGING INDUCTION STUDY

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Introduction: Upadacitinib (ABT-494) is an oral selective JAK1 inhibitor currently in development for the treatment of several inflammatory diseases including ulcerative colitis (UC).
Aims and Methods: To characterize the pharmacokinetics of upadacitinib and the exposure-response relationships for the effect of upadacitinib on different efficacy endpoints, following 8 week induction treatment in subjects with moderately to severely active UC who have had inadequate response, loss of response or intolerance to corticosteroids, immunosuppressants or biologic therapies in the Phase 2b Study U-Achieve. The analyses dataset included 250 subjects randomized to upadacitinib extended-release 7.5 mg [once-daily (QD); N = 47], 15 mg QD (N = 49), 30 mg QD (N = 52), 45 mg QD (N = 56) or placebo (N = 46). Upadacitinib population pharmacokinetic model was developed using pooled data from Phase 1 single and multiple ascending dose studies (intensive sampling), and available data from Phase 2 studies in subjects with rheumatoid arthritis, Crohn's disease, atopic dermatitis, and UC (sparse sampling). Quartile plots were generated for graphical exploration and population models using logistic regression analyses were developed to characterize the relationships between upadacitinib average plasma exposure over the dosing interval and efficacy endpoints (clinical response & clinical remission per adapted Mayo, clinical remission per full Mayo, endoscopic improvement and endoscopic remission) at Week 8. Effect of key demographic and baseline disease characteristics on upadacitinib exposure-response relationships was also explored.
Results: Upadacitinib plasma exposures increased dose proportionally in UC patients and were comparable to those previously observed in healthy subjects. A significant exposure-dependent increase in efficacy was observed. Highest percentage of subjects achieving clinical response per adapted Mayo, clinical remission per adapted and full Mayo, endoscopic improvement and endoscopic remission were associated with the upadacitinib exposures corresponding to the 45 mg QD dose. With the exception of endoscopic remission, the plateau of key efficacy endpoints (clinical remission, clinical response, and endoscopic improvement) was established at Week 8 within the range of exposures evaluated. The exposure-response relationship was comparable between percentage of subjects achieving clinical remission per adapted and full Mayo scores. Simulation results using the final exposure-response models for a population similar to that evaluated in Phase 2b are shown in the Table for the key efficacy endpoints at Week 8, and for different upadacitinib induction regimens. A dose lower than 45 mg QD is predicted to provide lower efficacy across endpoints (~2% to 10% relative to 45 mg QD).
Conclusion: Upadacitinib plasma exposures were comparable to those previously observed in healthy subjects. Upadacitinib exposures corresponding to the 45 mg QD regimen are predicted to maximize the efficacy in subjects with UC.

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Endpoint, Median Predicted Efficacy, % (5th-95th Percentile); NRI	Placebo	7.5 mg QD	15 mg QD	30 mg QD	45 mg QD
Clinical Remission per Adapted Mayo	0	7 (4–10)	12 (9–14)	16 (14–20)	19 (16–22)
Endoscopic Improvement	2 (0–4)	15 (13–18)	23 (20–27)	32 (28–36)	35 (31–38)
Clinical Remission per Full Mayo	0	6 (4–8)	10 (8–12)	15 (13–18)	17 (14–20)
Clinical Response per Adapted Mayo	12 (9–17)	28 (25–31)	38 (34–42)	47 (44–51)	52 (48–56)
Endoscopic Remission	2 (1–4)	3 (2–5)	4 (3–6)	9 (7–12)	19 (16–22)

NRI: Non-responder imputation
Clinical remission per adapted Mayo: stool frequency subscore ≤ 1, rectal bleeding subscore of 0, and endoscopic subscore ≤ 1
Endoscopic improvement: endoscopic subscore ≤ 1
Clinical remission per full Mayo: full Mayo score ≤ 2 with no subscore > 1
Clinical response per adapted Mayo: decrease from baseline in the adapted Mayo score ≥ 2 points and $\geq 30\%$ from baseline, PLUS a decrease in rectal bleeding subscore (RBS) ≥ 1 or an absolute RBS ≤ 1
Endoscopic remission: endoscopic subscore of 0.
*[Table Exposure-Response Model-Predicted Efficacy Endpoints at Week 8 In Subjects with UC for Different Upadacitinib Regimens**
**Simulation for 200 replicates, each with 600 subjects (400:200 upadacitinib:placebo) per dosing regimen. The 90% prediction intervals (5th-95th percentile) reflect the impact of random sampling of subjects and model parameters point estimates (i.e. prediction intervals do not reflect the model parameter uncertainty).]*
Disclosure: The study was funded by AbbVie. AbbVie contributed to the study design, research, and interpretation of the data, writing, reviewing and approving the abstract. All authors are AbbVie employees and may hold AbbVie stocks or options.

P0348 INDUCTION THERAPY OF UPADACITINIB IS ASSOCIATED WITH IMPROVED SYMPTOMS IN BOWEL URGENCY AND ABDOMINAL PAIN FOR PATIENTS WITH ULCERATIVE COLITIS: DATA FROM U-ACHIEVE

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Introduction: Upadacitinib (UPA) is an oral selective Janus kinase 1 inhibitor that is being assessed in patients with ulcerative colitis (UC). In addition to the symptoms captured in the Mayo score, the effects of UPA on other patient-reported UC symptoms including bowel urgency and abdominal pain were evaluated in the double-blind placebo-controlled dose-ranging 8-week induction portion of the phase 2b/3 study (U-ACHIEVE [NCT02819635]).
Aims and Methods: Adult patients with active UC (Adapted Mayo score [Mayo score without Physician Global Assessment] 5–9 points and centrally-read endoscopy subscore 2–3) who had inadequate response or intolerance to corticosteroids, immunosuppressants, or biologics were randomized to the modified-release formulation 7.5, 15, 30, or 45 mg once daily (QD) UPA or PBO (1:1:1:1:1) for 8 weeks. UC symptoms including bowel urgency (yes/no) and abdominal pain (0 = none, 1 = mild, 2 = moderate, 3 = severe) were collected in the patient daily diary. The total number of days with bowel urgency, average score of abdominal pain, Mayo rectal bleeding subscore (RBS), and stool frequency subscore (SFS) over the most recent 3-consecutive days prior to the study visits were calculated. The proportions of patients who reported no bowel urgency and abdominal pain score = 0 (which were considered the most stringent endpoints), along with RBS = 0 and SFS ≤ 1 at week 8, respectively, were compared between UPA and PBO groups using the Cochran-Mantel-Haenszel test adjusted for previous biologic use, baseline corticosteroid use, and baseline Adapted Mayo score (≤ 7 and > 7). Non-responder imputation was used for missing values. Sensitivity analyses were conducted by excluding patients with no bowel urgency or those with none to mild abdominal pain (average abdominal pain score ≤ 1) at baseline.
Results: A total of 250 patients with mean age 42.3 years, 60% males, and mean UC duration 8 years were analysed. At baseline, 83% of subjects reported 3 of 3 days with bowel urgency and 41% of subjects had an average abdominal pain score > 1. As early as week 2, more UPA-treated patients reported no bowel urgency over the 3 days and less abdominal pain compared with PBO. At week 8, significantly higher proportions of patients reported no bowel urgency over the 3 days; abdominal pain score = 0, RBS = 0, and SFS ≤ 1 in most UPA groups compared with the placebo group with a potential dose effect across the 7.5 mg, 15 mg, 30 mg, and 45 mg QD dose groups (Table). In the sensitivity analyses, the risk difference between UPA groups and PBO was similar to the primary analyses when excluding patients with no bowel urgency, or excluding those with none to mild abdominal pain at baseline.***, **, *, $^{+}$ statistically significant at 0.001, 0.01, 0.05, and 0.1 level for treatment group vs PBO.
[a]Patients with no bowel urgency at baseline were excluded.
[b]Patients with none or mild abdominal pain (≤ 1.0) at baseline were excluded.
[Table. Proportion of UC patients who reported UC symptoms at Week 8]
Conclusion: Patients with moderately to severely active UC treated with 8-week UPA induction therapy reported significant improvements as early as week 2 in meaningful UC symptoms of bowel urgency and abdominal pain in addition to the improvement in rectal bleeding and stool frequency.
Disclosure: Financial support for the study was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content. S Ghosh: Dr. Ghosh is a steering committee member for Pfizer, Janssen, AbbVie, BMS, Celgene and receives speaker honorarium from AbbVie, Janssen, Takeda, Shield, and Falk Pharma. E Louis has received Educational Grants from MSD, Abbvie, Takeda; and speaker fees from Abbvie, Ferring, MSD, Chiesi, Mitsubishi Pharma, Hospira, Janssen, Takeda. Advisory Board: Abbvie, Ferring, MSD, Takeda, Hospira, Mitsubishi Pharma, Celltrion, Prometheus. S Lee has received grant and research support from AbbVie, Arena, Atlantic, Celgene, Gilead Sciences, Janssen, Pfizer, Salix, Shield, Takeda, Tetherex, UCB Pharma and has performed consulting for Arena, Celgene, Celltrion Healthcare, Cornerstones, Eli Lilly and Company, Janssen, Mesoblast, Pfizer, Salix, Takeda, and UCB Pharma. EV Loftus Jr: Consulting for AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Eli Lilly, Celgene, Celltrion Healthcare. Research support from AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Genentech, Receptos, Gilead, Celgene, Seres, MedImmune, Robarts Clinical Trials. F Cataldi, B Huang, WJ Lee: employees of AbbVie and may own AbbVie stock.

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	PBO N = 46	UPA 7.5mg QD N = 47	UPA 15mg QD N = 49	UPA 30mg QD N = 52	UPA 45mg QD N = 56
Main analysis					
No bowel urgency	9%	19%	33%**	29%*	46%***
Abdominal pain score = 0	13%	21%	41%**	39%*	38%*
Mayo rectal bleeding subscore = 0	26%	36%	41%	52%**	59%**
Mayo stool frequency subscore ≤ 1	13%	34%**	27%$^{+}$	37%**	46%**
Sensitivity analysis					
No bowel urgency[a]	7% (n = 43)	17% (n = 41)	29%** (n = 45)	25%* (n = 48)	43%*** (n = 53)
Abdominal pain score = 0[b]	0% (n = 17)	9% (n = 22)	29% (n = 21)	23% (n = 22)	29%* (n = 21)

P0349 AN IBD RISK VARIANT WITHIN THE PTPN2 GENE LOCUS ENHANCES ANTI-INFLAMMATORY EFFECTS OF SPERMIDINE IN INTESTINAL EPITHELIAL CELLS AND PERIPHERAL BLOOD MONONUCLEAR CELLS FROM IBD PATIENTS

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Introduction: Genome-wide association studies revealed that single nucleotide polymorphisms within the gene encoding protein tyrosine phosphatise non-receptor type 2 (PTPN2) are associated with the onset of inflammatory bowel diseases (IBD) and other chronic inflammatory disorders. PTPN2 is involved in maintaining intestinal homeostasis *in vivo* via regulating inflammatory signalling pathways and protecting intestinal epithelial barrier function. Previously, we have shown that spermidine, a naturally occurring polyamine, exerts anti-inflammatory effects in mouse colitis models *in vivo* via pharmacologic activation of PTPN2 enzymatic phosphatase activity.

Aims and Methods: The aim of this study was to investigate the anti-inflammatory effect of spermidine in human colonic cell lines and in peripheral blood mononuclear cells (PBMC) isolated from IBD patients, and to investigate how presence of the PTPN2 risk allele (SNP rs1893217) affects the outcome of spermidine treatment.

T84 and HT29 human colonic cell lines, either homozygous for the major (TT) allele or heterozygous (CT) for SNP rs1893217 in PTPN2 respectively, were treated with IFN-γ (100ng/ml) and/or spermidine (10nM). PBMC were isolated from IBD patients heterozygous for SNP rs1893217 (CT; n = 4) or homozygous for the major allele (TT; n = 4), as well as from healthy controls (all TT; n = 5), and treated in the same manner. mRNA expression of *IFNG, PTPN2, ICAM1*(which encodes for intercellular adhesion molecule 1) and *NOD2* (encoding for nucleotide-binding oligomerization domain-containing protein 2) was analysed in both experiments by performing quantitative-PCR.

Results: IFN-γ treatment resulted in increased mRNA expression of *ICAM1, PTPN2* and *NOD2* genes in all cells. Of interest, however, in cells expressing CT genotype, basal mRNA expression of those genes was already elevated, and their mRNA expression level following IFN-γ treatment was clearly higher than those observed in PTPN2 wild-type cells. In line with this, cells carrying the CT variant showed reduced PTPN2 activity in basal and IFN-γ treated conditions. Activation of PTPN2 by spermidine clearly reduced IFN-γ induced elevation of *ICAM1, IFNG* and *NOD2* expression in T84 and HT29 cells ($p < 0.05$). Despite initially elevated IFN-γ responses, spermidine treatment was more effective in HT29 cells expressing the CT variant ($p < 0.05$), resulting in elevated activation of PTPN2, and more pronounced reduction of *ICAM1, INFG* and *NOD2* mRNA. In line with those findings, we observed that upon spermidine treatment, reduction of IFN-γ response was also more pronounced in PBMC from patients carrying the CT variant ($p < 0.05$).

Conclusion: Spermidine treatment effectively reduced inflammatory response in T84 and HT29 cell lines and in PBMC from IBD patients. Reduction of the inflammatory responses is more pronounced in case of the presence of C (variant) allele in PTPN2 SNP rs1893217 carriers. Taken together our data indicates that spermidine might be a new promising therapeutic agent in IBD treatment, furthermore the presence of the PTPN2 C allele might serve as a good prediction marker for treatment response.

Disclosure: Nothing to disclose

P0350 VEDOLIZUMAB IN REFRACTORY MICROSCOPIC COLITIS: AN INTERNATIONAL CASE SERIES

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Introduction: Most patients with microscopic colitis (MC) can be successfully treated with antidiarrheals or budesonide. Evidence for second-line therapy in patients failing budesonide is scarce, although anti-tumor necrosing factors (anti-TNFs), methotrexate and azathioprine have been reported to be effective in cases series. Vedolizumab, a monoclonal antibody targeting $\alpha 4\beta 7$-integrin, prevents homing of memory T-cells to the gut. We evaluated clinical and histological remission with vedolizumab in budesonide-refractory MC patients.

Aims and Methods: We solicited gastroenterologists in Europe and Canada for cases of MC treated with vedolizumab. All patients had histologically proven MC. Vedolizumab 300 mg IV was administered at weeks 0, 2 and 6, and then every 8 weeks. Clinical remission and histological remission were defined as < 3 stools per day and normalization of histology, respectively.

Results: Eleven cases were available for analysis from 4 referral centers in 4 different countries [9 females, median age at diagnosis 49 years, lymphocytic colitis (LC) n = 5, collagenous colitis (CC) n = 6]. Median (IQR) disease duration at vedolizumab initiation was 51 (29–70) months and median stool frequency was 8 (5–12) per day. All patients had previously received budesonide therapy. Patients had also been exposed to mesalamine (5/11), cholestyramine (5/11), azathioprine (6/11), methotrexate (3/11) and 10/11 had failed at least 1 anti-TNF agents (8/11 infliximab, 5/11 adalimumab, 1/11 golimumab). Reasons for anti-TNF cessation were inefficacy (8/10), loss of response (1/10) and delayed infusion reaction (1/10). After 3 infusions of vedolizumab, clinical remission was observed in 5/11 patients (2 LC and 3 CC) of whom 3 remained well with maintenance therapy (median duration of 13 months). Vedolizumab was stopped due to intolerance in 1 patient (post-infusion hypertensive crisis) and loss of response for 1 patient. Biopsies after induction were obtained from 9/11 patients. Histological remission was observed in 3/4 patients with clinical remission (2/3 CC, 1/1 LC) and 0/5 patients without clinical improvement. Rescue therapies in failures were budesonide (n = 1), systemic steroids (n = 1), methotrexate (n = 1), experimental drug (n = 1) and loop-ileostomy (n = 1).

Conclusion: In a series of highly refractory microscopic colitis patients, vedolizumab induced clinical remission in 5/11 subjects and disappearance of histological inflammation in 3/4. Larger randomized trials are needed to assess the efficacy of vedolizumab in patients with MC.

Disclosure: Nothing to disclose

P0351 DEFINING 'EARLY DISEASE' IN INFLAMMATORY BOWEL DISEASE: THE RESULTS OF A SYSTEMATIC LITERATURE REVIEW

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Introduction: Accumulating evidence indicates that early intervention may be the best way to change patients' (pts') disease course in Crohn's disease (CD) (1), however evidence to support an early intervention approach in ulcerative colitis (UC) is more limited. A consensus definition of early CD was published in 2012 (2), but early UC is less clearly defined. This systematic literature review (SLR) examined definitions of 'early disease' applied in CD and UC.

Aims and Methods: The Cochrane library, MEDLINE and EMBASE were searched using key words and indexing terms. Eligible papers reported the characteristics and/or treatment (tx) of adult pts (≥18 years) with 'early' inflammatory bowel disease (IBD) from clinical or observational studies published January 2008 - March 2018. There was no intervention or comparator restriction and no assumption on the definition of 'early'. Papers published before 2008, not in English, in paediatric or non-IBD pts were excluded. Uncertainty as to study eligibility was reconciled by a second independent reviewer.

Results: The SLR returned 1,742 abstracts; 107 papers (16 clinical studies; 91 observational studies) met inclusion criteria. A mean 6.2 papers per year (/yr)

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UC Patient characteristics, range (min-max) [n studies]		UC: clinical trial (n = 6)	UC: observational study (n = 49)	CD Patient characteristics, range (min-max) [n studies]		CD: clinical trial (n = 11)	CD: observational study (n = 63)
UC Treatment History	Prior IMM use (%)	6 [1]	0.2–21 [7]	**CD Treatment History**	Prior IMM use (%)	70–94 [2]	3–100 [9]
	Prior biologic use (%)	1 [1]	0–6 [5]		Prior biologic use (%)	0–27 [4]	0–27 [6]
	Prior surgery (%)		3–69 [4]		Prior surgery (%)	9 [1]	3–51 [7]
UC Disease Location	Ulcerative proctitis (%)	17–22 [4]	4–52 [33]	**CD Disease Location**	Ileum or colon only (%)	44–68 [5]	18–83 [44]
	Left–sided (%)	26–41 [4]	0–51 [32]		Ileocolon (%)	21–59 [7]	10–71 [48]
	Extensive / pancolitis (%)	39–55 [5]	9–100 [34]	**CD Disease Behaviour**	Stricturing (%)	8–18 [3]	0–64 [37]
					Non-stricturing (%)	64–92 [2]	6–100 [28]
					Penetrating (%)	0–12 [3]	4–48 [27]
					Active fistula (%)	10 [1]	9–14 [4]

were published 2008–2012 and 16.0/yr in 2013–2017. 'Early disease' was explicitly defined in 33 papers (19 CD; 7 UC; 1 CD and UC; 6 IBD overall): 22 (67%) used time since diagnosis (Dx) only; 9 (27%) combined this with tx history; 1 (3%) tx history and symptom duration; and 1 (3%) tx history and time since first IBD prescription. Definitions in UC used time since Dx only (6 papers), combined with tx history (1 paper), or tx history and symptom duration (1 paper). Cut-off points for time since Dx were applied in 30 papers: ≤3 months (20%), 3–6 months (17%), 6–12 months (27%), 1–2 yrs (17%) and >2 yrs (20%). Definitions based on tx history specified pts should be immunomodulator (IMM) and biologic naïve (7 papers) or additionally corticosteroid (CS) naïve (4 papers). 'Early disease' pt characteristics were stratified by CD and UC. Median disease duration ranged between 0.2–10.6 yrs in CD and 1.1–5.4 yrs in UC. CD cohorts included pts with stricturing (max 64%), penetrating (max 48%) or fistulising (max 14%) disease and prior surgery (max 51%); UC cohorts included pts with pancolitis (max 100%) and prior surgery (max 69%) (see Table). 'Early' CD cohorts met the consensus criteria (disease duration ≤18 months and IMM and biologic naïve) in only 2 papers published since 2012.

Conclusion: The characteristics of 'early' CD and UC pts have increasingly come under focus as the concept of early intervention in IBD has gained traction. Early disease has predominantly been defined by time since Dx (± other variables) but the disease duration of 'early' cohorts can be very long. Often 'early' pts already have complex disease, which may mean the 'window of opportunity' for intervention is missed. The consensus definition of 'early CD' has not been consistently applied since being developed. Robust definitions of early CD and UC are required to accurately evaluate the potential of early biologic tx to improve outcomes.

[Characteristics of 'early disease' UC and CD pts in clinical trials and observational studies]

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P0352 LACK OF EARLY RESPONSE AND MUCOSAL HEALING IS ASSOCIATED WITH COLECTOMY IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS TREATED WITH GOLIMUMAB IN THE PURSUIT-M TRIAL

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Introduction: In ulcerative colitis (UC), uncontrolled inflammation may result in disease progression requiring colectomy. Mucosal healing (MH) has been associated with avoidance of colectomy (1).

Aims and Methods: We investigated the rate and predictors of colectomy in the PURSUIT-Maintenance (PURSUIT-M) study of golimumab in patients with moderate to severe UC. Among 1228 patients in PURSUIT-M including the Induction Responders (IR; n = 593 who achieved clinical response at week 6 [Wk6]) and Induction Non-Responders (INR; n = 635), all colectomy cases were assessed through Wk54. MH at Wk6 was assessed by Mayo endoscopy score. Kaplan Meier (K-M) analysis was used to assess colectomy-free survival through Wk54.

Results: 47 patients required colectomy through Wk54 in PURSUIT-M. Most (34 [72.3%]) of the 47 colectomies occurred in INR, and a higher proportion of INR than IR required colectomy (5.4% vs 2.2%). Patients who responded to induction and still required colectomy (n = 13) had longer disease duration; they also tended to have more extensive disease, more severe UC, and more frequent extra-intestinal manifestations at baseline of induction, when compared to the IR without colectomy (Table). By K-M analysis, overall colectomy-free survival was significantly associated with Wk6 endoscopy score (p = 0.0077).

Conclusion: This post-hoc analysis of PURSUIT-M confirms that colectomy is associated with absence of early clinical response and MH at Wk6 in moderate to severe UC patients treated with golimumab. In patients who achieved clinical response at Wk6, colectomy was associated with longer disease duration.

	No n = 580	Yes n = 13	P-value (chi-square)
Parameter at Baseline (Wk 0 of induction)	n (%)	n (%)	
Duration of disease			
≤ 5 years	313 (53.97)	6 (46.15)	0.002
>5 to ≤ 15 years	212 (36.55)	2 (15.38)	
>15 years	55 (9.48)	5 (38.46)	
Extent of disease			
Limited	331 (57.07)	5 (38.46)	0.181
Extensive	249 (42.93)	8 (61.54)	
Mayo score			
<9	334 (57.59)	7 (53.85)	0.787
≥9	246 (42.41)	6 (46.15)	
Severity of UC disease			
Moderate (Mayo score ≥6 to ≤ 10)	538 (92.76)	11 (84.62)	0.268
Severe (Mayo score>10	42 (7.24)	2 (15.38)	
Extra-intestinal Manifestation			
Absent	447 (77.07)	8 (61.54)	0.190
Present	133 (22.93)	5 (38.46)	

[Colectomy through Week 54 in Induction Responders (N = 593)]

Disclosure: JF Colombel is a consultant, advisory board member, or speaker for Merck & Co., Inc. G. Philip, S. Huyck, and R. Yao are employees of Merck & Co., Inc., Kenilworth, NJ, USA and may hold stock and/or stock options in the company. C. Marano is an employee of Janssen Research & Development, LLC, Spring House, PA, USA and may hold stock and/or stock options in the company. F. Cornillie is an employee of MSD Switzerland and may hold stock and/or stock options in the company.

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P0353 VEDOLIZUMAB OUTCOMES IN REAL-WORLD BIO-NAIVE ULCERATIVE COLITIS AND CROHN'S DISEASE PATIENTS (EVOLVE) IN CANADA: TREATMENT PATTERNS, CLINICAL EFFECTIVENESS AND SAFETY

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Introduction: Vedolizumab (VDZ), a gut-selective humanised immunoglobulin G1 monoclonal antibody that binds to α4β7 integrin, is indicated in Canada for the treatment (Tx) of moderately-to-severely active ulcerative colitis (UC;19 May 2015) and Crohn's disease (CD;19 May 2016). Real-world data on Tx patterns, clinical effectiveness and safety outcomes in biologic (bio)-naïve patients treated with VDZ in Canada are limited.

Aims and Methods: A retrospective cohort study was conducted in adult (≥18 years) UC and CD patients who were bio-naïve and newly initiated VDZ between 19 May 2015 and 31 Dec 2016. Data collection spanned from Tx initiation to earliest of death, chart abstraction date or 6 months post-VDZ Tx discontinuation. Interim analysis used descriptive statistics. Time to first dose escalation and Tx persistence were analysed by Kaplan Meier method. Active disease, clinical remission and mucosal healing were assessed based on available data from symptomatic/endoscopic clinical assessments at baseline (closest assessment to index ≤6 months prior [active disease]) and follow-up (assessments closest to 6 and 12 months [±3 months] post-Tx initiation [remission, mucosal healing]).

Results: Interim analysis included 156 patients (UC: 108; CD: 48) from 11 sites: mean (SD) age, 42.1 (16.9) years, 61.5 % male, median (range: min-max) disease duration of 3.2 (0.01–35.0) years, and median (range) observation period of 16.5 (9.1–30.8) months. At VDZ initiation, 95.5% [85/89] of UC and 86.6% [26/30] of CD patients with assessable data had active disease. 41 patients (26.3%) had ≥1 VDZ dose escalation with a median (range) time to first dose escalation of 6.0 (2.4–22.7) months (UC: 6.6 [2.4–22.7]; CD: 5.7 [2.4–16.7]). At 12 months, 119 patients (83.8%) (UC: n = 85 [86.7%] and CD: n = 34 [77.3%]) persisted on VDZ Tx. Overall, 12.0% and 5.5% of UC and 8.3% and 6.3% of CD patients discontinued VDZ due to primary non-response and secondary loss of response, respectively. 2 CD patients discontinued Tx due to serious adverse events (neurological disorder and bronchitis; bronchitis related to VDZ). During VDZ Tx,12.0% of UC and 6.3% of CD patients had ≥1 IBD-related hospitalization and 5.6% of UC and 2.1% of CD patients had ≥1 surgical procedure. Additional outcomes are reported in Table 1.

[Concomitant Corticosteroid Use, Clinical Effectiveness and Safety Outcomes Among Bio-naïve Patients Treated with Vedolizumab]

Conclusion: These interim data support the long-term effectiveness and safety of VDZ in bio-naive UC and CD patients in real-world clinical practice. Findings will be confirmed in the final EVOLVE study cohort.

Disclosure: The study was funded by Takeda Pharmaceuticals Company Ltd. BB received honoraria from Takeda; MB, DS and MS are employees of Evidera

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	UC (N = 108)	CD (N = 48)
Concomitant corticosteroid (CS) Use and Discontinuation during Vedolizumab (VDZ) Treatment (Tx)		
Discontinuation of concomitant CS by 12 months, (%) [n/concomitant CS use n]* *discontinuation of all ongoing CSs during VDZ Tx without reinitiating new or repeat CS within 3 months of discontinuation	(47.5) [19/40]	(77.8) [7/9]
Clinical Effectiveness and Safety Outcomes		
Clinical remission at 6 months, (%) [n/available n]	(50.0) [34/68]	(29.6) [8/27]
Clinical remission at 12 months, (%) [n/available n]	(54.1) [20/37]	(28.6) [4/14]
Mucosal healing at 6 months, (%) [n/available n]	(53.3) [16/30]	(61.5) [8/13]
Mucosal healing at 12 months, (%) [n/available n]	(62.1) [18/29]	(75.0) [6/8]
Serious Adverse Events (SAEs) during VDZ Tx, n (%)	8 (7.4)	4 (8.3)
Serious infections during VDZ Tx, n (%)	1 (0.9)	3 (6.3)

which received funding from Takeda Pharmaceuticals Company Ltd. GR, MK and DD are employees of Takeda Pharmaceuticals Company Ltd.

P0354 FECAL MICROBIOTA TRANSPLANTATION IN CROHN'S DISEASE: A PILOT RANDOMIZED, SINGLE-BLIND, SHAM-CONTROLLED TRIAL

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Introduction: The role of the gut microbiota in inflammatory bowel disease (IBD) pathogenesis is established and fecal microbiota transplantation (FMT) has shown some efficacy inducing remission in active ulcerative colitis in three randomized controlled clinical trials (RCT) to date. However there is no RCT result available in Crohn's disease (CD). Moreover it is not known whether the best timing to perform FMT is during a flare or after having achieved remission.
Aims and Methods: A randomized, single-blind, sham-controlled pilot trial of FMT in adults with colonic or ileo-colonic CD was performed. Patients were included while in flare (Harvey Bradshaw index [HBI] > 4) and treated with oral corticosteroid. Following clinical remission (HBI < 5), patients were randomized to receive either FMT (50–100g of stool from a single donor suspended in 250–350ml of physiological serum and administered fresh) or sham transplantation (physiological serum) during a colonoscopy. Corticosteroids were tapered and a second colonoscopy was performed at week 6. Crohn's Disease Endoscopic Index of Severity (CDEIS) was assessed during each colonoscopy. The primary endpoint was the implantation of the donor microbiota in the receiver at week 6 defined by a receiver's fecal microbiota at week 6 closer to the donor (with Sorensen index $\geq$0.6 [Sorensen index = 1- Bray Curtis index]) than to the patient before FMT. Clinical, biological and endoscopic efficacy endpoints were also evaluated (NCT02097797).
Results: Overall, 21 patients were randomized, 8 received donor FMT, 9 received sham-transplantation and 4 were ineligible for transplantation (3 because of pathogen identification and 1 for unavailability of donor). In the FMT group, none of the patients reached the primary endpoint. However, patients from the FMT group had a microbiota composition at 6 weeks closer to donors compared to patients in the Sham-transplantation group ($p = 0.016$). The steroid-free clinical remission rate at 10 and 24 weeks were 44.4% and 33.3% in the Sham-transplantation group and 87.5% and 57.1% in the FMT group ($p = 0.13$ and $p = 0.6$ respectively at week 10 and 24). CDEIS decreased 6 weeks after FMT (8.5 [4.6;13.0] vs. 3.5 [1.0;8.9]; $p = 0.03$) but not after Sham-transplantation (2.4 [0.0;8.3] vs. 2.7 [0.7;10.0]; $p = 0.8$). Conversely, CRP level increased 6 weeks after Sham-transplantation (3.0 [3.0; 4.2] vs. 6.9 [4.0; 8.7] mg/l; $p = 0.008$) but not after FMT (3.0 [3.0;3.0] vs. 3.0 [3.0;14.2] mg/l; $p = 0.5$). Failure to achieve steroid-free clinical remission at week 24 in FMT group was associated with absence of donor microbiota engraftment at week 6 and with the absence of increase in alpha diversity. The microbiota composition at week 6 was predictive of steroid-free clinical remission at week 24. No safety signal was identified.
Conclusion: None of the patients reached the primary endpoint related to the level of implantation of the donor microbiota. However, this pilot study in CD suggests that FMT performed after achieving clinical remission by corticosteroids could be effective as a maintenance treatment. A larger randomized control trial is now required to confirm the efficacy of this strategy.
Disclosure: Nothing to disclose

P0355 TOPICAL APPLICATION OF HUMAN UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS GEL MATRIX ACCELERATE THE CLOSURE OF ENTEROCUTANEOUS FISTULA ON MOUSE MODEL

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Introduction: Mesenchymal stem cell therapy is an emerging field of regenerative medicine. However low ratio cell retention after transplantation limit the successful application of stem cell. Recently local application of MSCs represents a novel approach for the treatment of perianal fistula in patients with Crohn's disease. Engineered microenvironments of a gel matrix have been increasingly successful in protecting stem cell survival by mimicking niche of native stem cell.
Aims and Methods: To investigate the efficacy of Local application of human umbilical cord-derived Mesenchymal Stem Cells (hUSCs) supported by a gel matrix on the closure of enterocutaneous fistula of mouse model. Isolated hUSCs were labeled with luciferase and green fluorescent protein by lentivirus transfection and the distribution of implanted hUSCs were detected by BLI (bioluminescence). A caecostomy was used as a fistula model in 24 male BALB/c mice on day 0. Animals were randomly assigned to groups given daubs of hUSCs supported by a gel matrix (n = 8, group A), and blank gel matrix (n = 8, group B) or placebo (n = 8, group C) in the perifistular tissue after fistula formation. Fistula drainage assessment was used to evaluate the fistula healing on day 15. And their clinical and pathological conditions were evaluated by body weight, histological analysis of perifistular tissue. Simultaneously, Cell viability and distribution was detected using an IVIS Luminar camera on days 0, 2, 4 and 6 after application of D-luciferin.
Results: The fistula was identified as healed in 7 (87.5%) mice in group A vs. 3 case (37.5%) in group B vs. 1 case (12.5%) in group C on day 15. The body weight was minimum when the fistula was formed and recovered faster in group A comparing with the other 2 groups. Furthermore, histological analysis indicate more normalized histological structure of perifistular tissue in group A. The BLI was strongest immediately after administration of hUSCs and the values fell dramatically within the first 2 days but it was still higher in animals with healed fistulas 6 days after injection.
Conclusion: Local application of hUSCs supported by a gel matrix stimulated fistula healing with significantly higher fistula closure rate on an animal model. BLI monitoring showed rapid reduction of the hUSCs mass after application. More viable cells were detected in animals with healed fistula. Topical transplanted hUSCs may play a therapeutic role in fistula healing. Mesenchymal stem cells supported by gel matrix may be a promising therapeutic approach for fistulas of Crohn's disease.
Disclosure: Nothing to disclose

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P0356 MEASURING THIOGUANINE NUCLEOTIDE (6-TGN) LEVELS AND CLINICAL RESPONSE IN IBD

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Introduction: Monitoring levels of 6-TGN and titrating dose of Azathioprine (AZA) and Mercaptopurine (6-MP) accordingly to achieve therapeutic concentrations of 6-TGN has been reported to improve outcomes in the treatment of Ulcerative colitis (UC) and Crohn's Disease (CD).

Aims and Methods: The aim of our study was to show how levels of 6-TGN corresponds to clinical outcome. This was a single centre (Royal Free Hospital), retrospective study, of patients receiving AZA or 6MP. We identified our patients by collating those who had been dispensed AZA or 6MP over the past 2 years. We were then able to access their electronic database, and record whether 6-TGN levels were subsequently taken to titrate treatment, and assess clinical outcome.

Results: 359 from 426 patients have so far been analysed (F = 153 [42.6%], UC = 160 [44%], CD = 190 [53%], indeterminate/other colitis = 9 [3%]).

Mean duration on thiopurines was 5.7 years. Mean disease duration was 12.7 years. Out of 359 IBD patients on thiopurines, 275 [77%] had 6-TGN levels measured at some stage. 177/275 (64%) had therapeutic levels, whilst 98/275 (36%) did not. 166/275 (60.5%) were in clinical remission. 94/275 (34.5%) were not. For 15 patients (5%), no data was available. Of those that had therapeutic levels of 6-TGN, 112/177 (63%) were in clinical remission. 19/112 (17%) were in total remission (clinical, biochemical [normal CRP/WCC], endoscopic and histological). 60/112 (53%) were on Azathioprine (AZA), 48/112 (43%) were on mercaptopurine (6MP). For 4/112 (4%) patients there was no thiopurine treatment data or the treatment was stopped. 46/112 (41%) were on combined therapy with biologics. Of those that had non-therapeutic levels of 6-TGN, 54/98 (55%) were in clinical remission. 13/54 (24%) were in total remission. 37/54 (68%) AZA. 15/54 (28%) 6MP. 2/54 (4%) data not complete/purines were stopped. 24/54 (44%) were on combined therapy with biologics. Of those with therapeutic levels of 6-TGN, 53/177 (30%) were not in clinical remission. 30/53 (57%) AZA, 22/53 (41%) 6MP, 1/53 (2%) patient data not complete/purines were stopped. 41/53 (77%) were on combined therapy with biologics. Of the cohort that had non-therapeutic levels of 6-TGN, 41/98 (42%) were not in clinical remission. 21/41 (51%) AZA, 15/41 (37%) 6MP, 5/41 (12%) data not complete/purines were stopped. 29/41 (71%) were on combined therapy. (Note: 12 of the 177 patients with therapeutic 6-TGN had no data on remission status. 3 of the 98 patients with non-therapeutic levels of 6-TGN had no data on remission status).

Conclusion: Our study so far suggests that in IBD patients on thiopurines (sole or combined therapy), clinical remission rates were similar (63% vs. 55%) for those who had therapeutic 6-TGN levels and for those who had not. It also shows that even without achieving therapeutic levels of 6-TGN, 55% of patients were still in clinical remission. Moreover, there is no significant relationship between achieving therapeutic 6-TGN levels and clinical remission when looked separately for those only on thiopurines or on combined therapy (p = 0.074 and p = 0.13 respectively). Our study interestingly highlights that even with therapeutic levels of 6-TGN and with three quarters of patients on combined biologics - 30% were still not in remission. This preliminary study suggests interesting trends, that will be assessed further across the entire population (n = 426) and compared with other European data.

Disclosure: Nothing to disclose

P0357 EPIDEMIOLOGY, DIAGNOSTIC WORK-UP AND PHARMACOLOGICAL TREATMENTS OF INFLAMMATORY BOWEL DISEASE IN SPAIN: RESULTS FROM THE NATIONWIDE EPIDEMIBD STUDY OF GETECCU

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Introduction: This is the largest nationwide study to know the epidemiology of IBD in the 21th century in Spain.

Aims and Methods: i) to assess the incidence of inflammatory bowel disease (IBD) in Spain; ii) to describe the characteristics of patients at diagnosis, and iii) to evaluate the need for immunomodulators or biologics.

Prospective and population-based nationwide study in Spain. Adult patients diagnosed with IBD -Crohn's disease (CD), ulcerative colitis (UC) or indeterminate colitis (IC)- during 2017 in the 17 Spanish regions were included and followed-up for 12 months after diagnosis. Data were captured in a web-based database (AEG-REDCap).

Results: 3,469 incident cases from 116 centres covering approximately 50% of the Spanish population were included. The incidence of IBD was 16 per 100,000 person-years: 7.2 in CD, 8 in UC, and 0.7 per 100,000 person-years in IC. Median follow-up was 3 months both in UC and CD patients. Median age at diagnosis was lower in CD than in UC (40 vs. 45 years, $p < 0.01$). The mean time from symptoms onset to IBD diagnosis was longer in CD (5 vs. 2 months, $p < 0.01$); 10% of CD patients had no symptoms at diagnosis vs. 6% of UC ($p < 0.01$). The proportion of patients with family history of IBD was higher in CD (18 vs. 13%, $p < 0.01$). At the time of diagnosis, 12% of CD patients had extra-intestinal manifestations vs. 5.8% in UC. In CD patients, 55% had ileal location, 19% colonic, 26% ileocolonic, 3% upper gastrointestinal tract involvement, and 11% perianal disease. 11% of patients had stenosing and 7% fistulising behaviour at the time of diagnosis. 1.8% evolved to more severe phenotype after 3 months of follow-up. In UC patients, 34% had extensive colitis and 31% left-sided colitis at diagnosis, and 0.5% had progression of disease extension after 3 months. For the diagnosis work-up, 98% of patients underwent colonoscopy; among CD patients, 32% underwent MRI-enterography, 29% CT-scan, 13% upper endoscopy, 1.6% exploration under anesthesia, 5.6% capsule-endoscopy, 4% perianal MRI and 3% small bowel follow-through. Pharmacological exposures were higher in CD than in CU (table 1). The cumulative incidence of exposure to thiopurines was 32% at 3 months and 65% at 12 months in CD, and 6% at 3 months and 12% at 12 months in UC ($p < 0.01$). The cumulative incidence of anti-TNF exposure was 13% at 3 months and 35% at 12 months in CD, and 6% at 3 months and 12% at 12 months in UC ($p < 0.01$). There was not difference in median time to intravenous steroids, to thiopurines, methotrexate or anti-TNF treatment between UC and CD patients.

Conclusion: The incidence of IBD in Spain is high and similar to figures reported in the North of Europe. Up to 20% of CD patients showed an aggressive clinical phenotype -stenosing or fistulising- at diagnosis. The use of pharmacological treatments and diagnostic resources were remarkable in IBD patients, and were higher in CD than in CU patients.

	CD	UC	P
Oral mesalazine (%)	33	71	<0.01
Rectal mesalazine (%)	4	69	<0.01
Rectal budesonide (%)	0.6	4	<0.01
Oral budesonide/ beclomethasone dipropionate (%)	31	8	<0.01
Oral conventional steroids	36	22	<0.01
Intravenous steroids	13	12	N.S
Thiopurines	30	5	<0.01
Methotrexate	3.5	0.3	<0.01
Cyclosporine	0.1	0.5	<0.01
Anti-TNF agents	13.8	3.7	<0.01
Vedolizumab	0.5	0.2	N.S
Ustekinumab	0.3	–	–

[Table 1. Pharmacological treatments of IBD patients during follow-up (median 3 months, range 0–12 months).]

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P0358 ENDOSCOPIC DILATION THERAPY FOR STRICTURING CROHN'S DISEASE OF THE SMALL INTESTINE USING BALLOON-ASSISTED ENDOSCOPY - A COMBINED ANALYSIS OF 773 ENDOSCOPIC BALLOON DILATION PROCEDURES

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Introduction: Strictures are a common complication of Crohn's disease (CD) and may develop in all segments of the gastrointestinal (GI) tract. While colonoscopy has been proven suitable and effective for balloon dilation therapy of CD-associated strictures of the ileocecum (1,2), the published evidence on efficacy and safety of balloon-assisted endoscopy (BAE) for balloon dilation therapy of CD strictures of the small intestine is scarce. We therefore performed a combined efficacy and safety analysis based on all published studies of BAE for small intestinal strictures available in the literature.

Aims and Methods: A formal systematic literature review was performed to assess all relevant citations found in Embase, Medline and the Cochrane library regarding BAE used for EBD of small intestinal stricture. In addition, conference proceedings including Digestive Disease Week 2010–2017, European Crohn's and Colitis Foundation 2011–2017, United European Gastroenterology Week 2013–2016, Advances in IBD 2015–2017, American College of Gastroenterology 2016–2017, German Gastroenterology Congress 2013–2017 were screened for additional data. Available technical and clinical variables were extracted from all studies available for a descriptive pooled data analysis. Weighted efficacy averages were calculated for sub-groups.

Results: 18 publications with a total of 445 CD patients and 773 performed dilation procedures were included. 19.3% were anastomotic strictures. Technical success rate was 88.1%, resulting in clinical efficacy in 78% of patients. Major complications with regard to dilation, defined as perforation, bleeding or dilation-related surgery, occurred in 3.7% of all procedures. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgical intervention. Currently, there is no study available investigating the impact of concomitant therapeutic approaches such as steroid injection, cutting techniques or stent placement on the outcome of BAE EBD for small bowel GI strictures in CD patients.

Conclusion: BAE for dilatation therapy of CD-associated strictures of the small intestine possesses a high rate of short-term technical and clinical success and may represent an alternative to surgery in stricturing CD. BAE-associated complication rates appear comparable to those related to dilation therapy of ileocecal strictures during colonoscopy. Larger, controlled studies are warranted to further evaluate BAE for dilation therapy of CD strictures of the small intestine.

Disclosure: Nothing to disclose

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P0359 LONG-TERM SAFETY, EFFICACY AND PHARMACOKINETICS OF THE ANTI-MADCAM-1 MONOCLONCAL ANTIBODY SHP647 IN CROHN'S DISEASE: THE OPERA II STUDY

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Introduction: The endothelial adhesion protein MAdCAM-1 is a promising novel drug target in inflammatory bowel disease; the fully human IgG_2 anti-MAdCAM-1 monoclonal antibody SHP647 is in development for induction and maintenance of remission in patients with Crohn's disease (CD) and ulcerative colitis.

Aims and Methods: OPERA II was a multicentre, open-label, phase 2 extension study (NCT01298492), designed to assess the long-term safety and efficacy of SHP647 in patients with moderate-to-severe CD. Eligible patients had completed 12 weeks' induction treatment (placebo or 22.5 mg, 75 mg or 225 mg s.c. SHP647) in OPERA I (NCT01276509), or had a clinical response (≥3-point decrease in Harvey Bradshaw Index score) to 225 mg SHP647 in the open-label study, TOSCA (NCT01387594). Patients received SHP647 (75 mg, s.c.) every 4 weeks from baseline to week 72, and were followed up for safety assessments monthly for a further 24 weeks. Dose de-escalation to 22.5 mg owing to intolerance/treatment-emergent adverse events (TEAEs), or escalation to 225 mg owing to clinical deterioration/poor response, was allowed as judged by the investigator. Primary endpoints were frequency of TEAEs, TEAEs leading to withdrawal and SAEs. Concentrations of serum SHP647, high-sensitivity C-reactive protein (hsCRP) and faecal calprotectin (FC) were assessed as secondary endpoints.

Results: Of the 268 patients who enrolled and entered the treatment period, 149 completed the study. Table 1 shows the proportions of patients experiencing TEAEs, TEAEs leading to withdrawal and serious adverse events (SAEs). The most common treatment-related TEAEs in the treatment period were arthralgia (6.0%), nasopharyngitis (5.6%) and headache (5.2%). 2 patients died: 1 during treatment (75 mg) of multiple organ failure after postoperative aspiration following a resection of the terminal ileum (female, 30 years, SHP647 75 mg) and 1 during follow-up due to metastatic adenocarcinoma (unknown primary; male, 36 years, SHP647 225 mg); neither death was considered drug-related. No patients de-escalated their dose, and 157 patients increased their dose to 225 mg SHP647 after a median time of 28 weeks. Serum trough concentrations of SHP647 averaged 7051 ng/mL at week 4 and remained constant over time with a steady-state concentration of 7300 ng/mL at week 72. 3 months after dose escalation to 225 mg, patients achieved a new steady-state level of 16190 ng/mL, which is consistent with the pharmacokinetics determined previously. Patients whose dose escalated appeared to have more severe disease, with higher hsCRP (24.12±26.23 mg/L) and FC (2771.5±3583 mg/kg) levels at baseline than patients who remained on 75 mg, who had hsCRP and FC levels of 19.12±24.33 mg/L and 1823±2178 mg/Kg, respectively. Concentrations of hsCRP decreased steadily over time from week 0 to 72; the pattern was similar in patients who received 75 mg and those who escalated to 225 mg, though at the end of the study, patients who had escalated their dose had higher values than those who had not. FC levels decreased over time consistently in both groups.

Conclusion: SHP647 75 mg (with potential dose escalation to 225 mg) was generally well-tolerated in patients with Crohn's disease over 72 weeks. These results add to evidence for the long-term safety of SHP647.

[Table 1. All-cause and treatment-related adverse events in the treatment and follow-up periods.]

Disclosure: GRDH has been a consultant for Pfizer and Shire, and has received research support from Shire. WR has served as a speaker for Shire, and as a consultant and advisory board member for Pfizer. SDL has received grant and research support from and has been a consultant to Pfizer. DT has received research support from and has been a consultant to Pfizer. EL has received research grants and speaker fees from Pfizer. MK has received payments for lectures/advisory boards from Abbvie, Egis, Takeda, Janssen and Ferring. JK has received speaker fees from and served on advisory boards for Pfizer. SS has served on advisory boards for Pfizer and Shire. DIP has served on advisory boards for Shire. XH has served as a speaker, and as advisory board member for Pfizer. FC has been an employee of Pfizer and Shire, and holds stocks in Shire. SWM is an employee of Pfizer. SN is an employee of Pfizer. AB is an employee of Pfizer. KG is a consultant to Pfizer and Shire. WJS has been a consultant for Pfizer and Shire, and has received research support from Shire.

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	Treatment period: all-cause	Treatment period: treatment-related	Follow-up period: all-cause	Follow-up period: treatment-related
Number (%) of patients with TEAEs	249 (92.9)	124 (46.3)	133 (68.6)	31 (16.0)
Number (%) of patients with SAEs	80 (29.9)	10 (3.7)	57 (29.4)	1 (0.5)
Number (%) of patients who discontinued study owing to TEAEs	53 (19.8)	15 (5.6)	1 (0.5)	0

P0360 FMT CAPSULES DECREASES FECAL CALPROTECTIN AND IMPROVES SYMPTOMS IN ULCERATIVE COLITIS PATIENTS - A PILOT STUDY

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Introduction: There is growing evidence indicating that gut 'dysbiosis' is one of the factors in the pathogenesis of Inflammatory Bowel Disease IBD (1).
Fecal Microbiota Transplantation (FMT) from healthy donors is an effective treatment of recurrent *Clostridium difficile* infections both when administered by endoscopy or through oral capsules (2).
In addition, FMT appears to be promising in Ulcerative Colitis remission induction (3). However long-term safety and effects on ulcerative colitis remain unclear.
Aims and Methods: The aim was to test if multi-donor FMT capsules, manufactured at the laboratory at Aleris-Hamlet Hospital, Copenhagen, could lower Fecal (F) Calprotectin and improve symptoms in patients with Ulcerative Colitis and to test the safety of the treatment.
7 patients, aged 27 to 51 years, with Ulcerative Colitis, a Simple Clinical Colitis Activity Index (SCCAI) between 4 and 10, and F-Calprotectin $>$ 250 mg/kg were treated with 25 multi-donor FMT capsules daily for 50 days as a supplement to each individual patient's stable dose of standard treatment throughout the period of intervention. The 4 fecal donors were healthy individuals who were screened according to current guidelines (4) and recruited through postings in the area around the hospital. Participants were followed with fecal samples and SCAAI throughout the study period. We used Mann-Whitney U tests to compare F-Calprotectin and SCAAI levels at each time-point after baseline with the levels at baseline.
Results: Median F-Calprotectin at baseline was $\geq$1800 mg/kg (the upper limit for Calprotectin at our laboratory was 1800 mg/kg). After 4 weeks of treatment F-Calprotectin was lowered in 6 of the 7 participants, and there was a significant decrease in median F-Calprotectin of 912 mg/kg ($p = 0.004$). 1 week after the intervention had stopped, at 8 weeks from baseline, the median decrease in F-Calprotectin from baseline of 551 mg/kg was no longer statistically significant ($p = 0.14$).
The participants had a median SCAAI of 6 at baseline. After both 4 and 8 weeks all participants had lowered their SCAAI and there was a significant decrease in median SCAAI of, respectively, 5 ($p = 0.001$) and 6 ($p = 0.001$).
All participants completed the treatment and no serious adverse events were registered throughout the study period.
Conclusion: Daily multidonor FMT-capsules were safe and significantly lowered F-Calprotectin in Ulcerative Colitis patients with SCCAI between 4 and 10 after 4 weeks of active treatment. The participants also experienced a significant improvement in symptoms throughout the study period.
FMT administered in various forms appears promising in the treatment of Ulcerative Colitis but many questions remain. In particular, the type of administration, donor- and patient-selection, and dosing must be investigated in future placebo-controlled studies.
Disclosure: Nothing to disclose

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P0361 POPULATION PHARMACOKINETIC AND PHARMACODYNAMIC ANALYSIS OF SHP647, A FULLY HUMAN MONOCLONAL ANTIBODY AGAINST MUCOSAL ADDRESSIN CELL ADHESION MOLECULE 1 (ANTI-MADCAM-1), IN PATIENTS WITH ULCERATIVE COLITIS OR CROHN'S DISEASE

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Introduction: The mucosal addressin cell adhesion molecule-1 (MAdCAM-1) plays a role in gut immune surveillance and facilitates excessive lymphocyte infiltration under conditions of chronic gastrointestinal inflammation. SHP647 is a fully human immunoglobulin G2 anti-human MAdCAM-1 monoclonal antibody, which is being developed for the induction and maintenance of remission of ulcerative colitis (UC) and Crohn's disease (CD).
Aims and Methods: Clinical studies (NCT01276509; NCT01620255) were performed to assess efficacy, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of SHP647 in patients with UC or CD. Population PK and PK/PD analyses of SHP647 and MAdCAM-1 following repeated subcutaneous (SC) administration of 7.5, 22.5, 75, and 225 mg every 4 weeks was performed to identify sources of variability and support dosing in adult patients with UC/CD. A total of 440 patients were included in the analysis, of whom 249 (56.6%) had UC and 191 (43.4%) had CD. Population PK analysis of SHP647 included models with non-linear and/or linear elimination. Covariate analysis was performed using a stepwise covariate approach. The following covariates were explored: age, sex, race, markers of renal and liver function (i.e., creatinine clearance, bilirubin, AST, ALT) as well as renal impairment categories (normal, mild, moderate, severe), disease (UC/CD), anti-drug antibody (ADA), free MAdCAM-1 levels and various laboratory measurements (C-reactive protein [CRP], albumin, fecal calprotectin, and colonoscopy score). PK and PK/PD analyses were performed using nonlinear mixed effect modeling.
Results: Patients with UC/CD presented with similar mean age (40.4 and 36.0 years, respectively) and body weight (72.5 kg and 70.6, respectively). SHP647 was very well tolerated in patients with UC/CD. A 2-compartment model with linear and non-linear elimination resulted in an adequate characterization of concentration-time profiles. An empirical allometric function was used on clearance and volume parameters. The absorption of SHP647 was described with a first-order rate constant of absorption (Ka) and absorption lag time. Population estimates of apparent clearance (CL/F) and volume of distribution (Vc/F) were 0.0127 L/h (0.305 L/day) and 6.53 L, respectively. The CL/F was mainly dependent on baseline CRP and albumin while Vc/F was mainly dependent on body weight. No differences were observed in patients with UC/CD. ADA was not identified as a covariate explaining the variability of CL/F. The Michaelis-Menten constant (Km) was very low (19.0 ng/mL) suggesting that the nonlinear elimination (target-mediated) occurred at very low concentrations, and was less likely to contribute to the elimination half-life at therapeutic concentrations and under steady state conditions. The apparent SHP647 half-life associated with average steady state concentrations for the 7.5, 22.5, 75, and 225 mg dose levels were 7.04, 12.3, 16.5 and 18.6 days, respectively. A linear PK/PD model was used to describe the relationship between concentrations of SHP647 and MAdCAM-1 levels. Based on minimum concentrations of SHP647 under steady state conditions, the 75 and 225 mg doses were associated with $>$95% suppression of circulating MAdCAM-1 levels.
Conclusion: Nonlinear elimination of SHP647 occurred at very low concentrations and was less likely to contribute to the elimination half-life at therapeutic concentrations. Repeated SC administration of SHP647 resulted in a marked suppression of circulating MAdCAM-1 levels in patients with UC/CD.
Disclosure: Y Wang is an employee of Shire. JF Marier is a paid consultant of Certara. J Lavigne is a paid consultant of Certara. N Kassir is a paid consultant of Certara. P Martin is an employee of Shire.

P0362 EFFICACY OF TOFACITINIB AND BIOLOGICS AS INDUCTION AND MAINTENANCE THERAPY FOR MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: Tofacitinib (TOFA) is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). We performed a systematic literature review and network meta-analysis (NMA) to compare the efficacy of TOFA to other agents approved as induction and maintenance therapy in adults with moderately-to-severely active UC.
Aims and Methods: Literature searches were conducted in EMBASE, MEDLINE, CENTRAL, DARE, and CINAHL databases to identify randomized controlled trials published as of February 2017. Conference proceedings were also reviewed. 2 researchers independently assessed studies based on prespecified criteria. Feasibility assessments evaluated data availability, clinical heterogeneity, and risk of bias to identify studies suitable for inclusion. A Bayesian multinomial likelihood model with a probit link was conducted to compare induction and maintenance treatments on a 3-level mutually exclusive efficacy variable (no response, response without remission, remission) using the average placebo rate across trials as a common anchor. Results were stratified by prior tumor necrosis factor inhibitor (TNFi) exposure, where possible. Agents included in the analyses were TOFA, infliximab (IFX), golimumab (GOL), adalimumab (ADA), and vedolizumab (VDZ). 2 sets of maintenance analyses were conducted, 1 based on trials that re-randomized subjects between induction and maintenance phases (re-randomization or "RR") and the other based on trials that kept subjects on the treatment received during the induction phase (treat-through or "TT"). Data extrapolation methods were employed to integrate RR trials into the TT analyses. Results are reported as probability of response and remission along with 95% credible intervals; the probability of TOFA being superior to other treatments is also reported.
Results: 16 trials were included (10 induction only, 2 maintenance only, and 4 induction and maintenance). Among TNFi-naïve patients in induction, IFX had the greatest efficacy (response = 72%, remission = 36%). Among TNFi-exposed

patients in induction, TOFA 10mg BID had the greatest efficacy (60% and 18%) and had >99% probability of having better efficacy compared with ADA (36% and 7%). Among RR trials, TOFA had the greatest efficacy (5mg BID: 71% and 54%; 10mg BID: 72% and 56%) and had a 70–99% probability (depending on the comparator) of having better efficacy than other agents in the TNFi-naïve subpopulation. TOFA 10mg BID had the greatest efficacy (61% and 49%) and a 72–79% probability of having better efficacy than other agents in the TNFi-exposed subpopulation. Results among TT trials were similar. The probability of TOFA having better efficacy than other agents was 83–98% and 67–91% for TNFi-naïve and TNFi-exposed, respectively.
Conclusion: Except compared with IFX in the TNFi-naïve induction setting, TOFA has similar or superior efficacy compared with biologics as induction and maintenance therapy for moderately-to-severely active UC.
Disclosure: D Rubin has received research support from AbbVie, Genentech, Janssen, Takeda, UCB, and consultancy fees from AbbVie, Amgen, Janssen, Pfizer Inc, Takeda, UCB; A Ashaye, Y Zhang, K Fahrbach and A Freitag are/were employees of Evidera Inc at the time of analysis; C Kayhan, C Lohan, J Cappelleri and M DiBonaventura are employees and shareholders of Pfizer Inc

P0363 PREDICTING OUTCOME IN ACUTE SEVERE ULCERATIVE COLITIS: COMPARISON OF THE OXFORD, EDINBURGH, LINDGREN AND ENDOSCOPIC MAYO SCORES

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Introduction: Up to one-third of patients with acute severe Ulcerative Colitis (ASUC) will fail intravenous corticosteroids (IVCT) treatment, requiring rescue therapy with Cyclosporin (Cy), Infliximab (IFX) or colectomy. Although several scores for predicting response to IVCT exist, formal comparison is lacking.
Aims and Methods: This was a retrospective cohort single-center study. The endoscopic Mayo score and the Oxford, Edinburgh and Lindgren scores were determined at admission and on the 3rd day of IVCT treatment, respectively. Outcomes included prediction of steroid refractoriness, need for rescue medical therapy and surgery
Results: From 489 patients with Ulcerative Colitis, 112 presented with ASUC; 58% were male with a median age of 33.5 years (range 18–80). The median of Truelove and Witts score was 4 (range 2–5). 35% of patients showed an incomplete or absent response to IVCT, 28.6% received rescue medical therapy (65.6% with IFX, 31.3% with Cy and 3.1% received sequential therapy with Cy and IFX) and 13.4% were colectomized up to 1 year from admission. The Lindgren score was superior to the Edinburgh score (AUC 0.856 [0.784–0.928] vs 0.775 [0.682–0.869], p = 0.01) and the Mayo score (AUC 0,699 [0,597–0,801], p = 0,02), but not to the Oxford score (AUC 0.746 [9.651–0.841], p = 0.14) in predicting steroid refractoriness. The Lindgren score was superior to the Mayo (AUC 0.826 [0.749–0.902] vs 0.637 [0.525–0.749], p = 0.002) and Oxford scores (AUC 0.719 [0.617–0.821], p = 0.03), but similar to the Edinburgh score (AUC 0.771 [0.678–0.865], p = 0.18) in predicting the need for medical rescue therapy. Finally, the Lindgren score was also a better predictor of the need of colectomy than the Edinburgh (AUC 0.836 [0.712–0.960] vs 0.753 [0.608–0.897], p = 0.03) and Oxford scores (AUC 0.712 [0.587–0.837], p = 0.003), but not to Mayo score (AUC 0.782 [0.685–0.879], p = 0.47). In multivariate regression analysis, the Lindgren score was an independent predictor for steroid refractoriness (OR 1.647 1.111–2.441, p = 0.013) and need for medical rescue therapy (OR 1.410 1.033–1.926, p = 0.03). A Lindgren score >9 had a positive and negative predictive value for IVCT failure of
91.7% and 72.9%, respectively.
Conclusion: In our series, the Lindgren score was superior to the Edinburgh, Oxford and endoscopic Mayo scores in predicting steroid refractoriness, need for rescue medical therapy and colectomy.
Disclosure: Nothing to disclose

P0364 RISK OF VENOUS THROMBOEMBOLISM BY DISEASE ACTIVITY, HOSPITALIZATION, AND SURGERY IN INFLAMMATORY BOWEL DISEASE: A NATIONWIDE COHORT STUDY

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Introduction: Risk of venous thromboembolism (VTE) of inflammatory bowel disease (IBD) patient is higher than general population. Guidelines recommend primary prophylaxis of venous thromboembolism for certain periods. However, little is known about the magnitude of the risk of VTE development in those periods. We estimated the risk of VTE during a hospitalized flare, a non-hospitalized flare, a hospitalization without flare, IBD-related surgery, and other major surgeries.
Aims and Methods: Using the National Health Insurance claims data for the entire Korean population, we included 33,131 patients with IBD from January 2012 until December 2013 with 198,825 age- and sex-matched controls, and followed up until December 2016. We used Cox regression models to identify whether the risk of VTE varies by hospitalization, disease flare, surgery and/or presence of other risk factors.
Results: Of 33,131 patients with IBD and 198,825 matched controls, 110 patients and 376 controls developed VTE. The overall VTE risk was higher in patients with IBD [adjusted hazard ratio (aHR), 2.10; 95% confidence interval (CI), 1.70.–2.61], compared to controls. The risk of VTE during a non-hospitalized flare of IBD patients was higher compared with controls (aHR, 3.14; 95% CI, 1.90–5.19). The risks of VTE were increased much more during a hospitalization with non-flare (aHR, 16.23; 95% CI, 10.71–24.58) and a hospitalized flare (aHR, 27.20; 95% CI, 14.90–49.65). The risk of VTE was highest at the time of IBD-related surgery (aHR, 39.66; 95% CI, 9.87–159.33). Also, the risk at the time of other major surgeries was increased (aHR, 15.59; 95% CI, 7.73–31.43).
Conclusion: The prophylaxis of VTE for Asian patients with IBD should be considered at the time of a hospitalized flare and IBD-related surgery. However, the prevention of VTE is not needed for non-hospitalized patients with flare.
[Risk of venous thromboembolism by disease activity, hospitalization, and surgery.]
Disclosure: Nothing to disclose

Abstract No: P0364

	Events (n)	Person-years	Incidence (per 1000 person-years)	Adjusted HR* (95% CI)	P value
Disease activity					
IBD	110	99206.2	1.11	2.10 (1.70–2.61)	<0.001
Flare	27	9643.1	2.8	4.8 (3.23–7.11)	<0.001
Inactive (non-flare)	83	89563.1	0.93	1.73 (1.36–2.20)	<0.001
Control	376	595911.7	0.63	1.00 (reference)	
Disease activity and hospitalization					
IBD	110	99206.2	1.11	2.10 (1.70–2.61)	<0.001
Flare and hospitalization	11	720.7	15.26	27.20 (14.90–49.65)	<0.001
Flare and non-hospitalization	16	8922.5	1.79	3.14 (1.90–5.19)	<0.001
Non-flare and hospitalization	24	2441.3	9.83	16.23 (10.71–24.58)	<0.001
Non-flare and non-hospitalization	58	87121.8	0.67	1.29 (0.98–1.71)	0.0724
Control	376	595911.7	0.63	1.00 (reference)	
Surgery					
IBD	110	99206.2	1.11	2.10 (1.70–2.61)	<0.001
IBD-related surgery	2	152.3	13.13	39.66 (9.87–159.33)	<0.001
Other major surgeries	8	626.6	12.77	15.59 (7.73–31.43)	<0.001
Non-surgical period	99	98427.3	1.01	1.73 (1.38–2.16)	<0.001
Control	376	595911.7	0.63	1.00 (reference)	

P0365 SURGICAL AND HOSPITAL ADMISSION IN ADULTS NEWLY DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE IN THE BIOLOGICAL ERA IN SPAIN: RESULTS OF THE NATIONWIDE EPIDEMIBD STUDY OF GETECCU

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Introduction: The need for surgery and hospital admission in newly diagnosed inflammatory bowel disease (IBD) patients in the biological era is largely unknown.

Aims and Methods: i) To assess the frequency of surgery and hospital admission in an inception cohort of adults newly diagnosed with IBD; ii) to describe the characteristics and indications for surgical interventions; and iii) and to evaluate the causes of hospital admissions.

Prospective and population-based nationwide study in Spain. Adult patients diagnosed with IBD –Crohn's disease (CD), ulcerative colitis (UC) or indeterminate colitis (IC)– during 2017 in the 17 Spanish regions were included and followed-up for 12 months after diagnosis. Data were captured in a web-based database (AEG-REDCap).

Results: 3,469 incident cases from 116 centres covering approximately 50% of the Spanish population were included. Of them, 53% were males, with mean age of 43 years. 50% had UC, 45% CD, and 5% IC. About 14% of patients had a family history of IBD. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. 11% of patients had stenosing and 7% fistulising behaviour at the time of diagnosis. In UC patients, 34% had extensive colitis and 31% left-sided colitis at diagnosis. At present, median follow-up is 3 months (range 0–12 months). 149 patients (4.3%) underwent 188 surgical interventions: 131 (8.3%) in CD and 18 (0.9%) in UC ($p < 0.01$). Regarding the first surgical procedure, 60% were urgent and 60% entailed abdominal surgery (30% for perforation, 28% for stenosis and 26% for abdominal abscess). CD patients with inflammatory behaviour had lower rates of surgery than those with strictures or fistula (5.6%, 14%, and 32%, respectively, $p < 0.01$). Surgery was also more frequent among CD patients with perianal disease than in those without it (34 vs. 5.2%, $p = 0.01$). Other variables, such as family history of IBD, or smoking habit were not associated with the need of surgery. A total of 892 patients (26%) had 1,038 hospital admisions during follow-up, with disease diagnosis as major driver (81%). Median time from diagnosis to admission was 0 months (range 0–9 months). Reasons for hospital admissions are summarized in table 1.

Conclusion: In this large nationwide inception cohort in the biological era, a substantial proportion of IBD patients underwent surgery, which was urgent in over 2/3 of the cases. Stricturing and fistulizing complications in CD patients were the main drivers for surgery in these patients. 1/4 of patients were hospitalised –most of them at disease diagnosis– within the first 3 months of follow-up.

	CD (N = 507)	UC (N = 385)
Disease diagnosis, n (%)	373 (75)	335 (88)
Disease flare-up, n (%)	28 (5.7)	40 (10)
Perianal disease, n (%)	18 (3.6)	
Abdominal abscess, n (%)	11 (2.2)	
Thiopurine adverse event, n (%)	9 (1.8)	
Intestinal obstruction, n (%)	34 (6.9)	
Elective surgery, n (%)	2 (0.4)	
Infection, n (%)	4 (0.9)	4 (1.4)
Fever of unknown origin, n (%)	6 (0.6)	
Perforation, n (%)	4 (0.8)	1 (0.3)
Mesalazine induced pneumonitis, n (%)	2 (0.4)	1 (0.3)
Others, n (%)	19 (3.8%)	4 (1.2)

[Table 1. Reasons for hospital admissions during follow-up.]

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P0366 SHORT TERM AZATHIOPRINE CO-TREATMENT DOES NOT IMPACT LONG TERM CLINICAL OUTCOME IN INFLAMMATORY BOWEL DISEASE TREATED WITH INFLIXIMAB, BUT HAS INFLIXIMAB-SPARING EFFECT

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Introduction: It is usual clinical practice to start infliximab as combination treatment with azathioprine in patients with inflammatory bowel disease (IBD) and to de-escalate from combination treatment to infliximab (IFX) monotherapy once disease remission is reached. It is however unclear if the addition of azathioprine during introduction of IFX improves long-term clinical outcomes and pharmacokinetics in patients who previously failed azathioprine.

Aims and Methods: We aimed to study the effect of short-term (6–12 months) co-treatment with azathioprine on long-term clinical outcome and on consumption of IFX in patients who escalated from azathioprine to either IFX monotherapy or to combination of azathioprine and IFX due to inefficacy of azathioprine.

We included 149 patients (94 Crohn's disease, 55 ulcerative colitis) who started IFX between 2011 and 2016 for active IBD in a tertiary referral centre. To study the effect of azathioprine co-treatment we compared patients who started IFX as combination treatment with azathioprine and then de-escalated to IFX monotherapy after disease remission was reached (IFX combo) with patients who started IFX as monotherapy from the beginning (IFX mono).

Results: The study population included 78 (52%) IFX combo patients and 71 (48%) IFX mono patients. IFX combo (Crohn's disease: ileocolonic 71%, perianal 42%; ulcerative colitis: pancolitis 62%) and IFX mono (Crohn's disease: ileocolonic 74%, perianal 29%; ulcerative colitis: pancolitis 69%) groups did not differ in disease phenotype.

During a median follow-up of 19 months [interquartile range (IQR): 12–40 months] 38/149 (26%) patients permanently lost response to IFX.

Short-term (median 9 months [IQR: 6–13 months] azathioprine co-treatment did not impact clinical outcome after one year of treatment (loss of response in 8/78 (10.3%) in IFX mono vs. 12/71 (16.9%) in IFX combo ($p = 0.235$) nor did it impact long term outcome at the end of follow-up (loss of response in 18/71 (25.4%) in IFX mono vs. 20/78 (25.6 %) in IFX combo ($P = 0.968$).

However, azathioprine co-treatment decreased IFX consumption during the first year of treatment by approximately 25% and improved pharmacokinetics as the IFX combo group achieved higher IFX trough levels with lower IFX maintenance doses. However, at the end of follow-up, i.e. after a median of 14 months [IQR: 3–33 months] after withdrawal of azathioprine, the IFX-sparing effect, that was enjoyed while patients were co-treated with azathioprine, was attenuated with both groups of patents receiving similar doses of IFX and having similar IFX trough levels (Table 1).

Conclusion: Short-term (6–12 months) combination treatment with azathioprine after initiation of infliximab does not impact the long-term outcome of patients with inflammatory bowel disease but it decreases consumption of infliximab by approximately 25% during the first year of treatment. However, this infliximab-sparing effect is lost after de-escalation from combination treatment to infliximab monotherapy.

Abstract No: P0366

	Infliximab dose (mg/kg q 8 weeks)			Infliximab TL (μg/mL)	
	After induction	At year 1 after start	At the end of follow-up	TL at year 1	TL at the end of FU
Infliximab + azathioprine Median (IQR) (N = 75)	5.9 (5.1–7.4)	6.7 (5.25–9.0)	7.7 (6.5–10.7)	5.0 (2.5–.7)	5.2 (1.9–9.6)
Infliximab monotherapy Median (IQR) (N = 69)	6.2 (5.3–8.1)	8.9 (6.7–10.6)	8.4 (6.6–11.0)	1.8 (0.3–6.6)	3.4 (0.3–7.3)
P	0.237	0.019	0.335	0.012	0.080

*5 patients stopped treatment during induction

[Table 1: Effect of short term (6–12 months) azathioprine co-treatment on consumption of infliximab and trough levels. IQR - interquartile range, TL -]

Disclosure: Speaker, a consultant and an advisory board member for MSD, Abbvie, Takeda, Pfizer, Janssen, Krka.

P0367 MAINTENANCE OF REMISSION WITH TOFACITINIB IN PATIENTS WITH ULCERATIVE COLITIS: SUBPOPULATION ANALYSIS FROM AN OPEN-LABEL, LONG-TERM EXTENSION STUDY

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Introduction: Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). The efficacy and safety of tofacitinib were demonstrated in 3 Phase (P) 3, randomised, placebo-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458951; OCTAVE Sustain, NCT01458574) in patients (pts) with moderate to severe UC.[1] An ongoing P3, multicentre, open-label, long-term extension study (OLE; NCT01470612) included pts from OCTAVE Induction 1 or 2, or OCTAVE Sustain.

Aims and Methods: We present an update (as of 10 Nov 2017) of previous analyses of the OLE study maintenance remission subpopulation (pts in remission [total Mayo score ≤2, no individual subscore >1, rectal bleeding subscore of 0] at Week [Wk] 52 of OCTAVE Sustain).[2] Pts in remission at Wk 52 of OCTAVE Sustain received tofacitinib 5 mg twice daily (BID) in the OLE study. Efficacy data, including remission, mucosal healing (Mayo endoscopic subscore of 0 or 1), clinical response (decrease from induction baseline total Mayo score of ≥3 points and ≥30%, and decrease in rectal bleeding subscore ≥1 or absolute rectal bleeding subscore of 0 or 1; all based on local read) and partial Mayo score (PMS) remission (PMS ≤2, no individual subscore >1), up to Month 24 of the OLE study (as observed and with non-responder imputation), are presented for pts in remission after receiving tofacitinib in OCTAVE Sustain. Safety data are reported for all pts who received tofacitinib 5 mg BID in the OLE study.

Results: Of 944 pts who received ≥1 dose of study drug in the OLE study, 163 (mean age: 45 years; 46.0% female) were in remission at Wk 52 of OCTAVE Sustain. Of these, 142 had received tofacitinib 5 mg (n = 66) or 10 mg (n = 76) BID in OCTAVE Sustain. 40/163 (24.5%) pts discontinued in the OLE study (13 [8.0%] due to insufficient clinical response; 12 [7.4%] due to adverse events [AEs] excluding worsening UC).

Binary efficacy endpoints at baseline and up to Month 24 of the OLE study are shown in the Table. Efficacy over 24 months was similar irrespective of tofacitinib dose previously received in OCTAVE Sustain.

Among all pts receiving tofacitinib 5 mg BID in the OLE study, 78.9% reported treatment-emergent AEs (TEAEs). Serious and severe AEs occurred in 12.0% and 8.0% of pts, respectively. The most frequent TEAEs by preferred term were 'nasopharyngitis' and 'worsening of UC'. 5 pts (2.9%) had serious infections and 10 (5.7%) had herpes zoster (all mild or moderate severity). Malignancy excluding non-melanoma skin cancer was reported in 1 (0.6%) pt (lung cancer).

Conclusion: The majority of pts with moderate to severe UC who achieved remission after 52 wks of tofacitinib 5 or 10 mg BID in OCTAVE Sustain maintained remission, mucosal healing, clinical response and PMS remission with tofacitinib 5 mg BID for up to 24 months in the OLE study (up to 3 years from maintenance study baseline). No new safety risks were identified.

[Table]

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P0368 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF ULCERATIVE COLITIS: AN INTERIM ANALYSIS OF AN OPEN-LABEL, LONG-TERM EXTENSION STUDY WITH UP TO 4.9 YEARS OF TREATMENT

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). The efficacy and safety of tofacitinib was demonstrated as induction and maintenance therapy in patients (pts) with moderate to severe UC in 3 Phase (P) 3, randomised, placebo-controlled studies.[1] Safety and efficacy of tofacitinib for UC are being evaluated in an ongoing, open-label, long-term extension (OLE) study.[2]

Aims and Methods: We present an update (as of 10 Nov 2017) of previously presented safety and efficacy data[2] of an ongoing P3, multicentre, OLE study (NCT01470612) in pts who completed or demonstrated treatment failure in OCTAVE Sustain (NCT01458574) or were non-responders in OCTAVE Induction 1 or 2 (NCT01458951, NCT01458574). Eligibility was determined per Week (Wk) 8 data from OCTAVE Induction 1 & 2, or Wk 52 data (for completers) or early termination data from OCTAVE Sustain. Pts in remission (total Mayo score ≤2, no individual subscore >1, rectal bleeding subscore of 0) at Wk 52 of OCTAVE Sustain (per central read) were assigned to tofacitinib 5 mg twice daily (BID) in the OLE study; all others were assigned to 10 mg BID. At Month 2, all pts underwent endoscopy, and induction non-responders were mandated to withdraw if they did not show a clinical response. Binary efficacy endpoints were derived from Mayo score per local read.

Results: Of 944 pts who received ≥1 dose of study drug (for up to 4.9 years), 769 (81.5%) pts received tofacitinib 10 mg BID; 326 (34.5%) pts discontinued due to insufficient clinical response, and 65 (6.9%) discontinued due to adverse events [AEs] excluding worsening UC. Serious and severe AEs occurred in 14.8% and 9.9% of pts, respectively. The most frequent treatment-emergent AE (TEAE) classes were infections and gastrointestinal disorders. The most frequent TEAEs were nasopharyngitis, worsening UC and increased blood creatine phosphokinase. Serious infections were reported in 5 (2.9%) and 23 (3.0%) pts, herpes zoster in 10 (5.7%) and 47 (6.1%) pts, and major adverse cardiovascular events in 1 (0.6%) and 1 (0.1%) pts in the 5 and 10 mg BID groups, respectively. Malignancies excluding non-melanoma skin cancer (NMSC) were reported in 1 (0.6%) and 12 (1.6%) pts, and NMSC in 4 (2.3%) and 9 (1.2%) pts, in the 5 and 10 mg BID groups, respectively (with no clustering of malignancy type). No new safety risks were identified. Available remission, mucosal healing and clinical response data up to Month 24 are shown (Table).

Conclusion: In pts with moderate to severe UC in the OLE study, no new safety risks emerged compared with those observed with tofacitinib in rheumatoid arthritis. Efficacy data from the OLE study continue to support long-term efficacy with tofacitinib 5 or 10 mg BID up to 24 months beyond Wk 52 of OCTAVE Sustain.

[Table]

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Table: Efficacy of tofacitinib 5 mg BID in patients in the maintenance remission subpopulation of the OLE study[a] who previously received tofacitinib 5 or 10 mg BID in OCTAVE Sustain

	Tofacitinib 5 mg BID in OLE study, as observed		
Previous treatment in OCTAVE Sustain	Tofacitinib 5 mg BID N = 66	Tofacitinib 10 mg BID N = 76	Tofacitinib 5 or 10 mg BID N = 142
Remission, n/N1 (%)			
Baseline; central read	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	49/58 (84.5)	60/74 (81.1)	109/132 (82.6)
Month 12	50/58 (86.2)	56/68 (82.4)	106/126 (84.1)
Month 24	26/33 (78.8)	32/42 (76.2)	58/75 (77.3)
Mucosal healing, n/N1 (%)			
Baseline; central read	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	56/61 (91.8)	68/75 (90.7)	124/136 (91.2)
Month 12	51/58 (87.9)	63/70 (90.0)	114/128 (89.1)
Month 24	30/34 (88.2)	38/43 (88.4)	68/77 (88.3)
Clinical response, n/N1 (%)			
Baseline; central read	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	57/58 (98.3)	70/74 (94.6)	127/132 (96.2)
Month 12	58/58 (100.0)	63/68 (92.6)	121/126 (96.0)
Month 24	32/33 (97.0)	41/42 (97.6)	73/75 (97.3)
PMS remission, n/N1 (%)			
Baseline	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	60/62 (96.8)	67/74 (90.5)	127/136 (93.4)
Month 12	58/59 (98.3)	61/69 (88.4)	119/128 (93.0)
Month 24	33/34 (97.1)	42/44 (95.5)	75/78 (96.2)
	Tofacitinib 5 mg BID in OLE study, NRI[b]		
Previous treatment in OCTAVE Sustain	**Tofacitinib 5 mg BID N = 66**	**Tofacitinib 10 mg BID N = 76**	**Tofacitinib 5 or 10 mg BID N = 142**
Remission, n/N1 (%)			
Baseline; central read	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	49/60 (81.7)	60/76 (78.9)	109/136 (80.1)
Month 12	50/66 (75.8)	56/73 (76.7)	106/139 (76.3)
Month 24	26/42 (61.9)	32/52 (61.5)	58/94 (61.7)
Mucosal healing, n/N1 (%)			
Baseline; central read	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	56/63 (88.9)	68/76 (89.5)	124/139 (89.2)
Month 12	51/66 (77.3)	63/75 (84.0)	114/141 (80.9)
Month 24	30/43 (69.8)	38/53 (71.7)	68/96 (70.8)
Clinical response, n/N1 (%)			
Baseline; central read	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	57/60 (95.0)	70/76 (92.1)	127/136 (93.4)
Month 12	58/66 (87.9)	63/73 (86.3)	121/139 (87.1)
Month 24	32/42 (76.2)	41/52 (78.8)	73/94 (77.7)
PMS remission, n/N1 (%)			
Baseline	66/66 (100.0)	76/76 (100.0)	142/142 (100.0)
Month 2	60/63 (95.2)	67/76 (88.2)	127/139 (91.4)
Month 12	58/66 (87.9)	61/74 (82.4)	119/140 (85.0)
Month 24	33/43 (76.7)	42/53 (79.2)	75/96 (78.1)

[a]Patients in remission, based on central endoscopic reading, at Wk 52 of OCTAVE Sustain (all receiving tofacitinib 5 mg BID in OLE study); [b]Patients were treated as non-responders after the time of discontinuation up to the visit they would have reached if they had stayed in the study. No imputation for missing data was applied for ongoing patients.

All values are per local read of endoscopy, unless otherwise stated (baseline values are per central read). Remission was defined as a total Mayo score ≤2 with no individual subscore >1, and rectal bleeding subscore of 0; mucosal healing was defined by a Mayo endoscopic subscore ≤1; PMS remission was defined as a PMS ≤2 with no individual subscore >1.

BID, twice daily; n, number of patients in the maintenance remission subpopulation with the specified response within the given category; N, number of randomised patients in the maintenance remission subpopulation; N1, number of patients in the remission subpopulation who could have reached the specified time point (based on enrolment date and last non-missing total Mayo score [endoscopy for mucosal healing]); NRI, non-responder imputation; OLE, open-label long-term extension; PMS, partial Mayo score; Wk, Week.

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P0369 SEVEN-YEAR EFFICACY AND SAFETY OF AZATHIOPRINE TREATMENT IN THE MAINTAINANCE OF STEROID-FREE REMISSION IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Table: Summary of safety and efficacy in the OLE study

	Tofacitinib 5 mg BID N = 175	Tofacitinib 10 mg BID N = 769	Tofacitinib All N = 944
Baseline demographics and disease characteristics			
Female, n (%)	79 (45.1)	310 (40.3)	389 (41.2)
Age in years, mean (SD)	44.5 (14.6)	40.5 (13.5)	41.2 (13.8)
Total Mayo score, mean (SD)	1.2 (0.9)	8.1 (2.3)	6.8 (3.4)
Discontinuations, n (%)			
Due to AE excluding worsening UC[a]	12 (6.9)	53 (6.9)	65 (6.9)
Due to insufficient clinical response[b,c]	14 (8.0)	312 (40.6)	326 (34.5)
All-causality TEAEs, n (%)			
AEs			
SAEs	138 (78.9)	607 (78.9)	745 (78.9)
Severe AEs	21 (12.0)	119 (15.5)	140 (14.8)
Gastrointestinal AEs	14 (8.0)	79 (10.3)	93 (9.9)
Any infections	64 (36.6)	321 (41.7)	385 (40.8)
Serious infections	91 (52.0)	375 (48.8)	466 (49.4)
Herpes zoster	5 (2.9)[d]	23 (3.0)[e]	28 (3.0)
MACE[g]	10 (5.7)	47 (6.1)[f]	57 (6.0)
Malignancies excluding	1 (0.6)[h]	1 (0.1)[i]	2 (0.2)
NMSC[g]	1 (0.6)[j]	12 (1.6)[k]	13 (1.4)
NMSC[g]	4 (2.3)	9 (1.2)	13 (1.4)
Efficacy endpoints (FAS, as observed)			
Remission, n/N1 (%)			
Month 2	130/164 (79.3)	189/676 (28.0)	319/840 (38.0)
Month 12	129/154 (83.8)	278/449 (61.9)	407/603 (67.5)
Month 24	69/88 (78.4)	244/343 (71.1)	313/431 (72.6)
Mucosal healing, n/N1 (%)			
Month 2	152/169 (89.9)	280/690 (40.6)	432/859 (50.3)
Month 12	140/156 (89.7)	338/459 (73.6)	478/615 (77.7)
Month 24	79/90 (87.8)	286/354 (80.8)	365/444 (82.2)
Clinical response, n/N1 (%)			
Month 2	159/164 (97.0)	476/673 (70.7)	635/837 (75.9)
Month 12	147/154 (95.5)	413/449 (92.0)	560/603 (92.9)
Month 24	86/88 (97.7)	323/343 (94.2)	409/431 (94.9)
Efficacy endpoints (FAS, NRI)[l]			
Remission, n/N1 (%)			
Month 2	130/168 (77.4)	189/765 (24.7)	319/933 (34.2)
Month 12	129/172 (75.0)	278/758 (36.7)	407/930 (43.8)
Month 24	69/118 (58.5)	244/726 (33.6)	313/844 (37.1)
Mucosal healing, n/N1 (%)			
Month 2	152/172 (88.4)	280/767 (36.5)	432/939 (46.0)
Month 12	140/174 (80.5)	338/764 (44.2)	478/938 (51.0)
Month 24	79/120 (65.8)	286/731 (39.1)	365/851 (42.9)
Clinical response, n/N1 (%)			
Month 2	159/168 (94.6)	476/765 (62.2)	635/933 (68.1)
Month 12	147/172 (85.5)	413/758 (54.5)	560/930 (60.2)
Month 24	86/118 (72.9)	323/726 (44.5)	409/844 (48.5)

[a]Baseline mean total Mayo score was not available for 2 patients in the tofacitinib 10 mg BID group; therefore, Tofacitinib 10 mg BID, N = 767 and Tofacitinib All, N = 942; [b]AEs of worsening UC leading to discontinuation were designated as insufficient clinical response; [c]Induction non-responders were mandated to withdraw if they did not have evidence of clinical response at Month 2; [d]2 cases were reported as severe (number of cases): appendicitis (1), gastroenteritis norovirus (1); [e]9 cases were reported as severe (number of cases): appendicitis (3), arthritis bacterial (1), atypical pneumonia (1), herpes zoster (2), herpes zoster meningitis (1), meningitis herpes (1); [f]4 cases were reported as severe; [g]Adjudicated events; [h]A case of cerebellar haemorrhage; [i]A case of cerebrovascular accident; [j]Malignancy: pulmonary mass; [k]Malignancy (number of cases): cervical dysplasia (1), hepatic angiosarcoma (1), invasive ductal breast carcinoma (1), adenocarcinoma of colon (2), essential thrombocythaemia (1), acute myeloid leukaemia (1), cholangiocarcinoma (1), cutaneous leiomyosarcoma (1), Epstein-Barr virus-associated lymphoma (1), renal cell carcinoma (1), malignant melanoma (1); [l]Patients were treated as non-responders after the time of discontinuation up to the visit they would have reached if they had stayed in the study. No imputation for missing data was applied for ongoing patients.

Remission was defined as a Mayo score ≤2 with no individual subscore >1, and rectal bleeding subscore of 0; Mucosal healing was defined by a Mayo endoscopic subscore ≤1; Clinical response was defined by a decrease from study baseline Mayo score of ≥3 points and ≥30%, accompanied by a decrease in rectal bleeding subscore of ≥1 or an absolute rectal bleeding subscore of 0 or 1.

AE, adverse event; BID, twice daily; FAS, full analysis set; GI, gastrointestinal; n, number of patients with the specified response within the given category; MACE, major adverse cardiovascular event; N, number of randomised patients in the total population; N1, number of patients in the specified category with non-missing values; NMSC, non-melanoma skin cancer; NRI, non-responder imputation; OLE, open-label long-term extension; SAEs, serious AEs; SD, standard deviation; SOC, system organ class; TEAEs, treatment-emergent AEs; UC, ulcerative colitis.

Introduction: Azathioprine (AZA) and thiopurine are widely used for induction and maintenance of remission in steroid dependent patients with inflammatory bowel disease (IBD).

Aims and Methods: Aim of this study has been to investigate its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients seven year after the institution of treatment. Data from consecutive IBD outpatients referred in our Institution, between 1985–2016, were reviewed and all patients treated with AZA were included in this retrospective study. AZA was administered at the recommended dose of 2–2.5 mg/kg.

Results: Out of 2802 consecutive IBD outpatients visited in the index period, AZA was prescribed to 433 patients, 236 (54.5%) were affected by Crohn's disease (CD) and 197 (45.5%) by ulcerative colitis (UC). 179 patients with a follow-up < 84 months were excluded from the study. 254 patients were evaluated, 141 (55.5%) with CD and 113 (44.5%) with UC. 139 (54.7%) were male

and 115 (45.3%) female (average age of 35.62 ± 14.20 SD years, range 14–74 y.). 7 years after the institution of treatment, 127 (50%) patients still were in steroid-free remission (83 CD vs 44 UC, 58.8% and 38.9%, respectively, p = 0.0024), 71 (27.9%) had a relapse requiring retreatment with steroids (29 CD vs 42 UC, 20.6% and 37.2%, respectively, p = 0.0047), 56 (22.1%) discontinued the treatment due to side effects (29 CD vs 27 UC, 20.6% and 23.9%, respectively). Loss of response from 1st to 7th year of follow-up was low, about 20%.
Conclusion: 7 year after the onset of treatment 50% of patients did not require further steroid courses. After the first year loss of response was low in 6 subsequent years. In the present series the maintenance of steroid-free remission was significantly higher in CD than in UC patients. The occurrence of side effects leading to the withdrawal of AZA treatment has been low.
Disclosure: Nothing to disclose

P0370 EARLY CHANGE OF PATIENT-REPORTED RECTAL BLEEDING AND STOOL FREQUENCY SCORE AND FECAL CALPROTECTIN LEVEL ARE ASSOCIATED WITH COLECTOMY OUTCOME AT 1 YEAR IN PURSUIT-MAINTENANCE TRIAL

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Introduction: In ulcerative colitis (UC), uncontrolled inflammation may result in progressive mucosal damage requiring colectomy. Absence of short-term clinical response to medical therapy and absence of early mucosal healing (MH) are predictors of colectomy (1, 2).
Aims and Methods: We investigated the association of colectomy with early clinical and endoscopic response, and change of fecal calprotectin (FC) in the PURSUIT-Maintenance (PURSUIT-M) study of golimumab in patients with moderate to severe UC. We assessed whether early change of patient-reported outcomes (PRO) Mayo rectal bleeding score (RBS) and Mayo stool frequency score (SFS) and biomarker FC are associated with colectomy. PRO2 (RBS and SFS), Physician Global Assessment (PGA), Mayo score, Mayo endoscopic score (ES) and FC data were obtained at baseline and wk6 (end of induction). Data were compared between patients with and without colectomy by wk54 of maintenance in PURSUIT-M. A total of 1228 patients were included for colectomy analysis.
Results: N = 47 patients required colectomy by wk54 of maintenance in PURSUIT-M (3.8%). Of these, 34 (72.3%) were non-responders to sc or iv golimumab induction regimens. Responders to induction who underwent colectomy by wk54 (n = 9) received either 100mg (n = 2), 50mg (n = 4) or placebo (n = 3) maintenance therapy. 4 additional patients who responded to placebo induction and were maintained on placebo had colectomy. Baseline and wk6 Mayo score, Mayo ES, RBS, SFS, PGA, and log of FC value are shown in the table. At baseline, Mayo score, Mayo ES, and PGA were different between the 2 groups, whereas at wk6 Mayo score, Mayo ES, PGA as well as RBS, SFS and FC were different between the colectomy and non-colectomy groups.
Conclusion: This post-hoc analysis of colectomy outcome in PURSUIT-M shows that early (wk6 of induction) reductions of PRO2 (RBS and SFS) score and FC level are associated with a reduced likelihood of colectomy over 1 year of treatment. These data suggest that PRO2 (RBS and SFS) and FC are markers of disease activity that may inform colectomy risk stratification in UC patients treated with golimumab.

	No Colectomy		Colectomy		Total		Colectomy vs No Colectomy	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	Difference	P value (T test)
Age (years)	1152	40.8 (13.5)	47	40.7 (14.6)	1199	40.8 (13.5)	−0.13	0.9536
Disease duration (years)	1152	6.5 (6.5)	47	7.6 (8.2)	1199	6.5 (6.6)	1.12	0.3599
Mayo Score								
wk0	1151	8.4 (1.46)	47	8.9 (1.71)	1198	8.4 (1.48)	0.58	0.0260
wk6	1152	5.6 (2.96)	47	7.4 (3.48)	1199	5.7 (3.01)	1.86	0.0007
PGA								
wk0	1151	2.2 (0.43)	47	2.4 (0.49)	1198	2.2 (0.43)	0.20	0.0074
wk6	1152	1.5 (0.82)	47	1.9 (0.96)	1199	1.5 (0.83)	0.42	0.0046
RBS								
wk0	1151	1.5 (0.82)	47	1.5 (1.02)	1198	1.5 (0.82)	−0.01	0.9622
wk6	1152	0.7 (0.85)	47	1.2 (1.01)	1199	0.8 (0.86)	0.44	0.0046
SFS								
wk0	1151	2.3 (0.75)	47	2.5 (0.78)	1198	2.3 (0.75)	0.19	0.1067
wk6	1152	1.6 (1.07)	47	2.2 (1.09)	1199	1.7 (1.07)	0.60	0.0005
Mayo ES								
wk0	1151	2.4 (0.49)	47	2.6 (0.50)	1198	2.4 (0.49)	0.20	0.0100
wk6	1152	1.7 (0.90)	47	2.1 (0.93)	1199	1.7 (0.90)	0.39	0.0066
Log FC								

(continued)

Continued

	No Colectomy		Colectomy		Total		Colectomy vs No Colectomy	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	Difference	P value (T test)
wk0	1066	2.9 (0.69)	42	2.9 (0.46)	1108	2.9 (0.68)	0.02	0.8131
wk6	1149	2.5 (0.77)	47	2.9 (0.60)	1196	2.6 (0.77)	0.36	0.0002

P values were not adjusted for multiple comparisons.
[Table]
Disclosure: F. Cornillie and A. Khalifa are employees of Merck Sharp & Dohme Corp. (MSD) and may hold stock and/or stock options in the company. L. Peyrin-Biroulet is a member of the MSD global advisory board and received speaking fees from MSD. G. Philip is an employee of Merck & Co., Inc., Kenilworth, NJ, USA, and may hold stock and/or stock options in the company

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P0371 MEASURING THIOGUANINE NUCLEOTIDE (6-TGN) LEVELS AND CLINICAL RESPONSE IN IBD; COMPARING SINGLE AND COMBINED THERAPIES

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Introduction: Monitoring levels of 6-TGN and titrating dose of Azathioprine (AZA) and Mercaptopurine (6-MP) accordingly to achieve therapeutic concentrations of 6-TGN has been reported to improve outcomes in the treatment of Ulcerative colitis (UC) and Crohn's Disease (CD).
Aims and Methods: The aim of our study was to show how levels of 6-TGN corresponds to clinical outcome, and compare those on sole therapy and those combined with biologics. This was a single centre (Royal Free Hospital), retrospective study, of patients receiving AZA or 6MP. We identified our patients by collating those who had been dispensed AZA or 6MP over the past 2 years. We were then able to access their electronic database, and record whether 6-TGN levels were subsequently taken to titrate treatment, and assess clinical outcome.
Results: 359 from 426 patients have so far been analysed (F = 153 [42.6%], UC = 160 [44%], CD = 190 [53%], indeterminate/other colitis = 9 [3%]).
Mean duration on thiopurines was 5.7 years. Mean disease duration was 12.7 years.
Out of patients with IBD (359), 275 [77%] had 6-TGN levels measured at some stage.
177/275 (64%) had therapeutic levels, whilst 98/275 (36%) did not.
166/275 (60.5%) were in clinical remission. 94/275 (34.5%) were not. For 15 patients (5%), no data was available.
Of those that had therapeutic levels of 6-TGN, 112/177 (63%) were in clinical remission. 46/112 (41%) were on combined therapy with biologics. 66/112 (59%) were on purines alone. Of these 66, 37 (56%) were on Azathioprine (AZA), 26 (39%) were on mercaptopurine (6MP). For 3/66 (5%) patients there was no thiopurine treatment data or the treatment was stopped.
Of those that had non-therapeutic levels of 6-TGN, 54/98 (55%) were in clinical remission. 23/54 (44%) were on combined therapy with biologics. 31/54 (57%) were on purines alone. Of those who were not on biologics 21/31 (68%) were on AZA. 9/31 (29%) were on 6MP. 1/31 (3%) data not complete/purines were stopped.
Of those with therapeutic levels of 6-TGN, 53/177 (30%) were not in clinical remission. 40/53 (75%) were on combined therapy with biologics. 13/53 (25%) were on purines alone. Of those who were not on biologics 7/13 (54%) were on AZA, 5/13 (38%) were on 6MP, 1/13 (8%) data not complete/purines were stopped.
Of the cohort that had non-therapeutic levels of 6-TGN, 41/98 (42%) were not in clinical remission. 29/41 (71%) were on combined therapy. 12/41 (29%) were on purines alone. 9/12 (75%) were on AZA, 1/12 (8%) on 6MP, 2/12 (17%) data not complete/purines were stopped.
(Note: 12 of the 177 patients with therapeutic 6-TGN had no data on remission status. 3 of the 98 patients with non-therapeutic levels of 6-TGN had no data on remission status).
Conclusion: Interestingly our study suggests that if you had therapeutic levels of 6-TGN, you were more likely to be in clinical remission if you were on purines alone as compared to combined with biologics (59% vs. 41%). These interesting trends need further analysis to ascertain more comprehensive conclusions between the groups of sole therapy and combined biologics.
Disclosure: Nothing to disclose

P0372 SAFETY AND EFFECTIVENESS OF GRANULOCYTE AND MONOCYTE ADSORPTIVE APHERESIS FOR 90 PATIENTS WITH CORTICOSTEROIDS NAïVE ULCERATIVE COLITIS PATIENTS: A MULTICENTER COHORT STUDY

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Introduction: To evaluate the efficacy of granulocyte and monocyte apheresis (GMA) in corticosteroid naïve patients with active ulcerative colitis (UC) without concomitant corticosteroids therapy in remission induction and sustained remission.

Aims and Methods: In this multicenter retrospective study, ninety corticosteroids naïve patients with active UC received GMA as remission induction therapy between 2012 and 2018 in 4 Japanese institutes were enrolled. Each patient received weekly or intensive (2–3 sessions/week) GMA up to 11 sessions. Partial Mayo score ≤ 2 meant remission, while ≤ 1 in Mayo endoscopic subscore meant mucosal healing. Concomitant medication with corticosteroids, biologics or calcineurin inhibitors were not allowed, but medication with 5-ASA and immune-modulators were permitted.

Results: The overall remission and mucosal healing rates were 71.1% (64/90) and 64.5% (49/76), respectively. Subjects who achieved a remission were clinically and endoscopically followed for 12 months after a course of GMA. After 12 months follow up, a sustained remission was recorded in 66.7% (44/66) of those treated with GMA. The patients who had obtained a remission after a course of GMA showed relapses up to 33.3% (22/66) and mean time to relapse was 10.0 months.

Conclusion: The overall remission and mucosal healing rates were 71.1% (64/90) and 64.5% (49/76), respectively. Subjects who achieved a remission were clinically and endoscopically followed for 12 months after a course of GMA. After 12 months follow up, a sustained remission was recorded in 66.7% (44/66) of those treated with GMA. The patients who had obtained a remission after a course of GMA showed relapses up to 33.3% (22/66) and mean time to relapse was 10.0 months.

Disclosure: Nothing to disclose

P0373 ADVANCES IN OPTIMALIZATION OF THERAPEUTIC DRUG MONITORING USING MUCOSAL TNF EXPRESSION AND ANTI-TNF CONCENTRATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH BIOLOGICALS - PRELIMINARY RESULTS FROM A SINGLE CENTER STUDY

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Introduction: The introduction of anti-TNF therapy has dramatically changed the treatment of refractory inflammatory bowel disease (IBD-Crohn's disease [CD], ulcerative colitis [UC]). However, the clinical use of anti-TNF therapies is limited by loss of response posing significant challenge for clinicians. Therapeutic drug monitoring has gained increasing popularity in the management of IBD. However, relationship between clinical outcomes and serum anti-TNF levels is complex and controversial in many cases.

Aims and Methods: The aim of this study is to simultaneously analyse the serum, mucosal and fecal infliximab and adalimumab levels, to determine the mucosal expression of TNF-α and to assess the relationship between the levels of anti TNF-α in the above mentioned biological samples with endoscopic and clinical activities of IBD patients receiving anti-TNF maintenance therapy.

Patients with luminal CD and UC receiving maintenance anti TNF-α therapy have been started to enroll in the study and the enrollment is still ongoing. Clinical disease activity is assessed, blood samples and fecal specimens are collected and colonoscopy with biopsy samples is performed in every patient. Biopsy samples are obtained from inflamed and uninflamed tissue from the colon. Mucosal TNF-α expression is detected by confocal microscopy after immunofluorescent staining. Serum, mucosal and fecal anti TNF-α and anti drug antibody levels is determined by ELISA assay. Kendall-tau correlation coefficient was used to assess bivariate correlations.

Results: Data of 34 patients have been analyzed (20 CD, 14 UC; 17 infliximab, 17 adalimumab). The number of TNF-α positive cells was significantly higher in mucosal samples of active vs. inactive part of the bowel ($p < 0.001$). Mucosal drug level proved to be significantly higher in samples obtained from the inactive vs. active part of the bowel ($p < 0.001$). However, no association could be detected between the number of TNF-α positive cells and either endoscopic activity or mucosal drug levels. Serum drug level was significantly lower in patients who developed anti drug antibody ($p = 0.043$). We did not find any correlation between serum drug level and fecal calprotectin concentration, however, calprotectin level was higher in patients with anti-drug antibody positivity ($p = 0.0134$). No correlation was detected between serum and mucosal anti TNF levels.

Conclusion: Our study would be the first that simultaneously examine serum, tissue and fecal concentrations of anti TNF-α comparing with clinical and endoscopic activities. We were unable to find evidence against the hypothesis of no association between serum drug levels and mucosal anti TNF-α concentration. However, the sample size is currently very low, and more data is needed to be collected in order to better investigate the association between serum and tissue drug levels or disease activity. Nevertheless, it is hoped that these measurements will allow a better overview of the drug distribution and clearance and may help to identify a useful surrogate marker of clinical and endoscopic activity.

Disclosure: Nothing to disclose

P0374 ANTI-TNFα VS. CONVENTIONAL TREATMENT FOR THE PREVENTION OF POSTOPERATIVE RECURRENCE OF CROHN'S DISEASE. A META-ANALYSIS

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Introduction: The majority of patients with Crohn's disease (CD) need surgery during their lifetime. Within 1 year, 80% of the operated patients has endoscopic postoperative recurrence (POR). However, there is no widely accepted consensus on the prevention of POR.

Aims and Methods: Our aim was to compare the efficacy of biological agents and that of conventional therapy as prophylactic treatment options for POR and also to compare the efficacy of prophylactic biological treatment in high risk vs. non-selected patient populations. We searched Pubmed, Cochrane Library, EMBASE, and Web of Science for English-language studies published from inception up to 15 April 2017. The PICO items were, as follows: (P) adults with CD who had intestinal resection, (I) biological therapy (adalimumab, infliximab), (C) conventional therapies (mesalamine, thiopurines and placebo), and (O) clinical, endoscopic, and severe endoscopic POR. Patients were considered at 'high risk' for POR if they had ≥ 1 of the following risk factors: active smoking, young age at diagnosis, penetrating or perianal disease at diagnosis, ≥ 1 resections, and resection within 3 years. Odd ratios (OR) and 95% confidence intervals (CI) were calculated. PROSPERO registration number is CRD42017083679.

Results: The data of 2 observational and 8 randomized controlled trials, including 709 CD patients, were analysed. Anti-TNFα agents were significantly more effective in preventing clinical and endoscopic POR compared to conventional therapies (OR: 0.501, 0.319–0.786, $p = 0.003$, and OR: 0.157, 0.069–0.359, $p < 0.001$, respectively). We could demonstrate an overall benefit of biological therapy in unselected patient groups of CD patients regarding clinical, endoscopic and severe endoscopic POR (OR: 0.449, 0.272–0.741, $p = 0.002$; OR: 0.132, 0.055–0.317, $p < 0.001$, and OR: 0.263, 0.085–0.817, $p = 0.021$, respectively). In the course of direct comparison, there was no significant difference in POR rates between the 2 anti-TNF agents. Patients previously treated with biologics were less likely to maintain remission after surgery (OR: 0.509, 0.303–0.853, $p = 0.010$).

Conclusion: Compared to the conventional therapies, biological agents are more effective in preventing clinical and endoscopic POR both in unselected and high-risk CD patients. In addition, biologics should be continued after surgery in patients with preoperative anti-TNFα treatment to maintain remission.

Disclosure: Nothing to disclose

P0375 EFFICACY AND SAFETY OF GRANULOCYTE ADSORPTION APHERESIS IN ELDERLY PATIENTS WITH ULCERATIVE COLITIS

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Introduction: The number of elderly patients with ulcerative colitis (UC) has been increasing. Elderly UC patients differ from younger patients with respect to the course of their disease, response to treatment, risk of adverse effects, and influence of UC on the quality of life. At our hospital, granulocyte adsorption apheresis (CAP) is often used to treat elderly UC patients.

[A2] It is abbreviated as GCAP or GMA apheresis in other reports. GMA = granulocyte/monocyte absorption; this is logical.

GAA = granulocyte absorption apheresis is also logical.

Aims and Methods: Here we retrospectively analyzed the cases of elderly patients with moderate or severe UC who underwent CAP for remission induction therapy in a comparison with younger patients. From April 2000 to March 2016, 96 patients with UC underwent CAP at our hospital. Patients who concurrently received tacrolimus, biological agents, or high-dose steroid therapy (PSL at > 0.5 mg/kg) were excluded. The remaining 80 patients were evaluated. We divided them into an elderly group (aged ≥ 65 years) and a younger group (< 65 years old), and then we compared the groups' (1) clinical characteristics, (2) the efficacy and adverse effects of CAP, and (3) the complications of PSL therapy.

Results: The remission rate was 70.8% in the elderly group and 87.5% in the younger group, and CAP demonstrated efficacy in both groups. There were significant differences between the 2 groups with respect to the age at the onset

of UC, the estimated glomerular filtration rate on admission, underlying diseases, and complications of PSL therapy (all $p < 0.05$). Adverse effects of CAP included headache ($n = 2$ in both groups), complications of blood reinfusion ($n = 1$ in the younger group), heparin allergy ($n = 1$ in the younger group), hypotension ($n = 1$ in the elderly group), and failure of blood removal ($n = 2$ in the elderly group). There were significant differences between the 2 groups with respect to the complications of PSL therapy (all $p < 0.05$).
Conclusion: Although the elderly group had longer durations of UC, a higher prevalence of underlying diseases, and a higher frequency of adverse events due to PSL therapy, CAP was effective in both groups. No serious adverse effects that required the discontinuation of CAP occurred in either group. Thus, CAP was safe and effective in both younger and elderly UC patients. CAP should be considered as a useful treatment option for UC, especially in patients with adverse events due to PSL therapy and elderly patients with underlying diseases.
Disclosure: Nothing to disclose

P0376 DOES ANY CONNECTION EXIST BETWEEN BLOOD THIOPURINE LEVEL AND ANTI TNF DRUG LEVEL OR BODY COMPOSITION PARAMETERS - A CROSS-SECTIONAL STUDY IN A HUNGARIAN IBD CENTRE

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Introduction: Thiopurines are the most commonly used immunsuppressive therapies in mild-to-moderate IBD. Therapeutic concentration of 6-TG is between 235–450 pmol/8×10^8 red blood cell count (RBC). The effect of body composition on 6-TG level was never been studied. Furthermore clinical data suggests a synergistic effect between thiopurine and anti-tumour necrosis factor (anti-TNF) therapy in IBD.
Aims and Methods: This is a cross-sectional study involving 96 IBD patients. Consecutive IBD patients on maintenance AZA ($n = 32$) and on IFX/AZA or ADA/AZA combinations ($n = 32$) and activity indices-based pair-matched controls on IFX or ADA monotherapy ($n = 32$) were prospectively enrolled. 6-TG level was measured with high performance liquid chromatography, IFX and ADA levels were assessed by ELISA method. Body composition analysis was performed with bioelectrical impedance analysis.
Results: Therapeutic concentration of 6-TG was found in 50 patients (78%), they received AZA for a mean 5.9 years. 14 patients (21.8%) had lower blood 6-TG level, they received AZA for an average of 7.5 years. The level of AZA metabolite 6-TG correlated with body weight-based AZA doses ($p = 0.017$) however it did not correlate with body surface area-based AZA doses ($p = 0.081$). With statistical analysis correlation was found with some of the investigated body composition parameters: total body water ($r = -0.33$, $p = 0.011$), intra-, extracellular water ($r = -0.325$ and -0.334, $p = 0.008$ and $p = 0.008$, respectively), sceletal muscle mass ($r = -0.326$, $p = 0.01$). However no correlation was found with body fat mass ($r = -0.091$, $p = 0.487$). 32 patients received concomitant biological therapy (14 ADA, 18 IFX). Difference was found in ADA trough levels between those on combined ADA/AZA therapy and those on ADA monotherapy (5.22 ± 5.17 mcg/ml vs. 18.04 ± 14.84 mcg/ml, $p = 0.006$). In contrast, no difference was found in IFX trough levels between those on combined IFX/AZA therapy and those on IFX monotherapy (8.95 ± 10.08 mcg/ml vs. 12.13 ± 12.61 mcg/ml, $p = 0.374$).
Conclusion: Our study revealed that 6-TG level besides body weight-based AZA doses correlate with total body water, intra-, extracellular water and sceletal muscle mass. We found a significant difference in ADA trough levels between the ADA/AZA combination group and the ADA monotherapy group. Preliminary results of our study suggest that favourable outcomes of combination therapy may related to a synergistic effect between AZA metabolites and IFX or ADA trough levels. However the small number of the patients requires further investigations.
Disclosure: Nothing to disclose

P0377 STRICTURING CROHN'S DISEASE - CAN WE PREDICT NEED FOR SURGERY AT FIRST HOSPITALIZATION?

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Introduction: Patients with stricturing Crohn's disease (CD) are frequently hospitalized and a significant percentage requires surgery in the course of the disease.
Aims and Methods: We aimed to assess if there are any predictors of surgical management by the time of the first admission to hospital with obstructed bowel symptoms.
Retrospective unicentric study. Patients over 18 years old, with structuring ileal or ileocolonic involvement, with at least 1 hospitalization and a minimum follow-up of 1 year were included. Excluded patients with penetrating disease, those who had their first hospitalization before anti-TNF agents became available in our center and those without appropriate records. Several clinical, analytical and radiological variables were assessed. Statistical analysis was performed using SPSS v23.0.
Results: Included 43 patients of which 53.5% underwent surgery to treat structuring disease. Patients had a mean age of 43.3 ± 10.8 years, 53.5% were females and the median follow up time was 11.0 ± 7.0 years.
Comparing patients with and without need for surgery, no significant differences were found between groups regarding age at diagnosis, presence of perianal disease, family history and smoking habits, however females were more frequently submitted to surgery (73.9% vs 30.0%, $p = 0.004$) as well as patients who already had a structuring behavior at diagnosis when compared with those with inflammatory behavior at diagnosis (65.6% vs 18.2%, $p = 0.006$).
At the first hospitalization, patients with need for surgery were less frequently under anti-TNF (0.0% vs 20.0%, $p = 0.039$), presented with longer-standing obstructed bowel symptoms (3.0 ± 1.5 days vs 1.0 ± 1.0 days, $p = 0.010$), higher leukocytes count ($12.0 \pm 5.3 \times 10^3$/uL vs 9.2 ± 6.9 x10^3/uL, $p = 0.037$) and admission computerized tomography (CT) more frequently showed proximal small bowel dilation (86.4% vs 40.0%, $p = 0.002$) and longer extent of small bowel involved (8.0 ± 12.0cm vs 5.0 ± 7.0cm, $p = 0.016$). Also, patients that were diagnosed by the time of the first hospitalization were more frequently submitted to surgery than those who already had a CD diagnosis (60.9% vs 39.1%, $p = 0.043$).
Conclusion: Females, patients with structuring behavior from diagnosis and those diagnosed in the first hospitalization were more frequently submitted to surgery. Small bowel dilation and extent of small bowel involved in admission CT, leukocyte count and duration of obstructed bowel symptoms at the first admission were also predictors of need for surgery. Anti-TNF therapy before the first admission seems to reduce need for surgery in this group of patients.
Disclosure: Nothing to declare

P0378 THE ROLE OF STOMA FOR COLONIC AND PERIANAL CROHN'S DISEASE IN THE BIOLOGICAL ERA

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Introduction: In the biological era, surgical treatment continues to play an active role in some patients with colorectal or perianal Crohn's disease (CD).
Aims and Methods: Epidemiological analysis, surgical indication and clinical evolution of patients with CD with colorectal and/or perianal disease undergoing surgical treatment.
Retrospective study of patients with colonic and/or perianal CD who underwent colectomy, total proctocolectomy, or diverting ileostomy /colostomy between 2000–2016 in a tertiary hospital. Demographic and clinical data were collected.
Results: 20 patients were included, 70.0% were women, mean age was 44.5 years. The disease was located in the ileum and colon in 7, solely in the colon in 11 patients and in the ileum (L1p) in 2. 13 patients had perianal disease and 18 rectal involvement. The behaviour of CD according to the Vienna classification was non-stricturing non-penetrating in 12 patients, stricturing in 5 and penetrating in 3. Prior to surgery, 15 patients were treated with combination therapy, 2 with anti-TNF (previous withdrawal of azathioprine due to adverse events) and 3 had no medical treatment due to inaugural disease at the time of surgery. The mean duration of disease before colectomy was 9.1 years. Surgical indications were: refractoriness to medical treatment in 8 patients with luminal disease and 8 with perianal fistulizing disease, perforation in 3 and Hodgkińs lymphoma of the rectum in 1. 9 patients required more than 1 surgical intervention, including 4 urgent surgeries. The surgeries performed were proctocolectomy in 10 patients, total colectomy with ileostomy in 3, protectomy with colostomy in 2, segmental colectomy with colostomy in 1 and ostomy in 4 (3 colostomy and 1 ileostomy). The mean follow-up time was 5.4 years. Postoperative evolution: high-output ileostomy in 1 patient; pelvic floor dyssynergia in the patient with ileo-anal pouch; 5 patients with relapse of CD in the ileum; 2 with proctitis (1 underwent

proctectomy later); 1 with perianal disease and 1 death due to adenocarcinoma in fistulous tract. At the last follow-up, 9 patients were with combination therapy, 3 with biological therapy and 2 with methotrexate.
Conclusion: In this study, 95% remained with stoma. More than half of the patients maintain/restart biological treatment.
Disclosure: Nothing to disclose

P0379 ENTERIC RESECTION IN CROHN'S DISEASE - IS THERE A RELATIONSHIP BETWEEN THE TIMING OF IMMUNOSUPPRESSION ONSET AND THE EXTENSION OF THE RESSECTED SMALL BOWEL?

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Introduction: Intestinal function is closely related to its length. An individualized approach regarding the need for resection of each affected segment of the bowel should be applied to the patient with Crohn's disease (CD) requiring surgery. Several studies have been evaluating the relationship between the date of onset of anti-tumor necrosis factor (anti-TNF) agents or immunomodulators and the need of surgical procedures in CD.
However, it is still unclear if the timing of the immunosuppression onset has impact in the length of the resected small bowel.
Aims and Methods: We propose to evaluate the relationship between the early treatment of CD patients with anti-TNF agents or immunomodulators with the extension of the resected small bowel.
We perform a retrospective data analysis of a sample of cases with CD submitted to surgery. For each case, the date of diagnosis, immunomodulators or anti-TNF onset, and surgery was recorded. The extension of the resected small bowel was based on the anatomopathological report.
Results: A total of 314 cases diagnosed between 1975 and 2017 (172 men (50.7%), mean age at diagnosis 28.9 ± 12.8 years) were evaluated. Multiple surgeries were performed in 20% ($n = 63$) of the cases. The most frequently performed surgery was the right ileocolectomy (77.3%, $n = 245$).
The median time between diagnosis and the first surgery was 31 months (IQR 5–83 months). On average, the patients underwent resection of 23.6 ± 18.4cm of the small bowel. Prior to the first surgery, 46.7% ($n = 148$) of the patients were treated with an immunomodulator (median time of therapy 16 months, IQR 3–42 months) and 21.8% ($n = 69$) were treated with an anti-TNF agent (median time of therapy of 38 months, IQR 7–100 months). Neither immunomodulatory therapy (mean 23.2 ± 16.5cm vs. 24.3 ± 20.4cm, $p = 0.67$) nor anti-TNF therapy (mean 22.6 ± 15.9cm vs 24.0 ± 19.2cm, $p = 0.61$) was associated with lower extension of resected small bowel. No correlation was found between the time elapsed since diagnosis and introduction of the immunomodulator ($r = 0.07$, $p = 0.43$) or anti-TNF agent ($r = 0.06$, $p = 0.531$) and the extension of resected small bowel. Also, there was no correlation between the time elapsed between the introduction of immunomodulator ($r = 0.06$, $p = 0.47$) or anti-TNF agent ($r = 0.08$, $p = 0.53$) and time to surgery with the extension of resected small bowel.
Conclusion: In this group of patients, we found that the timing of introduction of immunomodulator or anti-TNF therapy did not influence the extent of the resected bowel.
Disclosure: Nothing to disclose

P0380 HIGHER BMI BUT NOT SYSTEMIC IMMUNE SUPPRESSION INCREASES THE RISK OF SHORT-TERM POSTOPERATIVE COMPLICATIONS IN CROHN'S DISEASE PATIENTS

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Introduction: Several studies have focused at the risk factors of postoperative complications in Crohn's disease (CD) patients with no conclusive results. Thus far, it is unclear whether immune suppression should be adjusted in a CD patient awaiting surgery for CD complications.
Aims and Methods: The aim of this study was to determine the risk factors associated with the postoperative complications in CD patients operated for luminal disease complications.
All consecutive CD patients operated on in 1 tertiary center between January 2015 and September 2017 were included. Complications within 30 days following surgery were categorized according to Clavian-Dindo classification. Patients' demographics, nutritional status, disease localization and behavior, type of medication, previous surgical interventions, type of surgical approach and duration of surgical intervention were noted. The association of postoperative complications with these factors was analyzed.
Results: In total, 91 procedures were performed in 86 CD patients (47.3% males; mean age 38 years, range 19–71; 56 pts (61.5%) with ileo-colonic disease, 11 pts (12.1%) with small bowel and 21 pts (23.1%) large bowel localization; 62 (68.1%) with stricturing disease). Based on body mass index, 23 (25.3%) patients were underweight, 42 (46.2%) had normal weight and 21 (23.1%) were overweighed. Minority of patients had steroids (16 pts; 17.6%); 36 pts (39.6%) were using azathioprine; 33 (36.3%) antiTNF; 7 (7.7%) vedolizumab and 1 patient was using trial medication.
The procedure was elective in 60.4% and one-third had repetitive surgery. Median duration of the procedure was 150 minutes (range 30–335) and median hospital stay was 6 days (range 3–32). 51 pts (56%) had simple resection, 24 (26.4%) had multiple resections, in 16 cases an ostomy was created. Laparoscopic approach was used in 44 cases (48.4%; 8 pts had single port laparoscopic procedure), 46 pts (50.5%) had laparotomy.
There were 10 complications (11%) out of which 5 (5.5%) major complications (Clavian-Dindo IIIb and above). There was a significant difference in BMI between patients with major complications compared with patients without complications (respective medians 26 and 21 in the group with major complications vs. group without complications; $p = 0.035$). None of the other factors were associated with unfavorable postoperative outcomes.
Conclusion: Overweight represents a risk factor for postoperative complications in Crohn's disease patients operated for luminal disease complications. Immune suppressive therapy, including systemic corticosteroids and antiTNF biologics does not seem to confer an increased risk for surgical complications.
Disclosure: Nothing to disclose

P0381 USING PATIENT'S PREFERENCE IN RANDOMIZED CONTROLLED TRIALS

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Introduction: Randomized controlled trials (RCT) are the gold standard of assessing efficacy in clinical medicine. However, many eligible trial participants have a preference for 1 of the intervention of the RCT, and therefore may decline randomization. Consequently, this could limit the extrapolation of the results to the clinical population (i.e. reduce external validity by randomization bias). Patients randomly allocated to their non-preferred intervention may experience resentful demoralization, which may lead to worse outcomes (i.e. reduce internal validity by preference bias). Especially studies with a substation difference in interventions (e.g. surgery vs. medication), and studies with a subjective primary outcome (e.g. quality of life), are prone for randomization and preference bias. The aim of this study was to determine whether preferences affect external and internal validity in trials.
Aims and Methods: A systematic review with meta-analyses was performed. 2 reviewers independently searched in MEDLINE, EMBASE, PsychINFO, and the Cochrane library for RCTs with a preference-arm published between 2005 and 2018. The trials that reported on allocation of patients to random or preference cohorts using the same inclusion criteria and protocol were included. We extracted data on study design, measurement of preference, recruitment, attrition, cross-over, and primary outcome at baseline and end of follow-up.
Results: In total 117 out of 3734 identified articles met screening criteria and 35 were eligible (to compare baseline and primary outcome difference between the randomised and preference cohort, 32 and 20 articles were included, resp.) Acceptance of randomization in all 35 trials varied from 1% to 81% and was lower than 50% in 23 of 35 studies. Higher education level, female, older age, race, and prior experience with 1 treatment arm were baseline characteristics of patients declining randomization. The primary outcome of the trials between randomized and preference groups was comparable, the difference in effect of the experimental intervention was 0.093 (95% CI −0.364–0.178), $p = 0.502$. After comparing only the 7 trials that adjusted for baseline difference the effect was even smaller, 0.026 (95%CI −0.211–0.263), $p = 0.832$.
Conclusion: Treatment preference led to a substantial proportion of a specific patient group refusing randomization, while it did not affect the primary outcome. Therefore, patients preference trials could increase external validity without compromising the internal validity compared to randomization controlled trials.
Disclosure: Nothing to disclose

P0382 EARLY CLOSURE OF ILEAL POUCH-ANAL ANASTOMOTIC LEAKAGE PRESERVES POUCH FUNCTION; A PROSPECTIVE COHORT STUDY

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Introduction: In case of ileal pouch-anal anastomotic (IPAA) leakage, Endosponge®-assisted early surgical closure prevents chronic presacral abscesses compared to conventional treatment (defunctioning ileostomy and passive drainage). It was hypothesised that early closure would also improve long-term pouch function. The aim of this study was to compare pouch function and failure after early closure to conventional management of anastomotic leakage and to control IPAA patients without anastomotic leakage.

Aims and Methods: In this prospective cohort study, all consecutive patients who underwent IPAA for ulcerative colitis (UC) between 2002 and 2016, were sent a validated pouch dysfunction questionnaire. Early surgical closure after Endosponge® treatment under a defunctioning ileostomy became standard practice in our center from 2010 onwards. The primary outcomes were pouch function (none-minor or some-major dysfunction) and pouch failure (defunctioning ileostomy or pouch excision) compared between control IPAA, early closure, and conventional management using a chi-square test for trend. Secondary outcomes were short-term outcomes, e.g. anastomotic healing at 6 months, and time to closure of anastomotic defect.
Results: In total, 308 patients were included and 84% returned the questionnaire (n = 255), of whom 41 patients had anastomotic leakage (n = 18 early closure and n = 23 conventional). Some-major pouch dysfunction was comparable between control IPAA (n = 75/216, 35%) and early closure (n = 7/17, 41%), but significantly more dysfunction after conventional management was seen (n = 15/22, 59%) (p = 0.03). Pouch failure was comparable between control IPAA (n = 11, 4%) and early closure (n = 1, 6%), while conventional management (n = 5, 22%) showed significantly more failures (p = 0.001). Early closure resulted in 100% (n:17/17) closed anastomosis at 6 months, compared to 64% (n:14/17) after conventional treatment (p = 0.006), and accelerated closure time 8 (7–15) days vs. after 76 (50–332) days, resp. (p < 0.001).
Conclusion: Early closure of IPAA leakage for UC patients is associated with a prevention of pouch failure and preservation of long-term pouch function compared to conventional management.
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00-17:00
Other Lower GI Disorders I - Hall X1____

P0384 CLINICOPATHOLOGICAL FEATURES OF NIVOLUMAB-INDUCED COLITIS

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Introduction: Nivolumab is a immune-checkpoint inhibitor and it enhances cancer-related immune responses by inhibiting programmed cell death protein (PD-1). Nivolumab is efficacious for the management of patients with metastatic melanoma and other solid tumors. However, immune-related adverse events (irAEs) are known as serious side effects of immune-checkpoint inhibitors. The purpose of this study is to clarify the clinicopathological characteristics of colitis occurring as an irAE in patients treated by nivolumab (nivolumab-induced colitis).
Aims and Methods: During a period from December 2015 until February 2018, we encountered 7 patients who were suspected of having nivolumab-induced colitis. There were 2 women and 5 men with ages ranging from 51 to 81 years (mean, 66 years). We retrospectively investigated clinical features, endoscopic findings and pathologic characteristics of the patients. Nivolumab-induced colitis was defined as 1) diarrhea occurring during nivolumab treatment, 2) exclusion of other causes of diarrhea, and 3) histological confirmation of apoptosis colonic epithelial cells.
Results: The underlying tumor was malignant melanoma in 3 patients, non-small cell lung cancer in 2 patients and renal cell carcinoma in 2 patients. In addition to diarrhea, 2 patients complained of hematochezia. C-reactive protein value at the time of colonoscopy ranged from 0.1 to 9.1 mg/dl with a mean of 2.0 mg/dl, and white blood cell count from 3330 to 10480/μl with a mean of 6430/μl. 3 of 7 patients fulfilled the diagnostic criteria of nivolumab-induced colitis. The remaining 4 patients manifested diarrhea and they were free from other causes of diarrhea, apoptosis was not evident in these patients. 3 patients with nivolumab-induced colitis manifested clinical symptoms after administrations of nivolumab for 4 to 5 times, and 2 patients complained of hematochezia. Colonoscopic findings of nivolumab-induced colitis included friable erythematous mucosa of the rectum and granular mucosa of the colon, which were apparently compatible with ulcerative colitis. These patients were treated by prednisolone, which was effective in patient. 2 patients intractable to prednisolone were treated by infliximab, but a patient failed to respond to infliximab. 4 patients without nivolumab-induced colitis had normal colonoscopic findings and they continued nivolumab without any specific treatment.
Conclusion: Colitis mimicking ulcerative colitis is 1 of irAEs induced nivolumab. Our diagnostic criteria, which include apoptosis of colonic epithelial cells, may be appropriate in consideration of mucosal damages and subsequent clinical course.
Disclosure: Nothing to disclose

P0385 FECAL TRANSPLANTATION FOR AUTISM SPECTRUM DISORDERS

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Introduction: The prevalence of children with autism spectrum disorders (ASD) is increasing worldwide (1). The cause of ASD is poorly understood and involves interplay of different genetic and environmental factors where gut microbiota could have a significant impact. The aims of the study were to evaluate fecal microbiota transplantation (FMT) effectiveness in children with ASD in treating autism spectrum disorders and gastrointestinal (GI) symptoms.
Aims and Methods: We performed FMT in 5 boys (5–8 yrs., every month, 3 times for every patient) with ASD and mild GI symptoms. The donor was the same 7 yrs. old healthy, unrelated girl. Her feces were infused into the cecum during colonoscopy. The patients' gut before FMT was prepared with polyethylene glycol 4000 (Fortrans). Symptoms were checked every week after FMT with parent global impression score (PGI-R; the symptoms were rated on a scale of 1–7, where 1 = much worse, 7 = much better compared to baseline) (2) for ASD and gastrointestinal symptom rating scale (GSRS; 1 represents absence of troublesome symptoms and 7 represents very troublesome symptoms) (3).
Results: We filled GSRS and PGI-R scores by asking parents about their child's health during phone call or when the patient came to the hospital for FMT. The total GSRS and PGI-R scores improved in all (1–5) patients after FMT (Table 1). The best improvement was seen after 2 wk. post FMT, less before second and third FMT. The FMT treatments were generally well-tolerated, without adverse effects.
[GSRS and PGI-R scores before and after FMT]
Conclusion: 1. FMT has positive effect on GI and autism spectrum disorders symptoms.
2. The FMT treatments were well-tolerated.
Disclosure: Nothing to disclose

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P0386 COMPARISON OF STAINING TECHNIQUES AND MULTIPLEX NESTED PCR FOR DIAGNOSIS AND TREATMENT OF ACUTE DIARRHEA

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Introduction: Although mortality is declining globally, acute diarrhea is leading cause more than 2 milion deaths annually and is a major cause of outpatient visits, hospitalizations, and reduced quality of life for domestic setting and traveling abroad.
Aims and Methods: We aimed to investigate whether stool PCR could have a beneficial effect on the duration of hospitalization induced by acute diarrhea. Between March 2015 and February 2018, patients were admitted with acute diarrhea, stool PCR was performed in 116 patients. Patients were divided into 2 groups: stool PCR (n = 58) and non-stool PCR (n = 58). The positive rate in stool PCR and the change in treatment modality were examined and the prognosis was compared between groups.

Abstract No: P0385

Patient	Before FMT	Before FMT	After 2 wks	After 2 wks	After 1 mo	After 1 mo	After 2 mo	After 2 mo
	GSRS	PGI-R	GSRS	PGI-R	GSRS	PGI-R	GSRS	PGI-R
1	35	–	20	53	22	50	23	49
2	33	–	19	56	21	52	22	53
3	33	–	20	55	20	52	20	51
4	36	–	21	52	25	52	24	50
5	37	–	26	56	27	55	28	54

Results: Overall, 29 (50%) of 58 samples were positive for pathogen at stool PCR. The positive rate for virus was 1.7%. Enteric adenovirus was detected in 1 sample, respectively. The positive rate for bacteria was 48.3% (28/58). *C. perfringens was* the most frequently detected, followed by *campylobacter spp*., *C.difficile toxin B*.
The rate of antibiotics change, antidiarrhea agent or probiotics change, additional endoscopy and image study(CT) were significantly higher in stool PCR positive group ($p = 0.007$, $p < 0.001$, $p = 0.018$ and $p = 0.027$, respectively).
There were no significant diffrences between groups in terms of antibiotics use and hospitalization, however, hospital of day decreased significantly in stool PCR positive group ($p = 0.032$).
On multivariate analysis, stool PCR positive was associated with increased rates of history of diabetes mellitus type 2, fluid therapy and anti-diarrheal agent use (HR, 8.357; 95% CI 2.381–29.328; $p = 0.001$ / HR 2.940; 95% CI 1.184–7.303; $p = 0.020$ / HR 2.945; 95% CI 1.522–5.699; $p = 0.001$).
Conclusion: With stool PCR positive, antibiotics changes and drug modification were associated shortening of hospitalization perioid, espicially in patients with diabetes.
Disclosure: Nothing to disclose

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P0387 FECAL MICROBIOTA TRANSPLANTATION IN CLOSTRIDIUM DIFFICILE INFECTION: REAL-LIFE EXPERIENCE FROM AN ACADEMIC ITALIAN HOSPITAL

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Introduction: Gut microbiota helps us to regulate homeostasis functions. Its key features are resilience and biodiversity. Antibiotic therapies can create an ecological vacuum, and some opportunistic pathogens, especially *Clostridium difficile*, may take advantage of it. Faecal microbiota transplantation (FMT), has been recently proven to be extremely effective ($\approx 80\%$) in controlling this infection.
Aims and Methods: The aim of the study is a preliminary clinical and microbiological evaluation of the implementation of faecal microbiota transplantation in Padua Hospital. In addition, efforts were made to provide guidance on the use of biodiversity indices to assess changes in intestinal microbiosis.
13 FMTs were performed in 12 patients (12 F/2 M, mean age 68.7) in 1 year. In 9 FMT donor and recipients faecal samples were collected before and after (2–8 days) transplantation, and in 4 patients even at 4–6 months (follow-up). In 1 patient faecal suspensions resulting from the combination of 2 donors were used, whereas in another patient frozen feces instead of fresh stool were infused. Stool samples were analyzed using the Illumina (NGS) technique. Statistical analysis was performed with the Wilcoxon Signed Ranks Test and a bilateral hypothesis system. We calculated Shannońs biodiversity indices and Simpsońs equipartition indices.
Results: The primary resolution of CDI was obtained in 100% of the cases, although an early relapse at 3-month from FMT was observed. Among the donors, the most numerous phyla were Bacteroidetes ($57.8\% \pm 23.45\%$) and Firmicutes ($35.0\% \pm 20.1\%$). Patients' fecal samples taken the day before FMT revealed a marked dysbiosis: Proteobacteria levels were excessively high ($58.1\% \pm 28.2\%$) compared to Bacteroidetes ($2.8\% \pm 4.8\%$), as usually occurs in CDI. In fecal samples taken after transplantation (between 2 and 8 days) an increase in Bacteroidetes levels ($65.2\% \pm 18.5\%$) and a specular decline in Proteobacteria were immediately observable ($10.6\% \pm 11.1\%$). The Shannon index correlated to changes in intestinal flora before and after faecal transplantation, with a good level of significance (p-value = 0.03906; $\Delta M = 0.67$). Using Simpson's equipartition index we showed that the 4 patients, in whom the microbial analysis was performed at 4–6 month, did not demonstrate significant changes compared to the samples taken immediately after FMT (p-value $\sim = 1$; $\Delta M = 0.01$). No safety issues were observed during the FMT and after it.
Conclusion: Our data confirmed that FMT is an effective, safe and simple practice for treating CDI. Even the transplant performed using frozen fecal material provided similar good results. Therefore, it is desirable to implement this procedure in clinical practice. Finally, the index of equipartition who seems able to provide us with a measure of disturbances of the microbiota in the long term, may prove to be a valuable tool to orient ourselves in the diagnosis, treatment and monitoring of many pathologies.
Disclosure: Nothing to disclose

P0388 GASTRIC ACID SUPPRESSION MAY LEAD TO AN INCREASED RISK OF VANCOMYCIN-RESISTANT ENTEROCOCCUS COLONIZATION

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Introduction: Gastric acid suppression therapy has been reported to change the gastrointestinal microbiome, resulting in increased gastrointestinal infections. However, the effect of gastric acid suppression therapy on vancomycin-resistant enterococcus (VRE) colonization has not been investigated.
Aims and Methods: Subjects who had surveillance rectal swabs for VRE at a university hospital were investigated. Surveillance was performed on subjects with prior hospitalization within 3 months, history of VRE colonization/infection, or positive VRE findings from an adjacent patient. Gastric acid suppression therapy was defined as use of proton pump inhibitor or histamine-receptor-2 antagonists.
Results: Of 886 subjects who underwent VRE screening, 452 were included with 69 VRE positive and 383 VRE negative subjects. In univariable analysis, gastric acid suppression therapy, antibiotics use, male gender and prior hospitalization were significant risk factors for VRE colonization. Multivariable analysis showed that gastric acid suppression therapy (OR 2.873, 95% CI 1.473–5.605, $p = 0.002$) and antibiotics use (OR 3.896, 95% CI 2.019–7.520, $p < 0.001$) significantly increased VRE risk. Of antibiotics, carbapenems (OR 3.836, 95% CI 1.603–9.182, $p = 0.003$) glycopeptides (OR 2.784, 95% CI 1.155–6.712, $p = 0.023$), and cephalosporins (OR 2.210, 95% CI 1.213–4.025, $p = 0.010$) were most significantly associated with VRE colonization. The unfavorable effect of gastric acid suppression therapy on VRE colonization was consistent, regardless of antibiotics type.
Conclusion: Gastric acid suppression therapy significantly increased VRE colonization risk. Gastric acid suppression should be administered according to strict guidelines. Physicians should be made aware of the increased VRE risk, and should consider VRE surveillance in those under long-term gastric suppression therapy.
Disclosure: Nothing to disclose

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P0389 FECAL MICROBIAL TRANSPLANTATION FOR CLOSTRIDIUM DIFFICILE INFECTION- A NATIONAL ISRAELI EXPERIENCE

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Introduction: Fecal microbial transplantation (FMT) has been established as an effective and safe therapy for recurrent *Clostridium difficile* infection (CDI), with cure rates of 85–95% [1]. In Israel, FMT for the treatment of recurrent CDI, has been approved for the past 5 years and is currently available in 5 medical centers, at which FMT is performed in ambulatory as well as in hospitalized patients using multiple methods including colonoscopy, gastroscopy, and capsules [2–3].
Aims and Methods: We evaluated and described the efficacy and safety of FMT for CDI patients in a national retrospective cohort of the 5 medical centers performing FMT in Israel. All patients who received FMT for recurrent (recurrence within 8 weeks of the previous treatment), refractory (ongoing diarrhea despite antimicrobial treatment) or severe CDI (WBC $\geq$ 15,000 c/μl $\pm$ Cr $\geq$ 1.5 times the premorbid level) from 2013 through 2017 were included.
Stool donors were screened according to the Israeli Ministry of Health guidelines. Fecal filtrates were locally prepared and stored frozen in -80^0c.
Clinical and laboratory data of patients were collected from patients' medical files in which indications for FMT, risk factors and outcomes at 1 week, 2 and 6 months post FMT are routinely recorded.
Results: A total of 111 FMTs for CDI were performed: 45% via the lower GI route (LGI) through a colonoscopy, 22% via gastroscopy or feeding tube (upper GI - UGI), and 33% via oral capsules. A summary of patients' characteristics, risk factors for CDI, indications and outcomes is depicted in Table 1.
Recurrent CDI was the leading indication for FMT in 74% of the patients while refractory and severe CDI were treated in 21% and 18% patients, respectively.

Abstract No: P0389

	Overall N (valid)	Overall % (IQR)	Upper GI N	Upper GI % (IQR)	Lower GI N	Lower GI % (IQR)	Capsules N	Capsules % (IQR)	p value
Patients, no.	111	100%	24	22%	50	45%	37	33%	
Male gender, no.	47 (111)	42%	16	67%	19	38%	12	32%	0.02
Age, median (IQR)	70 (111)	(53–82)	68	(51–86)	78	(61–83)	68	(45–75)	0.11
Charlson score, median	79±9 (81)	(69–93)	79±9	(69–93)	84±4	(75–93)	73±9	(69–98)	0.73
Abx use, past 3 months, no.	66 (108)	59%	15	63%	15	30%	36	97%	0.01
Previous CDI episode, median	2 (107)	(2–3)	2	(1–3)	2	(1–3)	3	(2–4)	0.29
Severe CDI, no.	20 (111)	18%	8	33.3%	10	20%	2	5.4%	0.02
Refractory, no.	23 (111)	21%	6	25%	13	26%	4	11%	0.19
Recurrent, no.	82 (111)	74%	18	75%	31	62%	33	89%	0.02
Outpatient, no.	78 (111)	70%	12	50%	36	72%	30	81%	0.03
Recurrence at 6 months	16 (99)	16.2%	3	15.8%	5	11.4%	8	22.2%	0.14
Total death, no.	11 (111)	9.9%	5	21%	6	12%	0	0%	0.02
No. of adverse events	19 (107)	17.1%	1	4%	14	28%	4	11%	0.01
Success	97 (111)	87.4%	19	79%	44	88%	34	92%	0.34

Overall success rate was 87.4% (97 patients), with no significant difference between administration routs.
Patients who achieved cure, were younger (age 63±22 compared with 73±12, $p < 0.05$), were less often defined as severe CDI, and were more likely to be treated as outpatients.
Patients who were younger than 60 years old (n = 35), were mostly outpatients, compared to the elderly group, (86% vs. 63%, respectively, $p < 0.05$) and underwent FMT at a much later time from first disease episode (mean time from 1st CDI −198±279 vs. 102±112 days, $p < 0.05$).
11 patients died during the follow-up, none was attributed to the FMT procedure itself; 2 patients suffered from post-endoscopy aspiration (1 UGI, 1 LGI). Other side effects were mild and self-limited. No FMT related infections were recorded.
Conclusion: FMT is a safe and effective treatment for CDI, which occurs in growing numbers in the young population. FMT via capsules emerges as a successful and well tolerated alternative for endoscopy.*[Study population characteristics and outcomes by FMT mode]*
Disclosure: Nothing to disclose

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P0390 THE IMPACT OF *CLOSTRIDIUM DIFFICILE* INFECTION ON HOSPITALIZATION IN VENETO REGION

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Introduction: *Clostridium difficile* infection (CDI) has emerged as a major healthcare-associated infection, because of the changing molecular epidemiology of the *C. difficile*, and the ageing of the population, without neglecting frequent exposure to broad-spectrum antibiotics and other predisposing medications, the presence of comorbidities, and the risk of hospitalization. In the last decade, analyses of hospitalization records and data on multiple causes of death demonstrated an important and constant increase in CDI rates.
Aims and Methods: To evaluate the impact of CDI on hospitalization in Veneto Region (North-East Italy, approximately 4,900,000 inhabitants), a retrospective analysis was carried out from a population-based archives represented by hospital discharge records (HDR) according to the ICD9-CM. All discharges from 1 January 2007 to 31 December 2016 of Veneto population with a code for CDI (008.45) ad principal or secondary diagnosis were extracted form the regional anonymous archive of discharge records. The Standardized Hospitalisation Rate (SHR) and in-hospital Mortality Rate (SMR) were calculated per 5-year age group (ref. pop. Veneto 2012) and expressed per 100 000 population.
Results: 7,557 discharges with CDI were tracked in the study period and **88%** of these hospitalizations **involved subjects aged over 65 years**, with CDI diagnosis as the primary in over 1-third of cases and an overall lenght of stay (LOS) of 25.6±22.7 days. Hospitalization distribution by gender showed a prevalence of **females** (63.2%) characterized by an **higher mean age** (80.2±14.6 vs. 75.6±16.4 yrs; $p < 0.001$). The **SHR** was 15.25 and **SMR** 1,72 both increased steeply and constantly in the analyzed period, and from the comparison of first and last year of the period emerged a rise of SHR (Chi square for trend: 141.702; $p < 0.001$) from 10.6 to 24.5 and also of SMR (Chi square for trend: 45.381; $p < 0.001$) from 0.6 to 3.7 per 100 000 inhabitants. **The rate of CDI** diagnoses per 100000 overall admissions **increased steeply with age**, and reached a peak of 222.4 every 100,000 discharges among the very elderly (> 85 years). In the frame of over 65 years patients the age class distribution showed an **higher risk in 75–84** (OR: 1.62; CI95%: 1.23–2.13; $p < 0.001$) and an almost **double in >85 years** (OR: 2.1; CI95%: 1.62–2.74; $p < 0.001$) **respect to 65–74 age class**.
Over 65 years patients admission with CDI diagnosis represent **2.1% of overall ordinary admission** and cause to the **LOS excess of 15.7 days and represent 5.4% of overall hospitalization days**. **Also in-hospital mortality rate showed an excess risk attributable to CDI** (OR: 1.91 95% CI: 1.77–2.05; $p < 0.001$).
Conclusion: In the observation period SHR for CDI was almost doubled and SMR even increased 6-fold in 2016 respect to 2007. What emerged confirms the literature's data about the time course of CD infections, with an increase in their frequency, as well as in their severity and in the additional days of hospitalization. These dramatic scenary imposing the adoption of adequate containment measures to deal with a now epidemic phenomenon, mainly through policies to optimize antibiotic therapy both in the intra- and extra-hospital environment.
Disclosure: Nothing to disclose

P0392 DECREASE OF BLOODSTREAM INFECTION RATES IN PATIENTS WITH *CLOSTRIDIUM DIFFICILE* INFECTION TREATED WITH FAECAL MICROBIOTA TRANSPLANTATION

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Introduction: *Clostridium difficile* infection, especially in its severe clinical picture, is a risk factor for bloodstream infections (BSI). A considerable body of evidence shows that fecal microbiota transplantation (FMT) is more effective than standard antibiotic regimens in treating recurrent CDI), although its efficacy in reducing CDI-related BSI has not yet been demonstrated.
Aims and Methods: The aim of this study is to assess the rate of BSI in a cohort of patients with CDI treated with FMT or with standard antibiotic therapy. This is a single-centre, retrospective cohort study of patients with CDI treated with FMT either with standard antibiotic regimens (metronidazole or vancomycin or fidaxomicin). The date of first fecal infusion and the starting date of antibiotic treatment were considered as time 0 for the analysis.
Results: At November 2017, 282 subjects (F = 91, M = 171, mean age 74 years) were analysed for this study. Of them, 101 patients (36%) were treated with FMT from healthy donor and 181 (64%) received antibiotic therapy for CDI. No differences were found on demographic and clinical characteristics of the 2 study groups.
47 patients developed a BSI after FMT or standard antibiotic therapy. Compared to those who received antibiotic treatment for CDI, patients in the FMT group had a significant lower risk of overall BSI (21.1% versus 8.9%; $p = 0.008$), fungal BSI (6.6% versus 1%, $p = 0.036$), polimicrobial BSI (6.1% versus 1%, $p = 0.016$). Subjects in the FMT group experienced also a significantly shorter length of hospitalisation compared to those in the antibiotic group (13.4 days versus 29.8 days on average; $p < 0.001$) and a reduced death risk at 60 days (7.7% versus 1%; $p = 0.015$). Adverse events were similar between the 2 groups.
Conclusion: In our cohort, subjects with recurrent CDI treated with FMT experienced a significantly lower incidence of bloodstream infections, a shorter length

of hospitalization and a reduced 60-day risk of death compared to those who received antibiotics. We can argue that a rapid restoration of healthy microbiota in people with CDI treated with FMT could explain the present results. Should these preliminary results be confirmed by prospective, randomized trials, the reduction of BSI in patients with recurrent CDI may be considered an additional relevant benefit of FMT.
Disclosure: Nothing to disclose

P0393 FAECAL MICROBIOTA TRANSPLANTATION: ESTABLISHMENT OF A DONOR STOOL BANK BASED ON TISSUE ACT CRITERIA

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Introduction: Faecal Microbiota Transplantation (FMT) is a promising therapeutic option, especially as a highly effective treatment for recurrent *Clostridium difficile* infection. However, implementing FMT as a treatment in a large-scale setting is very challenging due to safety issues and the need for immediate access to donor faeces.
Aims and Methods: We here describe the establishment of a donor stool bank for FMT in Region Zealand, Denmark.
Stool donors are recruited among blood donors. Donors are asked to donate 5 times within one month. Donors need to go through a screening-questionnaire, a medical consultation and a long list of blood and faecal tests. All this is repeated after the last donation.
Donations are made at home and immediately transported to the lab, where 50 g of filtered faeces are suspended with saline and 20 mL glycerol up to 170 mL before freezing at −80°C, no later than 2 hours after defecation.
A batch number is assigned and all critical material and steps are documented for traceability. All steps and passed lab reports are checked before quarantined material is released for clinical use. Material is stored for up to 1 year.
Procedures are based on the European Tissue Act, although there is currently no legislation on FMT in Denmark.
Results: At establishment, 8 donors were found eligible at the first screening and began donation. Reasons for not consenting were primarily logistic and aesthetic. Reasons for not being eligible were primarily BMI > 25 kg/m^3 or use of antimicrobials within 6 months.
All 8 donors donated 5 times each, each donation yielding 1–6 portions (median 3.5) and thus 86 portions in total. No donors had positive findings in any blood or faeces tests. At the second screening, after the last donation, 1 donor reported use of NSAIDS 2 days prior to a donation - material from this was destroyed (n = 2). No other findings were identified at the second screening. 84 portions were thus released for clinical use.
Conclusion: Recruiting stool donors among active blood donors is very feasible. Establishment of a donor stool bank with frozen pretested material secures effective and immediate access to FMT treatment.
Disclosure: Nothing to disclose

P0394 RISING BURDEN OF DIFFICULT TO TREAT AND MULTI-DRUG RESISTANT ABDOMINAL TUBERCULOSIS IN ASIAN CHILDREN

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Introduction: Incidence of tuberculosis (TB) especially multidrug resistant TB (MDR-TB) is steeply rising in developing countries despite efforts for global control. Abdominal MDR-TB is underreported, more so in children. Inaccessible tissue for histopathology or microbiology and poor sensitivity (64%) of molecular techniques from smear-negative, non-respiratory samples limit the confirmation of diagnosis. Hence, the choice of alternative drugs and duration of therapy in MDR-TB are based on clinical ± radiological assessments and drug toxicity profile.
Aims and Methods: We aimed to study the profile and predictors of difficult to treat (DTT-TB) inclusive of MDR-TB patients of all the confirmed cases of abdominal TB. Clinical, laboratory and radiological data of abdominal TB (n = 83) were analysed from 2012–2017. Disease rates of previous years (2000-11) were compared. DTT-TB was defined as 1 of the following: 1) prolonged (>9months) WHO category-1 antitubercular therapy (ATT), 2) MDR-TB (failed WHO category-2 ± category-1 ATT or proven on GeneXpert) requiring second line therapy. DTT-TB was compared with standard ATT (WHO category 1 or 2 responsive of ≤9months duration of therapy) cases.
Results: Of all abdominal TB, MDR-TB was diagnosed in 3 of 38 (8%; 2000-11)[1] and 13 of 83 (16%; 2012-17). An additional 7 of 83 children (2012-17) had prolonged category-1 ATT finally constituting 20 (24%) as DTT-TB. Table 1 shows the comparison of DTT-TB and standard therapy. Overall confirmation of diagnosis (n = 83) was 56 (67%) by microbiology or histology (caseating granuloma), the rest by discriminatory radiological ± laboratory features. Younger age, higher microbiological yield, presence of extra-abdominal, thoracic, and abdominal lymph node involvement and paucity of luminal involvement were significant in DTT-TB than standard therapy. In the DTT-TB group, prolonged ATT (n = 7) was administered for 17.7±5.1 months and MDR-TB (n = 13) for 18±6.9 months. At the end of 18 months, 3 of 13 (23%) MDR-TB were non-responsive to various second line agents and were labeled extended drug resistant TB.
Conclusion: An alarming rise of overall abdominal TB, MDR-TB and extended drug resistant TB is currently encountered in developing countries. MDR-TB is multibacillary and presents as disseminated disease affecting younger age groups*[Table 1: Comparison of difficult to treat TB versus standard therapy TB]*
Disclosure: Nothing to disclose

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	Difficult to treat TB (n = 20)	Standard therapy TB (n = 63)	p value	OR (95%CI)
Age (months)	125 ± 58	155 ± 46	**0.02**	–
Males, n (%)	9 (45)	32 (51)	0.6	0.7 (0.3–2.2)
Histological confirmation, n (%)	12 (60)	31 (49)	0.4	1.5 (0.6–4.3)
Microbiological confirmation*, n (%)	13 (65)	17 (27)	**0.003**	5.0 (1.7–14.7)
Abdominal lymph node (mesenteric + retroperitoneal), n (%)	16 (80)	34 (54)	**0.03**	3.6 (1.1–12.1)
Luminal involvement, n (%)	9 (45)	47 (75)	**0.01**	0.2 (0.1–0.8)
•Esophagus; stomach, n (%)	1 (5)	3 (5)	0.9	1.0 (0.1–10.7)
•Small bowel, n (%)	4 (20)	16 (25)	0.6	0.7 (0.2–2.5)
•Ileocecal; Colon, n (%)	4 (20)	28 (44)	**0.01**	0.1 (0.02–0.6)
Peritoneum/omentum, n (%)	4 (20)	22 (35)	0.2	0.4 (0.1–1.5)
Liver, spleen, pancreas, n (%)	5 (25)	14 (22)	0.8	1.2 (0.3–3.7)
Extra-abdominal involvement, n (%)	14 (70)	18 (29)	**0.001**	5.8 (1.9–17.6)
•Thorax, n (%)	11 (55)	19 (30)	**0.04**	2.8 (1–7.9)
•Cerebrospinal, n (%)	2 (10)	6 (10)	0.06	1.0 (0.2–5.7)
•Genitourinary, n (%)	2 (10)	3 (5)	0.4	2.2 (0.3–14.3)
ATT hepatotoxicity, n (%)	4 (20)	7 (11)	0.3	2.0 (0.5–7.7)

ATT: anti-tubercular therapy, *Microbiological confirmation includes Zeihl-Neelsen stain for acid-fast bacilli, rapid solid medium culture, real-time polymerase chain reaction for M.tuberculosis and GeneXpert molecular technique

P0395 IMMUNOHISTOCHEMISTRY APPLICATION AS ONE STEP FOR DIAGNOSING HUMAN INTESTINAL SPIROCHETOSIS

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Introduction: Diagnosing human intestinal spirochetosis (HIS), a colorectal infectious disease caused by *Brachyspira* species bacteria, depends on pathologists finding the so-called fringes on the mucosal epithelial surface. In routine practice, cases in which hematoxylin-eosin (HE) sections raise suspicions of HIS are further examined using Giemsa or silver stain, or immunohistochemistry (IHC). Whether IHC could itself raise suspicion of HIS is unexploited.
Aims and Methods: We aimed to elucidate whether an initial IHC application might increase the proportion of cases considering HIS-suspicious. Focusing on the so-called fringes, we compared HE and IHC (using a polyclonal anti-Treponema pallidum antibody) results in 1 month's consecutive lower GI endoscopic specimens in the pathology department at a single hospital.
Results: Among the 140 individuals examined (M:F = 86:54; 20–94 yrs; median 64 yrs) during the period, 10 HIS-IHC cases (7.1%; M:F = 5:5; 34–75 yrs; median 57 yrs) were diagnosed, while HE pathology found eight HIS-HE cases (so-called fringes were thick and distinct; 5.7%) and 2 possible cases. All 8 HIS-HE cases matched HIS-IHC cases. However, the 2 possible HIS-HE cases were denied by IHC, while another 2 of the HIS-IHC cases were overlooked by HE. In the HIS-IHC cases, so-called fringes were confirmed in 73.9% of the sections. At this time, four HIS-IHC cases have received endoscopy as follow-up for polyps, 1 for ulcerative colitis, 2 for fecal occult blood, and 1 for watery diarrhea.
Conclusion: The hallmark of HIS can be overlooked histologically, and an initial IHC application might find more HIS cases in routine practice.
Disclosure: Nothing to disclose

P0396 LOW INTESTINAL BLEEDING: WHAT AND WHEN WE SHOULD BE LOOKING AT COLONOSCOPY?

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Introduction: The recommended strategy of the use of colonoscopy after preparation by oral lavage at patients with low-intestinal bleeding identifies the source of bleeding in 25% -40%. The frequency of these sources are significantly different. Incorrect identification of the source of bleeding involves the wrong tactics and volume of treatment. What is more important at low intestinal bleeding: total colonoscopy or search for the true source of the bleeding?
Aims and Methods: Compare the structure identified during colonoscopy sources of lower intestinal bleeding at patients prepared by oral lavage versus patients who performed urgent colonoscopy without bowel preparation.
A randomized cohort study. Included 252 patients admitted from the signs of intestinal hemorrhage in 2006–2015. 118 men, women 134. The average age of the patients was 60.15 ± 15.7 years. In Hosp No 29 colonoscopy was performed at admission without prior preparation of the colon, the patient in Hosp No 1 performed lavage or enema preparation prior to colonoscopy within 24–48 hours of hospital stay.
Results: Significant differences in the structure of intestinal bleeding sources ($\chi 2 = 4.500000$, $p = 0.03390$) are revealed. In patients without bowel preparation the most frequently detected were bleeding diverticula and cancers - 17%, ulcerative colitis - 10%, intestinal bleeding - 16%, upper bleeding - 16%. In preliminary bowel preparation the most often likely causes of bleeding detected were cancers - 22%, ulcerative colitis - 15%, angiodysplasia - 13%. The number of endoscopic findings in bowel preparation was 1.5 times higher against emergency colonoscopy without bowel preparation. The number and structure of the observed changes were significantly different between both groups, and depending on the sex of patients ($\chi 2 = 112.4894$, $p < 0.0000$). There were no complications in both groups. Another aspect of the question consists of the need to use hemostasis methods. In our observations at active bleedings we used hemostasis methods in only 3 patients (1.2%). It not in favor of an early colonoscopy without preliminary preparation of a colon. These data differ from other authors who use a hemostasis in 25% or 40%. Apparently, tactical decisions in favor of using a colonoscopy without bowel preparation should be based on experience of clinic and regional features of nosological forms.
Conclusion: Performing a colonoscopy at an altitude of bleeding without colon preparation is safe, but significantly alters the structure of the true sources (causes) of bleeding. Colonoscopy after preliminary bowel preparation has significantly higher diagnostic capabilities, which complicates the identification of the true source of bleeding. The choice in favor of a colonoscopy without intestinal preparation should be individual.
Disclosure: Nothing to disclose

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P0397 DO CLINICAL CHARACTERISTICS AND OUTCOME IN NONAGENARIANS WITH ACUTE LOWER GASTROINTESTINAL BLEEDING DIFFER FROM YOUNGER PATIENTS?

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Introduction: The number of nonagenarians hospitalized for various reasons including acute lower gastrointestinal bleeding (ALGIB) is increasing worldwide.
Aims and Methods: Our aim was to evaluate whether clinical characteristics and outcome in nonagenarians with ALGIB differ from younger patients.
Data from all nonagenarians with ALGIB hospitalized in our hospital over a 7s-year period were compared with those < 90 years old. Hemodynamic resuscitation, management of antithrombotic agents, early colonoscopy following bowel cleansing, capsule enteroscopy and endoscopic hemostasis when needed were the main steps in the management of patients with ALGIB. In cases of hemodynamic instability, emergent CTA was performed with embolization when appropriate.
Results: Data of 32 nonagenarians (91.8 ± 2.1, 90–99) were compared with that of 496 patients <90years (68.8 ± 14.1, 17–89). Nonagenarians were more commonly female (24/32 vs 232/496, $p = 0.003$) with higher serum creatinine levels (1.4 ± 0.8 vs 1.0 ± 0.7, $p = 0.046$) and higher rate of coexisting diseases (32/32 vs 430/496, $p = 0.023$), mainly cardiovascular (23/32 vs 241/496, $p = 0.017$). Proper bowel preparation (25/32 vs 438/496) and endoscopic examination (29/32 vs 477/496) did not differ. The cause of bleeding was not different (mainly diverticula, ischemic colitis and neoplasia in 8, 9 and 4/32 nonagenarians respectively). No significant difference was observed between the 2 groups regarding transfusions (1.1±1.8 vs 0.9±1.9, $p = 0.524$), hospitalization days (5.0 ± 2.6 vs 4.3 ± 3.2, $p = 0.150$), recurrence of bleeding (1/32 vs 36/496, $p = 0.72$), urgent surgical hemostasis (0/32 vs 6/496, $p = 0.69$) and mortality (2/32 vs 11/496, $p = 0.19$).
Conclusion: Despite the age and the higher prevalence of concomitant diseases, management of ALGIBs in nonagenarians should not differ from that of younger patients.
Disclosure: Nothing to disclose

P0398 MANAGEMENT OF ANTITHROMBOTIC AGENTS IN PATIENTS WITH PRESUMPTIVE DIVERTICULAR HEMORRHAGE

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Introduction: It has been reported 5~15% of definite diverticular hemorrhage patients experience re-bleeding within 30 days regardless of status of re-initiation of antithrombotic agents. However, about 65% of diverticular hemorrhage patients are diagnosed as presumptive hemorrhage.
Aims and Methods: This study aimed to elucidate risk factors predicting re-bleeding in patients with presumptive diverticular hemorrhage. A total of 231 patients with presumptive diverticular hemorrhage from January 2004 to September 2017 were included retrospectively. The primary outcome was post-endoscopy re-bleeding among patients with presumptive diverticular hemorrhage. Age, sex, past medical history, laboratory results, colonoscopy procedure length, and site of diverticula, as well as use of antithrombotic agents were compared between patient with and without re-bleeding. In addition, among patients with presumptive diverticular hemorrhage using antithrombotic agents, we examined relationship between re-bleeding and when they restart their agents.
Results: 63 (27.3%) patients experienced re-bleeding. Colonoscopy procedure was longer in patients who had re-bleeding afterward (46.8 minutes VS 40.2 minutes $p = 0.01$). None of other variables including use of antithrombotic agents was associated with re-bleeding. 23 (38.1%) of the 63 re-bleeding patients were taking antithrombotic agents. Duration from colonoscopy to re-bleeding in patients taking antithrombotic agents and those not taking was 1.70 and 1.92 days, respectively ($p = 0.23$). In addition, 17 of the 23 re-bleeding patients under antithrombotic agents had their antithrombotic agents re-initiated after the index

re-bleeding, with none of them experiencing another re-bleeding during the follow-up.
Conclusion: Use of antithrombotic agents was not associated with re-bleeding in patients with presumptive diverticular hemorrhage after colonoscopy, potentially indicating the safety of reinitiating antithrombotic agents.

	re-bleedng (n = 63)	non re-bleeding (n = 168)	P-value
Antithrombotic agents,n(%)	23 (37)	56 (33)	0.38
Hypertention,n(%)	37 (59)	99 (59)	0.55
Diabetes mellitus,n(%)	14 (22)	34 (20)	0.44
Hemoglobin(g/dl), mean(SD)	11.83 (2.00)	11.50 (2.36)	0.40
C reactive protein(mg/dl), mean(SD)	0.21 (0.35)	0.31 (0.66)	0.26
colonoscopy time(minutes), mean(SD)	47 (16)	40 (20)	0.012
Location			
-Cecum,n(%)	15 (24)	44 (26)	0.40
-Asecending colon,n(%)	52 (83)	143 (85)	0.31
-Transverse colon,n(%)	18 (29)	51 (30)	0.45
-Descending colon,n(%)	21 (33)	56 (33)	0.57
-Sigmoid colon,n(%)	40 (64)	115 (69)	0.29

[Risk factor of re-bleeding in patients with presumptive diverticular hemorrhage]
Disclosure: Nothing to disclose

P0399 CUMULATIVE LEVELS OF FAECAL HAEMOGLOBIN IN CONSECUTIVE ROUNDS OF FIT NEGATIVE PARTICIPANTS FOR IMPROVING COLORECTAL CANCER SCREENING MANAGEMENT

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Introduction: Faecal Immunochemical Test (FIT) for haemoglobin is widely used in colorectal cancer screening programmes to select those participants with higher risk of neoplasia undergoing to colonoscopy. However excretion of haemoglobin to faeces (fHb) is intermittent and can be due to difference causes other than neoplasia. Moreover, it has been shown that FIT pre analytics have sources of variability and that the concentration of fHb is related with age and gender. For instances, an individual may present a positive result followed by a negative result or vice versa only in a few days.
Aims and Methods: Our hypothesis is that the cumulative concentration of fHb in consecutive rounds might be useful to detect those individuals with high risk neoplasia (HRN), even amongst FIT negative participants. We have evaluated 1771 average-risk participants (50–69 years old) from the Barcelona colorectal cancer screening programme with a negative FIT (< 20 μg Hb/g faeces) in the first and second round and with a positive test in the third round. We have established 3 groups based on the mean fHb concentration of the 2 first rounds (< 4 μg/g; 4–9 μg/g; >9 μg/g). This classification, in combination with gender and age, has been correlated to endoscopic findings. The principal outcome has been HRN defined as colorectal cancer and/or 5 ≥ adenoma / serrated lesions and/or lesion size ≥20 mm.
Results: A multivariate logistic regression analysis identified gender (men: odds ratio [OR], 1.70; 95% confidence interval (CI), 1.30–2.22), and mean fHb concentration of the first 2 rounds (>9 μg/g: OR, 3.08; 95% CI, 2.02–4.70) as independent predictive factors for HRN. Combining these factors, different risk categories have been established. A 6.59-fold (95% CI, 3.80–11.42) higher risk of HRN was found between the 2 extremes categories (see table). The positive predictive value for HRN ranged from 8.8% to 38.9%. Interestingly, negative predictive values for CRC, ranged from 93.1% to 98.5%.
Conclusion: Cumulative fHb concentration together with gender in FIT negative participants could be a useful tool to assess the presence or absence of HRN in subsequent screening rounds and can help in the design of strategies and the management of the programmes to enhance their efficiency.

	Women	Men
<4 μg/g	1 (613)	1.82 [1.26–2.61] p = 0.001 (543)
4–9 μg/g	2.35 [1.51–3.64] P < .001 (222)	3.08 [2.07–4.59] p < 0.001 (266)
>9 μg/g	2.30 [1.10–4.83] P = .027 (55)	6.59 [3.80–11.42] p < 0.001 (72)

[Table. Risk of HRN According to Gender and fHb. Odds ratios [95% confidence interval]. The number of individuals is shown in parentheses.]
Disclosure: Nothing to disclose

P0400 TO IDENTIFY A LOW-RISK GROUP OF INDIVIDUALS WITH IRON DEFICIENCY ANAEMIA WITHOUT GASTROINTESTINAL SYMPTOMS

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Introduction: Iron deficiency anemia (IDA) is one of the most common indications for investigation with gastroscopy and colonoscopy. However, there is a dearth of data on the diagnostic yield of endoscopic evaluation in patients with asymptomatic IDA. Identification of a low-risk subgroup without compromising the diagnosis of clinically significant lesions can have the potential to avoid invasive investigations and reduce burden on endoscopy departments. The aims of this study were:
1) To identify positive predictors of malignancy in patients with IDA.
2) To use the negative predictive values of the above to identify patients who can safely avoid bidirectional endoscopy (BDE) (low probability of significant gastrointestinal malignancy).
Aims and Methods: This was a retrospective study of consecutive subjects who underwent BDE between July 2014 and July 2017 for IDA. Patients with a history of GI bleeding, active gastrointestinal symptoms, and/or signs of overt gastrointestinal bleeding were excluded. Endoscopic findings were documented as presence/absence of a bleeding related lesion. Gastrointestinal neoplasm was the primary outcome. Model discrimination was defined using ROC curves and calibration assessed using the Hosmer-Lemeshow statistic.
Results: A total of 158 patients were included, of whom 94 (59.0%) were female with a median age of 59 years (IQR: 48–71). The mean Hb was 97 g/L (IQR: 80–116). The mean MCV was 79 fL. A total of 6 patients (3.2%) had gastrointestinal malignancy, all of which were colorectal. 50 (31.6%) had a cause for their IDA identified on BDE. 27 patients had causes identified on gastroscopy, 14 patients had causes identified on colonoscopy and 9 patients had causes identified on both procedures. Logistic regression analysis revealed that cancer was almost 3 times more likely to be diagnosed for every 10 years of increased age (OR 2.5, 95%CI 1.1–6.1, p = 0.04) and 51% more likely for every 10g/L reduction in Hb (OR 1.51, 95% CI 1.1–2.3, p = 0.04). When applying an age threshold of greater than or equal to 70, the OR was 6.0 (95% CI 1.1–34.1, p = 0.04). We found that other biochemical variables (such as iron, ferritin and transferrin saturation) and clinical variables (such as presence of weight loss, smoking and family history of gastrointestinal cancer) do not appear to contribute to cancer risk prediction. The statistically significant parameters of age and Hb demonstrate satisfactory calibration (Hosmer-Lemeshow p = 0.96) and similar discrimination (C-statistic 0.93). Using the cut off age of less than 55 and Hb greater than 105, this can exclude all patients with gastrointestinal pathology and malignancy.
Conclusion: Age and serum Hb can provide useful discrimination for significant gastrointestinal pathology in patients with asymptomatic IDA. These findings need further validation in large scale cohorts. In doing so, we can identify patients with a low pre-test probability to reduce the number of low-value investigations in IDA.
Disclosure: Nothing to disclose

P0401 ASSOCIATION OF COLORECTAL CANCERS AND SYNCHRONOUS POLYPS IN A PERIOD OF 15 YEARS: CHANGING PATTERN?

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Introduction: Primary tumor location is an important prognostic factor owing to distinct biological features. Moreover right colon polyps are recognised as a cause of interval cancers. Thus characterization of colorectal cancer (CRC) and synchronous polyps has emerged as an important feature of current endoscopic practices.
Aims and Methods: To investigate possible changes in CRC characteristics as well as their association with synchronous polyps in a 15 year period (2000–2015)

	G1: 2001-2005	G2: 2006-2010	G3: 2011-2015
Left colon	153 (71.5%)	177 (64.36%)	189 (62.79%)
Right colon	61 (28.5%)	98 (35.64%)	112 (37.21%)

[table]
All patients with a CRC diagnosis, identified by total colonoscopy in a time frame of 15 years (2000–2015) in a tertiary medical center in Greece, were included in the study. Patients with familial polyposis syndromes were excluded. Data regarding year of diagnosis, location of CRC, sex, presence of synchronous polyps and their location were collected. Patients were categorized in 3 groups according to year of CRC diagnosis: G1 (2000–2005), G2 (2006–2010), G3 (2011–2015). X^2 and t-test were used for statistical analysis.
Results: 790 CRC cases (404 men, 51.1%) and 443 synchronous polyps were identified. CRC was equally diagnosed in men and women throughout the 3 studied periods (p > 0.05). Right-sided CRCs were significantly increased in G3 compared to G1 (37.21% vs 28.5%, p = 0.04), while in G2 compared to G1 the

increase did not reach statistical significance (35.64% vs 28.5%, p = .09). Location of CRC in the 3 different groups is depicted in the table.
Synchronous polyps were more commonly found in the right colon during G3 compared to G2 and G1 (G3 = 40.76% vs G2 = 17.12% vs G1 = 23.14%, $p < 0.0001$). Statistical significance remained even when analyzed separately for sex (females-right colon polyps G3 = 35.94% vs G2 = 2.7% vs G1 = 8.7%, $p < 0.0001$ and males right colon polyps G3 = 42.86% vs G2 = 24.32% vs G1 = 32%, p = 0.019).
Conclusion: Right colon CRCs as well as synchronous right colon polyps are significantly more frequently diagnosed in a single endoscopic center during the last 15 years. This may be due to better colon preparation, use of high definition endoscopes or increased awareness of right colon cancers by gastroenterologists.
Disclosure: Nothing to disclose

P0402 AGE AT MENARCHE AND RISK OF COLORECTAL ADENOMA

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Introduction: Limited data are available regarding the association between age at menarche and the risk of colorectal adenoma. Therefore, we aimed to evaluate the relationship between reproductive factors including age at menarche and the risk of colorectal adenoma.
Aims and Methods: A cross-sectional study was performed on asymptomatic female subjects who underwent colonoscopy between 2010 and 2014 as part of a comprehensive health screening program in Korea. The association between reproductive factors including age at menarche and the presence of adenomas was assessed using multivariate logistic regression analysis.
Results: Among 32,620 asymptomatic female subjects, the proportion of patients with menarche at 10–11, 12–13, 14–15, 16–17, and 18–19 years of age was 4.1%, 31.7%, 45.4%, 14.9%, and 4.0%, respectively. Age at menarche was not significantly associated with the risk of any adenoma (adjusted odds ratio [AOR], 0.99; 95% confidence interval [CI], 0.97 to 1.02; p = 0.500) and advanced adenoma (AOR, 0.98; 95% CI, 0.91 to 1.04; p = 0.468) after adjusting for confounding factors. Age at menarche was not significantly associated with the risk of adenoma even among the similar age group. In addition, parity, use of female hormones, and menopause were not associated with the risk of adenoma.
Conclusion: Age at menarche, parity, use of female hormones, and menopause were not significantly associated with the risk of colorectal adenoma. Our findings indicate that reproductive factors including age at menarche do not affect the development of colorectal adenoma.

	Any Adenoma		Advanced Adenoma	
Participants' age groups	adjusted odds ratio(95% CI)	p value	adjusted odds ratio(95% CI)	p value
30–34 (years)	1.01 (0.93–1.99)	0.816	0.98 (0.78–1.24)	0.880
35–39	0.94 (0.88–1.00)	0.052	1.04 (0.88–1.21)	0.672
40–44	0.97 (0.92–1.04)	0.403	0.89 (0.75–1.07)	0.231
45–49	1.06 (0.99–1.14)	0.098	1.11 (0.90–1.36)	0.327
50–54	1.10 (0.95–1.09)	0.688	1.02 (0.85–1.24)	0.810
≥ 55	1.03 (0.98–1.08)	0.291	0.94 (0.85–1.05)	0.301

[Risk of colorectal adenoma according to the age at menarche among similar age groups]
Disclosure: Nothing to disclose

P0403 METABOLIC FACTORS, LIFESTYLE HABITS AND AGING ARE ASSOCIATED WITH DEVELOPMENT OF COLORECTAL NEOPLASIA IN JAPAN

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Introduction: For the past decades, the incidence and mortality rate of colorectal cancer (CRC) has been increased in Japan and CRC is the third leading cause of cancer death in Japan. This may reflect economic development and concomitant shifts from traditional lifestyle towards a westernized lifestyle. The association of metabolic syndrome (MetS) and CRC has been reported in several studies, however, individual factors contributing to CRC occurrence have been obscure, especially in Japan.
Aims and Methods: In the present study, we investigated the risk factors such as metabolic and lifestyle factors for the occurrence of colorectal neoplasia (CRN; adenomatous polyp ≥ 5 mm in size and cancer) and advanced neoplasia (AN; advanced adenoma and cancer, ref.) by using comprehensive health checkup data. We conducted a retrospective analysis in clinical practice at a single center. Among 10138 subjects who took comprehensive health checkup at our hospital between in August 2012 and December 2016, 2769 subjects who also underwent screening colonoscopy were enrolled. A diagnosis of MetS was made by Metabolic Syndrome Diagnostic Criteria Exploratory Committee in Japan. Demographic characteristics, anthropometric measurements, visceral fat area (VFA) measured at the umbilical level by CT, hematological metabolic parameters, degree of liver fat evaluated by ultrasonography, and current smoking and drinking habits were assessed. Association between variables and CRN or AN was evaluated by univariate analysis using t-test, X^2 test, Mann-Whitney test, and then by multivariate analysis using multiple logistic regression model. A $p\ value < 0.05$ was considered statistically significant.
Results: Of 2769 subjects analyzed, 327 subjects had CRN (11.8%) and 99 had AN (3.3%). 676 subjects were diagnosed as MetS (24.4%) and presence of MetS was significantly associated with CRN and AN. (p = 0.000, 0.004). Univariate analysis identified significant association of CRN with sex, age, body mass index (BMI), VFA, systolic and diastolic blood pressure (SBP/DBP), low-density lipoprotein (LDL)-cholesterol, triglycerides (TG), fasting plasma glucose (FBS), hemoglobin A1c (HbA1c), fatty liver, smoking habits, drinking habits and ≥ 10 kg weight gain compared with the body weight at the age of 20. Logistic regression analysis revealed that age, BMI, SBP, LDL TG, current smoking and drinking habits were independent factors associated with CRN (Table). Moreover, age, LDL TG and current smoking were recognized as independent factors associated with AN.
Conclusion: The present study demonstrated that metabolic factors, especially dyslipidemia, aging and current smoking were risk factors for development of colorectal neoplasia in Japan.
[Results of logistic regression analyzes]
Disclosure: Nothing to disclose

Reference

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P0404 COMPARISON OF COLORECTAL POLYPS WITH SIZE BETWEEN 6 AND 20 MILLIMETERS IN YOUNGER AND OLDER INDIVIDUALS

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Introduction: According to the recommendation by the U.S. Multi-Society Task Force on Colorectal Cancer, colonoscopy screening for colorectal neoplasm should be performed for individuals for 50 years old and over. Over the last decades, the incidence and mortality of colorectal cancers (CRCs) in individuals who are 50 or more years old have been decreasing. In contrast, the incidence of CRCs in individuals less than 50 years old has been increasing. Several studies demonstrated that CRCs in older individuals have a different biology compared to younger individuals. However, the data on the characteristics of colon polyp in individuals aged < 50 years is limited.
Aims and Methods: The aim of this study was to investigate the characteristics of colorectal neoplasm in individuals aged < 50 years and to compared them to those of individuals > = 50 years old. From Jan 1, 2015, to Jan 31, 2017, patients

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	for CRN			for AN		
	OR	95% CI	p value	OR	95% CI	p value
Age (per 1 year increment)	1.041	1.029–1.053	0.000	1.051	1.032–1.070	0.000
BMI (per 1 kg/m2 increment)	1.049	1.013–1.086	0.008			N.S.
systolic blood pressure (per 1 mmHg increment)	1.011	1.005–1.018	0.001			N.S.
LDL-cholesterol (per 1 mg/dL increment)	1.009	1.005–1.013	0.000	1.007	1.000–1.014	0.048
triglyceride (per 1 mg/dL increment)	1.001	1.000–1.002	0.028	1.002	1.001–1.003	0.002
current smoking (vs non-smoker)	2.205	1.562–3.113	0.000	1.923	1.114–3.317	0.019
drinking habits (vs those without habits)	1.567	1.216–2.017	0.001			N.S.

who underwent snare polypectomy with polyp's size between 6 and 20 millimeters (mm) were enrolled in this study in a tertiary medical center of northern Taiwan. The demography of patients and the polyp characteristics, including pathological findings, size, morphology and location, were recorded. Descriptive statistics and frequency distributions were calculated. The data were analyzed by using either the Mann-Whitney U test for continuous variables or chi-square test for categorical variables. Statistical significance was defined as $p < 0.05$.
Results: A total of 1925 polyps in 1424 patients were included in this study. There were 323 polyps in 264 patients < 50 years old (younger group) and 1602 polyps in 1160 patients $>= 50$ years old (older group). In the younger group, 183 patients were male (69.3 %), with a median age of 44 years old (range: 19–49 years old). The median size of polyps was 10 mm (range: 6–20 mm) in the younger group. Most polyps in the younger group were in the distal colon (62.8%) and had a sessile shape (83.6%). Compared to the older group, the prevalence of the distal colon polyp and pedunculated polyp was significantly higher in the younger group (62.8% vs. 55.2%, $p = 0.011$; 16.4% vs 12.3%, $p = 0.045$) respectively. In the polyp pathological findings, there were 57 (17.6%) hyperplastic polyps, 20 (6.2%) sessile serrated adenomas, 158 (48.9%) tubular adenoma, 52 (16.1%) tubulovillous adenoma, 6 (1.9%) villous adenoma and 2 (0.6%) high-grade dysplasia in the younger group. In the high-risk polyp subgroup, the prevalence of sessile serrated adenoma and $\geq$10 mm serrated adenoma was significantly higher in the younger group compared to the older group (6.2% vs 2.7%, $p = 0.002$; 3.4% vs. 1.4%, $p = 0.042$) respectively. The prevalence of polyps with high-grade dysplasia was significantly higher in the older group (3.0 % vs 0.6 %, $p = 0.014$). There was no significant difference between both groups in terms of polyps with size $>= 10$ mm and polyps with villous component.
Conclusion: In the polyps with size between 6 and 20 mm, the prevalence of left side colon polyp and pedunculated polyp is significantly higher in patients < 50 years old. In the high-risk polyp subgroup, the prevalence of sessile serrated adenoma is higher in younger group.
Disclosure: Nothing to disclose

P0405 SHORTER LIFE EXPECTANCY OF INTERVAL COLORECTAL CANCER AND LEAD TIME BIAS

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Introduction: The outcomes of interval colorectal cancer (ICRC) varied in previous studies without accounting for lead time bias.
Aims and Methods: This nationwide cohort analysis estimates expected years of life lost (EYLL) to adjust for lead time bias and comparison between patients with ICRC and detectable colorectal cancer (DCRC). Patients with colorectal cancer (CRC) registered in Taiwan Cancer Registry during 2002 to 2009 were enrolled, including 22,169 CRC confirmed within 6 months after colonoscopy grouped as detected CRC (DCRC) and 1,653 CRC diagnosed during 6–60 months after a negative colonoscopy grouped as ICRC. All patients were followed up until the end of 2011. We simulated age- and sex-matched references from life tables in Taiwan National Vital Statistics using Monte Carlo method. Lifetime survival function of the cancer patients was obtained from extrapolation of logit transform of the survival ratio between cancer cohorts and age- and sex-matched references. The LE (life expectancy) and EYLL were calculated after stratification by genders and tumor stages.
Results: Comparing with DCRC, ICRC were predominantly older age, more on proximal sites, and more endoscopic polypectomy procedures ($p < 0.001$). Patients with ICRC had consistently shorter LEs than those of DCRC after stratification by genders and stages (all $p < 0.001$). There is no such trend if the comparison is performed through EYLL, or, adjustment for age at diagnosis and/or lead time bias. There is a linear trend for increasing proportion of ICRC from distal to proximal colon, which seems to corroborate with different cancer registries internationally.
Conclusion: The evidence corroborates the hypothesis that the worse long-term outcome or shorter LE of ICRC largely results from lead time bias. Improving the quality of colonoscopy and regular surveillance of patients with detected and resected polyp are crucial to reduce ICRC.
Disclosure: Nothing to disclose

P0406 ACTIVATION OF STAT3 MEDIATES SURVIVAL OF CANCER STEM-LIKE TUMORSPHERES IN EGFR-POSITIVE COLORECTAL CANCERS: ANALYSIS BY RNASEQ AND THERAPEUTICS SCREENING

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Introduction: Cancer stem cells are capable of cell division and survival against cancer therapies, leading to tumor progression and recurrence. The inhibitory agents against cancer stem cells may be efficient for eradicating tumors.
Aims and Methods: This study aimed to uncover the relevant driver genes maintaining cancer stemness in epidermal growth factor receptor (EGFR)-positive colorectal cancer cells, and to discover the efficiently therapeutic agents. EGFR-positive HCT116- and HT29-derived cancer stem-like cells (CSCs) were induced *in vitro* as studying models in this study. RNAseq technique following by bioinformatics analysis was applied to identify the differential genes maintaining CSCs. Moreover, a panel containing 172 therapeutic agents targeting to the documental pathways of stem cells were applied to search for the efficient therapeutics against CSCs.
Results: RNAseq revealed that 654 genes were significantly up-regulated and 840 genes were down-regulated in the HCT16CSCs. Among the genes, notably, plateletderived growth factorA (PDGFA) and signal transducer and activator of transcription 3 (STAT3) were relevant to Pathway in Cancer analyzed by NetworkAnalyst. Furthermore, the therapeutics screening indicated that the agents targeting to STAT3 and Wnt signaling pathways were efficient to reduce the cell viabilities of HCT116 and HT29 cells. Consequently, we figured out that inhibition of STAT3 by its specific inhibitors such as homoharringtonine and knockdown technique significantly reduced the formation and survival of the HT29-derived tumorspheres, whereas STAT3 phosphorylation was majorly regulated by EGF to induce PDGFA and Wnt signaling cascade.
Conclusion: This study demonstrated the potential genes involving in the tumorsphere formation and survival in the selective EGFR-positive colorectal cancers. The data suggested that EGF-STAT3 signaling pathway promoted and maintained the colorectal cancer stemness as a putative therapeutic target, where STAT3 may be through inducing PDGFA to activate Wnt signaling pathway.
Disclosure: Nothing to disclose

P0407 PATIENT-DERIVED COLORECTAL CANCER EXPLANTS - ADEQUATE MODELS FOR CHEMOTHERAPY TESTING?

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Introduction: Colorectal cancer (CRC) is the second most common cancer in developed countries. More than a quarter of these patients eventually receive chemotherapy. Several pathways leading to CRC are currently recognized, which may impact on therapy success. Although both short-term culture of tumor sections and xeno-transplantation have been used to determine drug efficacy, there are no available long-term validated models to test chemotherapy in patient-derived cultures, namely in the different carcinogenesis pathways.
Aims and Methods: We aim to develop an efficient methodology for culture of CRC samples originated from different carcinogenesis pathways.
In this prospective study we cultured patient-derived tissue microfragments in stirred-tank culture systems (PDEs) - we studied culture viability (metabolic and morphologic evaluations), phenotype [gland and/or villi formation, mucin production, presence of tumor infiltrating lymphocytes (TILs), p53 staining, mismatch repair protein expression, microsatellite instability] and *KRAS* (exon 2) and *BRAF*V600E mutational status in *in vitro* cultures; we correlated culture progression to the primary tumor features.
Results: 11 CRCs were collected. All tumors were successfully cultured as PDEs for 28 to 122 days. Culture duration was determined by the frequency of sampling along culture time to assure a minimum PDE concentration. PDEs ($N = 11/11$) retained their originals' architecture. There was always viable tumor for at least 28 days (~46 days, range 28–87 days) and for most cases ($N = 7/11$) viable stroma was retained for as long as the neoplastic cells. Capillaries were not preserved. PDEs ($N = 10/11$) considerably lost tumor architectural complexity, stroma cellularity and inflammatory cells, specifically TILs, at the first histological evaluation (days 7–11), but less significantly thereafter. After the first week of culture, PDE tumor cells progressively acquired a senescent phenotype. PDEs ($N = 10/11$) replicate the original tumors' immunohistochemical and genetic key features. One PDE showed a *KRAS* mutation undetected in the primary tumor, from day 0; p53 staining was also consistently different in the PDE. *KRAS* mutated clones seem to be positively selected in culture ($N = 3/5$).
Conclusion: PDE dynamic culture is an efficient method to culture human CRC. Overall the key pathological features of the primary tumors are retained over time, which supports the potential use in drug predictive assays. Divergent results may be due to intratumoral heterogeneity and optimization in tumor collection may be required to improve PDE representation of the primary tumor.
Disclosure: Isadora Rosa reports personal fees and/or non-financial support from MSD, Abbvie, Ferring, Dr Falk Pharma, Pharmakern, Hospira, Janssen and Takeda, outside the submitted work.

P0408 HDAC6 SELECTIVE INHIBITOR, ACY1215, INHIBIT CELL GROWTH OF COLON CANCER CELL LINE HCT116

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Introduction: Colorectal cancer is the third leading cause of cancer death around the world, and 5-FU is the most common used chemotheraputic drugs for colorectal cancer, however chemoresistence do occur. HDAC6 is a unique member of HDACs, and is involved in regulating diverse key biological processes including cell motility, cell division, protein trafficking, and apoptosis, thus playing important role in carcinogenesis. HDAC6 inhibitors have emerged as promising agents for the treatment of various forms of cancer, and ACY1215, the first oral HDAC6 inhibitor, has showed promising results for treatment of multiple myeloma in phase I and II clinical trials, however little is known about its role in colorectal cancer.

Aims and Methods: We aimed to explore the effect of Rocilinostat (ACY1215), a specific HDAC6 inhibitor, on the cell growth, migration and apoptosis of HCT116 cells, as well as its influence on the chemotheraputic effect of 5-Fluoracil (5-FU) on colon cancer.

Treating HCT116 cells with different concentration of ACY1215, and explore its effect on cell viability, cell proliferation, cell migration and apoptosis, and explore the potential mechanism of ACY1215 via detecting some cell signal related protein by western blot. And them explore the influence of ACY1215 treatment on the chemotheraputic effect of 5-FU.

Results: 1. After treating HCT116 cells with ACY1215, the cell viability, colony formation, wound closure and migrated cell numbers were significantly reduced with the increasing concentration of ACY1215, and the propotion of apoptosis cells were significantly increased with the increased concentration of ACY1215 ($p<0.05$), as well as the expression of apoptosis-related protein (PARP and Cleaved-Caspase 3). After treating HCT116 cells with ACY1215, the expression of p-MEK and p-ERK were decreased, while no obvious changes were noticed regarding the expression of MEK and ERK. Treating HCT116 cells with ACY1215 and/or 5-FU, we found that the cell viability, colony formation, wound closure and migrated cell numbers were significantly reduced when comparing control with single drug, or comparing single drug with combined drugs ($p<0.05$). The same tendency was noticed in regarding to the expression of apoptosis related protein (PARP and Cleaved-Caspase 3).

Conclusion: HDAC6 specific inhibitor, ACY1215, could inhibit the cell growth, proliferation and migration, and promote apoptosis of HCT116 colon cancer cells. ACY1215 exibits its tumor suppression role via inhibition of the MEK/ERK signal pathway. ACY1215 may enhance the chemotheraputic effect of 5-FU on colon cancer cells.

Disclosure: Nothing to disclose

P0409 PEDIATRIC COLORECTAL CANCER - A HETEROGENEOUS ENTITY

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Introduction: Colorectal cancer (CRC) is extremely rare in pediatric patients. A poor outcome has been reported in parallel with unfavorable prognostic factors.

Aims and Methods: We aimed to characterize at clinical, pathological and molecular level a group of pediatric CRC patients (< 18 years) - and evaluate overall and disease-free survival.

Included pediatric CRC patients diagnosed from January 2002 to January 2016. Clinical data, tumor features, and survival were evaluated.

Microsatellite instability (MSI) status, loss of heterozygosity for the dinucleotide Bethesda microsatellite markers and expression of the DNA mismatch repair (MMR) proteins were analyzed. Germline mutation analysis was performed for a multigene panel of 94 genes associated to increased cancer risk (including genes associated to CRC hereditary syndromes), using next generation sequencing and MLPA.

Results: 5 patients were included, 3 of them males, mean age at diagnosis 14.2 years (9–17 years). 4 out of 5 had family history of cancer in 2nd degree relatives: 2/4 corresponded to CRC (in 1/2 the parents had consanguinity), whereas the remaining 2 corresponded to other cancers. 4 out of 5 CRC were located in the right colon. Regarding histology subtype, 2/5 (40%) were mucinous with signet ring cells, 1 had signet ring cells, and 2 had no other specification (NOS). Lymphovascular invasion was present in 4/5 (80%) and perineural invasion in 3/5 (60%) of them. "*Crohn-like*" lymphoid reaction and tumor budding was not observed. All tumors were ≥ pT3N2.

Patients had a mean follow-up of 5.6 years (10 months to 14 years). 1 patient recurred after 15 months and 2 (40%) died after 24 and 10 months. A likely pathogenic germline mutation was identified in only 1/5 patients (heterozygous *MSH2* mutation), although not explaining by itself the diagnosis of CRC at pediatric age.

All CRC analyzed (n = 4) were microsatellite stable (MSS) and/or expressed all MMR proteins. Three CRC were analyzed for Bethesda microsatellite markers and one showed LOH for the 3 dinucleotide markers (chromosomes 2p, 5q and 17p), suggesting the presence of chromosomal instability. This 4 corresponded to the patient diagnosed at an earlier age (9 years), without any family history of cancer, presenting a NOS tumor.

Conclusion: Pediatric CRC presented with advanced disease and had a poor prognosis, however, its molecular cause(s) need yet to be clarified. These CRCs had distinct histological and molecular presentations, resembling features from different carcinogenic pathways, thus suggesting a heterogeneous nature.

Disclosure: Nothing to disclose

P0410 CANCER-ASSOCIATED FIBROBLASTS PROMOTES COLORECTAL CANCER THROUGH SECREATION OF TNFSF4 AND IGF2

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Introduction: As an essential part in stromal cells, cancer-associated fibroblast (CAF) plays an important role in the tumor microenvironment and exerts promoting effect in colorectal neoplastic progression. However, the detailed molecular mechanism is elusive.

Aims and Methods: In this study, we proposed to reveal the oncogenic role of CAF in colorectal cancer (CRC) progression. The primary culture was employed for isolation of CAF and adjacent normal fibroblast (NF). The CRC cells were treated with conditional medium (CM) from NF and CAF for the assessment of cell proliferation rate and invasion ability. RNA-Seq analysis was applied to identify the differentially expressed genes in 3 paired NF and CAF samples. The candidate genes were validated by qRT-PCR in 18 paired primary samples and 2 top genes, TNFSF4 and IGF2, were selected for functional studies.

Results: In primary culture, CAF-produced CM exhibited oncogenic function through promoting CRC cell proliferation and invasion. TNFSF4 and IGF2 were screened out showing the highest expression in CAFs compared with NFs with 14 and 12-time upregulation respectively. qRT-PCR confirmed the abundance of TNFSF4 ($p < 0.001$) and IGF2 ($p = 0.006$) in CAF. Immunohistochemistry staining on the tissue microarray demonstrated that TNFSF4 was predominantly expressed in fibroblasts but IGF2 was located both in the cancer cells and fibroblasts. Their receptors, OX40 and IGF1R were expressed in immune cells and cancer cells respectively. In the functional studies, both rhIGF2 and IGF2 CM promotes CRC cell proliferation and invasion *in vitro*.

Conclusion: In colorectal CAF, TNFSF4 and IGF2 are abundantly expressed, whose secretion plays oncogenic role through promoting CRC growth. CAF enhances CRC progression via immune suppression and direct influence on tumor cells. Our study not only revealed novel mechanisms for the CAF in tumorigenesis but also provided a rational therapeutic strategy.

Disclosure: All authors have declared no conflicts of interest.

P0411 MALIGNANT POTENTIAL OF EARLY-STAGE SERRATED ADENOCARCINOMA BASED ON GENETIC ANALYSIS

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Introduction: Serrated adenocarcinoma (SAC) is one of several end-points of the serrated neoplasia pathway progression pattern. Although SAC prognosis is not widely recognized, the serrated pathway-associated subtype consistently exhibits unfavorable prognosis in genetic studies.

Aims and Methods: The aim of this study was to classify molecularly distinct subtypes for serrated carcinomas and clarify their associated clinicopathological characteristics and genetic changes.

We examined 38 early-stage colorectal SACs from 1142 consecutive patients (895 with Tis and 247 with T1 carcinoma) who were treated at Hiroshima University Hospital between January 2009 and January 2016. Of these, 24 were classified into 3 molecularly distinct groups by colon cancer subtyping (CCS) (De Sousa de Melo et al., Nat Med 19, 2013). Clinicopathologic characteristics, Ki 67 labeling index (LI), and SAC epithelial serration were assessed. DNA from carcinomas and normal tissue/adenoma was extracted using laser microdissection, sequenced by next generation sequencing, and mutation number and pattern for a 15-oncogene panel were determined.

Results: CCS groups included CCS1: CDX (+) and MSI-L/MSS (14 cases), CCS2: MSI-H (5 cases), and CCS3: CDX (−) and MSI-L/MSS (5 cases). Invasive cancer was significantly higher in CCS3 than CCS1 (CCS1:CCS3, 3/14:5/5, $p = 0.0048$). Ki67 LI and epithelial serration were higher in CCS3 than in CCS1 (CCS1:CCS3, 65.4 ± 4.0: 83.0 ± 5.8, 3/14:5/5, $p = 0.0048$, 0.031). CCS2 showed the highest mutation number, whereas *KRAS* and/or *BRAF* mutation number were higher in CCS3 than CCS1 (2/14 vs. 4/5, $p = 0.038$).
Conclusion: Early-stage SACs can be classified into 3 molecularly distinct subtypes with different clinicopathological and genetic characteristics.
Disclosure: Nothing to disclose

Reference

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P0412 MBD2 AND EZH2 REGULATE SFRP1 EXPRESSION WITHOUT AFFECTING ITS HYPERMETHYLATION IN COLORECTAL CANCER CELL LINE

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Introduction: The Secreted frizzled related proteins 1 (SFRP1) as extracellular inhibitors of Wnt signaling is downregulated by high frequency of promoter hypermethylation in the early stage of colorectal tumorigenesis. PCG proteins and MBD proteins important for gene epigenetic regulation have the ability to regulate gene expression. We aim to figure out the role of the specified PCG and MBD proteins in the regulation of SFRP1 gene expression.
Aims and Methods: The methylation status and mRNA expression of SFRP1 in CRC cell lines and human embryo intestinal mucosa cell CCC-HIE-2 are analyzed by Methylation-specific PCR (MSP) and real-time qPCR. The combination of PCG proteins, MBD proteins with SFRP1 gene is studied and the related proteins are screened by chromatin immunoprecipitation (ChIP). We knock down related genes by RNA interference to clear its role in the regulation of SFRP1 gene expression and the effect on proliferation of colorectal tumor cells.
Results: The promoter of SFRP1 was completely methylated in CRC cell lines, and partly methylated in normal cell line CCC-HIE-2. The mRNA expression level of SFRP1 was down-regulated significantly in CRC cell lines compared to CCC-HIE-2 ($p < 0.05$). SFRP1 promoter region was enriched with EZH2 in CCC-HIE-2 ($p < 0.05$) and it was enriched with EZH2 and MBD2 in SW480 ($p < 0.05$), but none of BMI1, EZH2 and MBD2 proteins bound to SFRP1 in HCT116 ($p > 0.05$). The expression of SFRP1 is reactivated by MBD2 siRNA ($p < 0.05$), but not by EZH2 siRNA in SW480 ($p > 0.05$). However, knockdown the MBD2 and EZH2 together can restore SFRP1 gene expression more effectively and inhibit the proliferation of SW480. All of those inhibitions cannot change the status of SFRP1 promoter methylation.
Conclusion: MBD2 and EZH2 regulate SRPF1 expression without affecting the hypermethylation of SFRP1 in colorectal cancer cell line, they may regulate the SFRP1 expression through other mechanisms system which need further research.
Disclosure: Nothing to disclose

P0413 IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS IN THE TUMOR MICROENVIRONMENT OF COLORECTAL CANCER

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Introduction: Cancer microenvironment, including tumor endothelial cells (TECs) and cancer associated fibroblasts (CAFs), plays an important role in the pathogenesis of cancer and is considered as a potential therapeutic target.
Aims and Methods: We aimed to understand the molecular mechanism of microenvironment of colorectal cancer (CRC) and to identify novel therapeutic targets. To this end, we isolated stromal cells in primary CRC and performed transcriptome analysis. Stromal cells and epithelial cells from surgically resected primary CRC ($n = 14$) and corresponding normal colonic tissues ($n = 14$) by using CD146 and EpCAM as markers. RNA sequencing (RNA-seq) was performed in 3 pairs of normal and tumor stromal cells. Expression of the gene was validated by quantitative RT-PCR (qRT-PCR) and immunohistochemistry. To analyze the gene function, human umbilical vein endothelial cells (HUVECs) and culturedCAFs were transfected with specific siRNAs after which cell viability assay and gene expression microarray were performed.
Results: RNA-seq analysis identified a series of 18 genes upregulated in tumor stromal cells isolated from primary CRC tissues. Through validating the results by qRT-PCR and immunohistochemistry, we identified AEBP1, as a novel candidate of CRC stroma-related gene. AEBP1 is expressed in TECs and CAFsin CRC tissues, and that the expression was higher in the invasive front. The Cancer Genome Atlas (TCGA) datasets revealed that higher expression of AEBP1 is associated with worse overall survival of CRC patients. Expression of AEBP1 was also upregulated in HUVECs treated with TCM obtained from CRC cell lines. Knockdown of AEBP1 in HUVECs suppressed *in vitro* tube formation. Knockdown of AEBP1 in HUVECs and CAFs suppressed cell proliferation and induced G1 cell cycle arrest. Microarray analysis revealed that knockdown of AEBP1 in HUVECs significantly affected the expression signature of angiogenesis-related genes including AQP1 and POSTN1. To confirm our findings *in vivo*, we co-transplanted CRC cells with HUVECs into nude mice. We found that knockdown of AEBP1 in HUVECs resulted in reduced micro vessel formations in the xenograft tissues. Moreover, we found that injection of siRNAs targeting mouse AEBP1 suppressed *in vivo* tumor growth.
Conclusion: Our results suggest that AEBP1 may play an important role in the microenvironment in CRC, and that it could be a potential therapeutic target.
Disclosure: Nothing to disclose

P0414 SYSTEMATIC REVIEW AND META-ANALYSIS: DIAGNOSTIC ACCURACY OF QUANTITATIVE FECAL IMMUNOCHEMICAL TESTS FOR COLORECTAL CANCER DETECTION IN SYMPTOMATIC PATIENTS

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Introduction: The quantitative fecal immunochemical test (FIT) is a non-invasive biomarker for the early detection of colorectal cancer (CRC). Recently, the National Institute for Health and Care Excellence (NICE) has recommended the adoption of FIT in primary care to guide referral for suspected colorectal cancer in people without rectal bleeding who have unexplained symptoms but do not meet the criteria for a suspected cancer pathway referral (1).
Aims and Methods: Our goal is to assess the diagnostic accuracy of FIT for CRC detection in symptomatic patients.
2 searchers independently reviewed online databases including MEDLINE, EMBASE expanding the search to bibliography and authors of relevant studies. All studies evaluating the diagnostic accuracy of quantitative FIT for CRC in symptomatic patients until May 2017 were included.
Studies were classified by FIT threshold, brand, percentage of symptoms and CRC prevalence. Quality of studies was evaluated, and global sensitivity and specificity were estimated in addition to the ROC curve (sROC) taking the area under the curve (AUC) as a global precision estimator in those subgroups formed by at least three studies, using a random effect model. Heterogeneity was determined by means of the Q statistic of Cochran. Threshold effect was examined by calculating Spearman's rank correlation.
Results: 13 studies were included in our review accumulating a sample of 12,584 patients (52% women). Data from 7 cohorts were obtained for patients scheduled consecutively to undergo elective colonoscopy due to several indications, with their CRC prevalence ranging from 0.4 to 7.1%. The remaining 6 were carried out on purely symptomatic patients with CRC prevalence ranging from 2.3 to 16.8%.
The pooled sensitivity for CRC detection of OC-Sensor® at the 0, 10 and 20 μg/g of feces was 98% (95% confidence interval CI 96–99%), 91% (95% CI 88–93%) and 90% (95% CI 87–93%), respectively. Conversely, pooled specificity at the same thresholds was 36% (95% CI, 34–37%), 80% (95% CI 79–81) and 83% (95% CI 83–84%). At the threshold with the best discriminatory ability (20 μg/g of feces) the AUC was 0.93 (95% CI, 0.91–0.96).
The number of available studies performed with the OC-Sensor® allowed for the conduct of a subgroup analysis based on the prevalence of CRC and the percentage of symptoms at the 10 μg/g cut-off. Pooled sensitivities were higher in the studies reporting a CRC prevalence ≥3% (92%, 95% CI; 89–94%) and in those performed only on a symptomatic population (94%, 95% CI, 91–97%); Conversely, the test's specificity in those subgroups was 70% (5% CI; 68–71%) and 66% (95% CI; 64–67%) respectively.
3 studies using OC-Sensor® with the same threshold identified 79% (95% CI; 76–81%) of patients with significative colonic lesions (SCL), with a 70% (95% CI; 68–72%) specificity, respectively.
Only 3 studies evaluated HM-Jack® at different thresholds. The AUC was 0.88 (95% CI, 0.77–0.98). There was substantial heterogeneity between studies specially in the pooled specificity estimates.
Conclusion: The quantitative FIT is highly sensitive for CRC detection in symptomatic patients. However, its global accuracy may depend on the prevalence of another SCL. Caution is recommended when using it to rule out CRC in this setting.
Disclosure: The work described in this abstract has been previously presented as an oral presentation at a spanish scientific meeting (Asociación Española de Gastroenterología) in Madrid in March 2018.

Reference

1. National Institute for Health and Care Excellence (NICE). Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care. Diagnostics guidance [DG30]. 2017.

P0415 ACCURACY OF QUANTITATIVE FECAL IMMUNOCHEMICAL TEST TO DETECT COLORECTAL CANCER. REAL-LIFE DATA IN 22,819 PATIENTS FROM THE GENERAL PRACTICE SETTING IN SPAIN

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Introduction: The quantitative immunochemical fecal occult blood test (FIT) has proved its worth on both CRC screening and in the timely assessment of patients with symptoms of lower bowel disease (1). However, its use in routine clinical practice remains unknown, as does its accuracy to detect CRC in this setting.

Aims and Methods: Our purpose is to describe the use of FIT in 2 Spanish regions and estimate its accuracy in real practice, in order to consider whether or not it is comparable to theoretical values.

Retrospective observational study with long-term follow-up. We included all subjects from the metropolitan area of San Sebastian (SS) and the province of Ourense (Ou) who had been performed a FIT determination (OC-Sensor®) requested at their primary care center between January 2009 and May 2015. CRC diagnosis was determined in the following 2 years using discharge information obtained from the national surveillance system for hospital data, Conjunto Mínimo Básico de Datos (CMBD), provided by the Ministry of Health. Global accuracy for detecting CRC was assessed by means of the receiver operating characteristics (ROC) curve and its area under the curve (AUC). Sensitivity and specificity were calculated using 10 and 20 μg/g feces as thresholds. Subgroup analysis were conducted using 10 μg/g cut-off to assess differences between center, age, sex and test indication (CRC screening / symptom evaluation).

Results: During the studied period, at least 1 FIT determination was requested to 22,819 patients (54.1% women). 5,265 people were from SS and 17,554 from Ou with significant differences with regard to age (SS = 60.4±16.3, Ou = 64.9±16.1; $p < 0.001$) and CRC prevalence (SS = 1.1%, Ou = 2.1%; $p < 0.001$). The reason for requesting the test was available for SS subjects (53.9% symptom evaluation). Overall, the AUC of FIT to detect CRC was 0.85 (CI 95% 0.84–0.87). Sensitivity and specificity at the 10 and 20 μg/g cut-offs were 91% (CI 95% 87.6–93.5) vs 88% (CI 95% 84.3–90.9) and 77.8% (CI 95% 77.2–78.4) vs 85.2% (CI 95% 84.7–85.8) respectively.

With regard to subgroup analysis, no differences were found in sensitivity between regions (SS 85.0, CI 95% 73.9–91.9, Ou 91%, CI 95% 87.6–93.5; $p = 0.15$), sex (men 90.5%, CI 95% 86.5–93.5, women 89.5% CI 95% 83.6–93.4; $p = 0.72$), age ('< 50y' 85.0%, CI 95% 64.0–94.8, '50–79y' 91.2%, CI 95% 87.3–94.0, '>79y' 88.7%, CI 95% 82.2–93.0; $p = 0.53$) or test indication (symptom evaluation 85.7%, CI 95%70.6–93.7, screening CRC 81.8%, CI 95% 61.5–92.7; $p = 0.70$).

Specificity was different between all analyzed subgroups except for test indication (SS 89.6%, CI 95% 88.8–90.4, Ou 77.8%, CI 95% 77.2–78.4; $p < 0.01$); (men 79.0%, CI 95% 78.2–79.8, women 81.9%, CI 95% 81.2–82.5; $p < 0.01$); ('< 50y' 87.6%, CI 95% 86.6–88.5, '50–79y' 80.5, CI 95% 79.9–81.2, '>79y' 71.7%, CI 95% 70.3–73.2; $p < 0.01$); (symptom evaluation 89.5%, CI 95% 88.3–90.6, CRC screening 89.7%, CI 95% 88.3–90.9; $p = 0.84$).

Conclusion: This analysis confirms the high diagnostic accuracy of FIT for the detection of CRC in routine clinical practice for both studied areas, no matter of age, sex nor the test indication.

Disclosure: The work described in this abstract has been previously presented as an oral presentation at a spanish scientific meeting (Asociación Española de Gastroenterología) in Madrid in March 2018.

Reference

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P0416 HIGH-QUALITY CLEANSING IMPROVES LESION DETECTION DURING COLONOSCOPY COMPARED TO ADEQUATE CLEANSING: POST HOC ANALYSIS OF 1170 CENTRAL-READER ASSESSED PATIENTS IN THREE RANDOMISED PHASE 3 TRIALS

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Introduction: Effective colonoscopy requires successful bowel preparation. 'Adequate' preparation allows detection of lesions >5mm and has been defined as a Boston Bowel Preparation Scale (BBPS) score of ≥2 per segment. This post hoc analysis determined the relationship between BBPS scores and adenoma and polyp detection rates in patients who had identical scores in each of the 3 colon segments, using pooled data from 3 identically designed Phase 3, multicentre, randomised trials.

Aims and Methods: Analysed patients had: treatment-blinded central reader assessed BBPS scores where the BBPS score was identical in each segment; and recorded polyp and adenoma counts. Patients were stratified to assess the relationship between low-quality cleansing (BBPS of 1+1+1), adequate cleansing (BBPS of 2+2+2) or high-quality cleansing (BBPS of 3+3+3), and ADR and PDR. A logistic regression (LR) model was fitted to assess whether ≥1 polyps and, separately, ≥1 adenomas, were detected including the BBPS score group and study as fixed effects.

Results: 1170 patients were analysed (Table 1). For low, adequate and high-quality cleansing, the PDRs were: 40.7%, 41.7%, 54.8%, and the ADRs were: 27.8%, 26.0% and 42.8%. The odds ratio (OR) for detection were significantly higher with high-quality versus adequate cleansing (PDR OR: 1.60, 95% confidence interval [CI] 1.14–2.24, $p = 0.0067$; ADR OR: 1.97, 95% CI 1.39–2.80, $p = 0.0001$). LR analysis revealed a significant correlation between BBPS score and PDR ($p = 0.0239$) and ADR ($p = 0.0006$).

Conclusion: In patients who had uniform low, adequate or high-quality cleansing in each respective colon segment, there was a strong correlation between higher cleansing scores and increased PDR and ADR.

[Table 1. PDR and ADR by uniform BBPS score]

Disclosure: Cesare Hassan was an investigator in the DAYB study and received honoraria from Norgine Ltd or investigator advisory board attendance; Jonathan Manning was an investigator in the MORA study and has received honoraria from Norgine Ltd. For investigator advisory board attendance and clinical conference attendance as a presenting author; Juha Halonen and Bharat Amlani are employees of Norgine Ltd; Michael Epstein was an investigator in the NOCT study and has acted as a safety advisor for Aspire Bariatrics, a consultant for Zx Pharma and IM HealthScience, as a speaker for Daichi Sankyo and Pfizer.

P0417 HIGHER HAREFIELD CLEANSING SCALE SCORES ARE ASSOCIATED WITH IMPROVED LESION DETECTION: POST HOC ANALYSIS OF THREE RANDOMISED AND CENTRAL READER-ASSESSED PHASE 3 CLINICAL TRIALS

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Introduction: Effective colonoscopy requires successful bowel cleansing. The bowel preparation NER1006 was assessed in 3 identically designed randomised phase 3 clinical trials. These trials used validated cleansing scales and treatment-blinded central readers for a standardised cleansing quality assessment. This post hoc analysis assessed the relationship between colon cleansing quality using the Harefield Cleansing Scale (HCS), and overall colon detection rates for adenomas (ADR) and polyps (PDR).

Abstract No: P0416

Overall colon lesion detection rates	High-Quality (N = 166)	Adequate (N = 950)	Low-Quality (N = 54)	Odds ratio High-Quality: Adequate (95% CI) [P-value]	Odds ratio Adequate: Low-Quality (95% CI) [P-value]
PDR, n (%)	91 (54.8)	396 (41.7)	22 (40.7)	1.60 (1.14–2.24) [0.0067]	0.90 (0.50–1.60) [0.7104]
ADR, n (%)	71 (42.8)	247 (26.0)	15 (27.8)	1.97 (1.39–2.80) [0.0001]	0.75 (0.39–1.43) [0.3829]
LR Analysis of Association between Uniform BBPS Score Group and PDR, P-value	0.0239				
LR Analysis of Association between Uniform BBPS Score Group and ADR, P-value	0.0006				

Abstract No: P0417: Table 1. Uniform segmental HCS scores vs lesion detection rates

	0/0/0/0/0 N = 4	1/1/1/1/1 N = 10	2/2/2/2/2 N = 379	3/3/3/3/3 N = 37	4/4/4/4/4 N = 39
ADR, n (%)	0	1 (10.0)	97 (25.6)	12 (32.4)	21 (53.8)
PDR, n (%)	0	3 (30.0)	164 (43.3)	19 (51.4)	24 (61.5)
Logistic regression analysis of the trend for uniform HCS scores vs ADR: Odds ratio (95% CI) [P-value]	1.61 (1.182–2.199) [0.0026]				
Logistic regression analysis of the trend for uniform HCS scores vs PDR: Odds ratio (95% CI) [P-value]	1.38 (1.021–1.863) [0.0361]				

Aims and Methods: Patients aged 18–85 years were included if they had fully reported HCS scores, adenoma and polyp counts, and also identical segmental HCS scores (range 0–4) in all 5 HCS colon segments. A logistic regression analysis examined the odds ratio (OR), 95% confidence interval (CI) and p-value (p) for the resulting trend in lesion detection, when segmental HCS scores increased incrementally from 0 to 4.
Results: 469 patients were included in this analysis (Table 1). When uniform segmental HCS scores were increased from 0, 1, 2, 3, and 4, the resulting ADRs increased continuously (0%, 10.0%, 25.6%, 32.4% and 53.8%) as did the PDRs (0%, 30%, 43.3%, 51.4%, and 61.5%). The corresponding OR (CI) and [P] were, for ADR 1.61 (1.182–2.199) [0.0026], and for PDR 1.38 (1.021–1.863) [0.0361].
Conclusion: ADR and PDR increased continuously with improved colon cleansing quality. There was a strong association between uniform segmental HCS scores and both ADR and PDR.
Disclosure: Jonathan Manning was an investigator in the MORA study and has received honoraria from Norgine Ltd. for investigator advisory board attendance and clinical conference attendance as a presenting author; Cesare Hassan was an investigator in the DAYB study and received honoraria from Norgine Ltd. For investigator advisory board attendance; Juha Halonen and Bharat Amlani are employees of Norgine Ltd; Michael Epstein was an investigator in the NOCT study and has acted as a safety advisor for Aspire Bariatrics, a consultant for Zx Pharma and IM HealthScience, as a speaker for Daichi Sankyo and Pfizer.

P0418 RAID-CRC: A NOVEL NON-INVASIVE TOOL FOR COLORECTAL CANCER SCREENING BASED ON BACTERIAL SIGNATURES CAPABLE OF REDUCING THE FAECAL IMMUNOCHEMICAL TEST FALSE-POSITIVE RESULTS

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Introduction: Colorectal cancer (CRC) is the third main cause of cancer mortality. Around 75% of CRC are sporadic and they usually develop without symptomatology. Therefore, some countries are implementing CRC national screening politics in order to detect lesions at an early stage by using non-invasive tools. One of the most common tools is the faecal immunochemical test (FIT). Despite affordability, FIT shows a low sensitivity for precancerous lesions (29%) and a low positive predictive value (8%), which produces a high rate of false positive results. Hence, CRC-screening organizations are demanding new, non-invasive tools, capable of decreasing false positive rates, thus reducing the number of unnecessary colonoscopies. The aim of this study was to develop a new, non-invasive CRC screening tool based on bacterial faecal markers, which in combination with FIT (hereby named RAID-CRC), could reduce the false-positive rate.
Aims and Methods: We performed the FIT analysis (OC-Sensor® Kit) and the bacterial markers analysis (CRC1-CRC10) in stool samples from individuals with normal colonoscopy (167), non-advanced adenomas (88), advanced adenomas (30) and CRC (48). All participants showed CRC-associated symptoms. The RAID-CRC algorithm was designed using machine learning technology.
Results: Performance of FIT for advanced neoplasia (i.e. advanced adenoma and CRC) was determined by using the cut-off value established in Catalonia (OC-Sensor®, 20 μg Haemoglobin/g of faeces) for a population-based screening approach. Sensitivity and specificity values of 83% and 80%, respectively, and positive and negative predictive values of 56% and 94%, respectively, were obtained. When RAID-CRC was used, the corresponding values were 80% and 90% for sensitivity and specificity, respectively, and 70% and 94% for positive and negative predictive values, respectively, resulting in a 50% reduction of the false-positive rate.
Conclusion: RAID-CRC is a promising tool for CRC screening because of its non-invasiveness, its low cost and its capacity for lowering the number of false-positive results associated with the use of FIT. Therefore, RAID-CRC use would lead to a reduction up to 30% of unnecessary colonoscopies and their derived costs. However, since our study was performed in symptomatic individuals, this new approach warrants to be validated in a screening scenario.
Disclosure: Prof. Garcia-Gil, Dr. Aldeguer, Dr. Serra-Pagès, Dr. Serrano, Dr. Ramió-Pujol, Mr. Amoedo, Ms. Oliver are employees from GoodGut, company who has received private and public funding. The rest of the authors have nothing to disclose.

P0419 CLINICAL AND PATHOLOGICAL OVERLAP AMONG THE HAMARTOMATOUS POLYPOSIS SYNDROMES CAN RESULT IN ERRONEOUS DIAGNOSIS

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Introduction: Hamartomatous polyposis-syndromes (HPS) are a group of rare autosomal-dominant syndromes, associated with hamartomatous polyps and gastrointestinal (GI) tract malignancies, including- Juvenile polyposis (JPS), Peutz-Jeghers syndrome (PJS) and Cowden disease (CD). There is a known clinical and histological overlap between syndromes. Appropriate diagnosis dictates cancer preventing surveillance for the proband and family carriers. Yet, more than 50% of clinically diagnosed cases have no genetic diagnosis.
Aims and Methods: We aimed to describe phenotype, genotype, histology and outcomes of individuals/families with HPS, study overlap between syndromes and erroneous diagnosis according to genetic findings.
Retrospective cohort-study of consecutive HPS patients. Demographic, clinico-pathological and genetic data were obtained from computerized-medical-records.
Results: 52 individuals from 34 families were included. Phenotypic, oncologic and genetic findings of the 3 syndromes are described in Table 1.
Clinical manifestations included mainly rectal bleeding (40% JPS, 23% PJS, 25% CD) and bowel obstruction (46.15% PJS, 11.4% JPS). Pathological report varied widely, with 75% of JPS, 61% of PJS and 50% of CD having a polyp diagnosis different from the syndrome hallmark, with some patients having up to 6 different types of polyps. Overall 22/52 (42.3%) of patients had a histological diagnosis of adenoma during follow up (48.5% of JPS, 38.4% of PJS and 25% of CD). 4 patients had an initial incorrect diagnosis, with subsequent review of pathology and genetic testing unveiling the correct syndrome. Gastrointestinal cancer history was positive in 65%, 40% and 50% of JPS, PJS and CD families, respectively. 5 patients developed cancers (2 gastrointestinal, 1 thyroid, 1 breast and 1 with both breast cancer and liposarcoma of the chest). 18 (34.6%) patients tested positive for mutations in either STK11, PTEN, SMAD4 or BMPR1A. 2 additional patients were found to harbour novel gene mutations in AKT1 and TM7SF3. Sanger sequencing had a positive detection rate of 45.4% while next generation sequencing (NGS) had a 100% detection rate.
Conclusion: HPS present versatile phenotypes with apparent redundancy in histological diagnosis, requiring pathology review. Cancer rates are low at this cohort, potentially due to the young mean age. The NGS era should shed light on further candidate-genes and genetic alterations in order to better understand cancer related mechanisms and prevent malignancy.
Disclosure: Nothing to disclose

P0420 ERCC6L PROMOTES CELL GROWTH AND INVASION IN HUMAN COLORECTAL CANCER

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Introduction: Excision repair cross-complementation group 6 like (ERCC6L), a newly discovered DNA helicase, has been discoverd highly expressed in diverse human cancers. However, the precise role of ERCC6L in colorectal cancer (CRC) remains unclear.
Aims and Methods: This study aimed to explore the potential role of ERCC6L in the development and progression of CRC. Real-time quantitative polymerase chain reaction (qRT-PCR) and western blot were used to detect the expression of ERCC6L in 30 colorectal cancer patients. 9 pairs of CRC tissues were examed

Abstract No: P0420: Table 1. Phenotypic, oncologic and genetic findings of HPS carriers

	JPS	PJS	CD	Total
Number of families	20	10	4	34
Number of patients	35	13	4	52
Mean age at diagnosis	23.9	24.6	42.6	25.3
Main polyp location	Colon and rectum	Small intestine	Stomach, small intestine and colon	
Cumulative polyp number - dozens	15 (42.8%)	7 (53.8%)	2 (50%)	25 (46.1%)
Cumulative polyp number - hundreds	3 (8.5%)	2 (15.3%)	0	5 (9.6%)
Patients with max polyp size <1 cm	8 (22.8%)	1 (7.69%)	2 (50%)	11 (21.1%)
Patients with max polyp size >4 cm	8 (22.8%)	4 (30.7%)	0	12 (23.07%)
Mutations found (no. of patients/families)	11/7	6/4	3/3	20/14

by immunohistochemistry. The function of ERCC6L in cell proliferation, cycle, apoptosis, invasion and colony-forming ability was examined in CRC cell lines.
Results: ERCC6L was highly expressed in CRC tissues and CRC cell lines. The expression of ERCC6L was related to tumor size, but not to other clinical features such as age, gender, differentiation and clinical stage. we found that silencing of ERCC6L by small interfering RNA (siRNA) remarkably inhibited the proliferation rate and colony-forming ability of CRC cell lines. Flow cytometry analysis shown that knockdown of ERCC6L in CRC cells blocked the cell cycle progression and more cells were delayed in G0/G1 phase without affecting apoptosis. Moreover, knockdown of ERCC6L remarkably decreased the invaded number of CRC cells compared with the cells treated with negative control.
Conclusion: Our results suggest that ERCC6L can stimulate cancer cell proliferation by promoting cell cycle progression, and it may be a potential target for cancer therapy.
Disclosure: Nothing to disclose

P0421 TARGETED UPLC-MS METABOLOMIC ANALYSIS OF HUMAN FAECES REVEALS NOVEL LOW-INVASIVE CANDIDATE MARKERS FOR COLORECTAL CANCER

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Introduction: A simple, low invasive test with high sensitivity for both colorectal cancer and advanced precancerous lesions might increase uptake and adherence rates, which could improve clinical outcomes. Thanks to the technological advances, these days metabolomics technology offers a powerful tool for biomarker discovery.
Aims and Methods: In this study we have performed a targeted ultra-performance liquid chromatography/time-of-flight mass spectrometry (UPLC-(TOF) MS)-based metabolomics approach to identify faecal biomarkers for the detection of patients with advanced neoplasia. A cohort of 80 patients with advanced neoplasia (40 advanced adenomas and 40 cancers) and 49 healthy subjects were analyzed in the study. We evaluated the faecal levels of 105 metabolites including glycerolipids, glycerophospholipids, sterol lipids and sphingolipids.
Results: We found a panel of 18 metabolites that were significantly altered in patients with advanced neoplasia compared to healthy controls. Combinations of seven of these metabolites including ChoE(18:1), ChoE(18:2), ChoE(20:4), PE (16:0/18:1), SM(d18:1/23:0), SM(42:3) and TG(54:1) were employed to construct a predictive model that provide an area under the curve (AUC) value of 0.821. Furthermore, the levels of the cholesteryl esters correlated positively with the faecal haemoglobin concentration and its inclusion in the metabolomics signature improved the predictive model to an AUC of 0.885.
Conclusion: Faecal levels of ChoE(18:1), ChoE(18:2), ChoE(20:4), PE (16:0/18:1), SM(d18:1/23:0), SM(42:3) and TG(54:1) discriminated advanced neoplasia patients from healthy controls. Our data highlight the potential clinical use of these molecular signatures for low invasive screening of patients with colorectal neoplasia.
Disclosure: Nothing to disclose

P0422 CLINICOPATHOLOGICAL STUDY OF SERRATED LESIONS OF THE COLORECTUM

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Introduction: Serrated lesions of the colorectum are the precursors of microsatellite unstable carcinomas. However, their clinical and pathologic features are still unclear and need further exploration.
Aims and Methods: The aims of this study was to clarify the clinicopathological features of colorectal serrated lesions. We reviewed clinical charts and pathology files of 6243 endoscopically resected specimens performed during January 2007 and December 2017 in our hospital. A total of 559 serrated lesions (9.0%) resected were classified into 3 categories: HP (hyperplastic polyp), SSA/P (sessile serrated adenomas/ polyps), and TSA (traditional serrated adenoma), according to the WHO criteria. We examined the features of these cases and evaluate the morphologic characteristics by using immunochemical staining for Ki-67 and the expression of MUCs (MUC2, MUC5AC and MUC6) in differentiating serrated lesions.
Results: Of these 559 lesions, a total of 291 (52.0%) were HP, 137 (24.5%) SSA/P, and 131 (23.5%) TSA. Male to female ratio (M/F) was 2.36 for HP, 0.98 for SSA/P, and 2.18 for TSA. Mean size of SSA/Ps (13.3mm) and TSAs (10.5mm) were significantly larger than that of HP (8.1mm) ($p < 0.005$, respectively). SSA/Ps were located predominantly in the proximal colon, whereas HP and TSA were mainly located in the sigmoid colon and rectum. 82% of SSA/Ps were flat in macroscopic appearance. SSA/Ps and HPs were whitish or almost the same as adjacent mucosa in color, whereas TSAs had a tendency to be reddish. Magnified colonoscopy showed Type II open pit pattern as characteristic of SSA/Ps, whereas pinecone-shaped pit pattern as that of TSAs. Incidences of concomitant carcinomas in HP, SSA/P, and TSA were 0% (0 out of 291), 2.9% (4 out of 137), and 3.8% (5 out of 131), respectively. Ki-67 positive cells in HP showed regular, symmetric distribution, and those in SSA/P did irregular asymmetrical pattern, whereas most of those cells in TSA distributed in the so-called ectopic crypts. Expression levels of MUC2, MUC5AC and MUC6 were significantly different between serrated lesions, SSA/Ps and HPs were positive for MUC5AC in comparison with TSAs.
Conclusion: Our studies showed the 3 types of serrated lesions have their own distinct features and could be helpful to distinguish between them. SSA/P and TSA are premalignant lesions of colorectum and we should detect these lesions and completely remove endoscopically.
Disclosure: Nothing to disclose

P0423 PEDUNCULATED MORPHOLOGY IS AN INDEPENDENT RISK FACTOR FOR A FAVORABLE ONCOLOGIC OUTCOME IN PATIENTS WITH T1 COLORECTAL CANCER

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Introduction: Large-scale comparison studies of pedunculated versus non-pedunculated T1 colorectal cancer (CRC) have not been performed and current risk stratification for adverse events such as lymph node metastasis is based on histology only.
Aims and Methods: We aimed to compare adverse oncologic outcomes of pedunculated versus non-pedunculated T1 CRCs. Patients diagnosed with T1 CRC between 2000 and 2014 in 14 Dutch hospitals were included. We evaluated the association between morphology and the primary composite endpoint adverse oncologic outcome adjusted for clinical variables, histological variables and treatment approach. Adverse oncologic outcome was defined as lymph node metastasis, distant metastasis, local recurrence or residual tissue. Secondary endpoints were metastasis, recurrence and incomplete resection.
Results: In total, 1,656 patients with T1 CRC with a median follow-up time of 42.5 months (IQR 18.5-77.5) were included. Adverse oncologic outcomes were observed in 9.3% (67/723) of pedunculated T1 CRCs vs 16.6% (155/933) of non-pedunculated T1 CRCs. Pedunculated morphology was independently associated with a decreased risk for adverse oncologic outcomes (adjusted OR 0.61; 95% CI 0.43–0.86; $p = 0.005$). Metastasis, incomplete resection and recurrence were observed in 8.5%, 6.5% and 5.4% of patients, respectively. Pedunculated morphology was also independently associated with a reduced risk for metastasis (adjusted OR 0.62; 95% CI 0.41–0.95; $p = 0.03$), incomplete resection (adjusted OR 0.60; 95% CI 0.38–0.98, $p = 0.03$) and recurrence (adjusted HR 0.51; 95% CI 0.32–0.84; $p = 0.007$).
Conclusion: Pedunculated morphology is independently associated with a better oncologic outcome in patients with T1 CRC. Incorporating morphology in future risk assessment is therefore likely to refine risk prediction in T1 CRC, thereby improving patient selection for surgery.
Disclosure: Nothing to disclose

P0424 LONG-TERM ONCOLOGIC OUTCOMES OF SELF-EXPANDING METALLIC STENTS AS A BRIDGE TO SURGERY IN MALIGNANT LEFT-SIDED COLON OBSTRUCTION COMPARED WITH EMERGENCY SURGERY

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Introduction: Self-expandable metallic stents (SEMS) are used as a bridge to surgery in malignant left-sided large bowel obstruction (MLLO). However, the oncologic outcome after endoscopic stenting remains to be assessed.
Aims and Methods: The aim of this study is to compare the oncologic outcomes of SEMS with those of emergency surgery for MLLO. A database of MLLO between January 2001 and December 2012 were reviewed. They were divided into those who underwent bridge-to-surgery with SEMS and those who underwent emergency surgery (ES). The 2 groups were compared in terms of disease-free survival (DFS) and overall survival (OS).
Results: 93 patients underwent SEMS and 41 patients underwent ES. Clinicopathological features did not differ significantly between the SEMS and ES groups. 28 (30.1%) patients suffered recurrence in SEMS group and 14 (34.1%) patients suffered recurrence in ES group. There were no differences in 5-year DFS (67.6%vs. 64.6%; $p = 0.761$) and OS rates (71.0% vs. 64.9%; $p = 0.554$) between the 2 groups.
Conclusion: The SEMS as a bridge to surgery is equivalent to emergency surgery for MLLO with regards to oncologic safety.
Disclosure: Nothing to disclose

P0425 HIGH PRETREATMENT PLASMA D-DIMER LEVELS ARE ASSOCIATED WITH POOR SURVIVAL AFTER CURATIVE RESECTION IN PATIENTS WITH COLON CANCER

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Introduction: Coagulation pathways are activated in patients with malignancies. Previous studies showed association between coagulation parameters (platelet count and plasma fibrinogen levels) and poor prognosis in patients with colon cancer. D-dimer is a stable end product of fibrin degradation. Here we investigated the association of the pretreatment plasma D-dimer levels and clinical characteristics or pathological features in patients with colon cancer.
Aims and Methods: We evaluated the medical records of 378 patients who underwent curative resection for colorectal cancer in our institution from 2013 to 2015. Information about all clinical parameters, complete follow-up, and pretreatment plasma D-dimer measurements was available for 207 patients. The normal cut-off level of 1.0 mg/L was used for distinguishing the negative from the positive D-dimer results. We retrospectively investigated the association between preoperative plasma D-dimer levels on clinicopathologic parameters and the 3-year overall survival (OS) rate in patients after curative resection of colorectal cancer.
Results: High preoperative plasma D-dimer levels were positively correlated with age at surgery and tumor depth. There were no statistically significant differences between the D-dimer normal group and D-dimer high group in terms of sex, tumor location (left colon or right colon), and histologic grade. A univariate 3-year survival analysis showed that lymph node metastasis (N factor) and high preoperative D-dimer levels were independent prognostic factors. The multivariate survival analysis using Cox regression model showed that the preoperative plasma D-dimer level was an independent prognostic factor with an odds ratio [95% confidence interval] of 4.04 (1.24–15.5). In stage III colon cancer, high pretreatment D-dimer levels were associated with a poor 3-year OS rate.
Conclusion: Elevated pretreatment plasma D-dimer levels in patients with colon cancer are associated with lower OS; patients with stage III colon cancer with high pretreatment D-dimer levels showed extremely poor OS. Preoperative D-dimer levels may be useful as a predictor of survival after curative surgery in patients with colon cancer.
Disclosure: Nothing to disclose

P0426 ARE ADDITIONAL TREATMENTS REALLY NEEDED AFTER ENDOSCOPIC RESECTION FOR RECTAL SMALL NEUROENDOCRINE TUMORS?

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Introduction: Little is known about the long-term outcomes of endoscopically resected rectal neuroendocrine tumors (NETs).
Aims and Methods: The present study aimed to investigate treatment strategies determining additional treatment after endoscopic resection (ER) of rectal NETs and long-term outcomes of endoscopically resected rectal NETs. We analyzed medical records of patients who underwent ER for rectal NETs from January 2005 to December 2016. The clinicopathological characteristics of these lesions were analyzed and long-term outcomes were evaluated.
Results: A total of 322 patients were studied. The complete and curative resection rate were 76.4% and 55.9%, respectively. Rectal NETs initially resected as polyps and treated with conventional EMR were observed more frequently in the non-curative group ($p = 0.041$ and $p = 0.012$, respectively). After ER, only 44 of the 142 patients (31.0%) who did not meet the criteria for curative resection received additional salvage treatment. In multivariate analysis, lesions diagnosed via biopsies (OR, 0.096; $p = 0.002$) or suspected as NETs initially (OR, 0.04; $p = 0.001$) were less likely to undergo additional treatment. Positive lymphovascular invasion (OR 61.971; $p < 0.001$), positive (OR 75.993; $p < 0.001$), or indeterminate (OR 13.203; $p = 0.001$) resection margins were more likely to undergo additional treatment. Although lymph node metastasis was found in 6 patients, none experienced local or metastatic tumor recurrence during the median follow-up of 40.49 months.
Conclusion: Long-term outcomes after ER for rectal NETs were excellent. The prognosis showed favorable outcomes regardless of whether patients receive additional salvage treatments.
Disclosure: Nothing to disclose

P0427 IMPACT OF PRIMARY TUMOR LOCATION AS A PREDICTIVE FACTOR IN CYTOTOXIC ANTI-CANCER AGENT FOR COLORECTAL CANCER (CRC) BASED ON COLLAGEN GEL DROPLET-EMBEDDED DRUG SENSITIVITY TEST (CD-DST)

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Introduction: We have reported the usefulness of CD-DST for the individualization of first-line treatment in CRC (UEGW: 2014; P1538, 2015; P1681, 2016; P0929, 2017; P0466).
In recent years, primary tumor location in CRC as a predictive factor has attracted attention. Several reports have recently addressed the predictive impact of primary tumor location in CRC. A better outcome for left-sided colon cancer (CC) compared with right-sided CC has been reported. However, in those reports, the chemotherapy regimens always included molecularly-targeted agents. To the best of our knowledge, the impact of primary tumor location as a predictive factor in cytotoxic anti-cancer agent alone (FOLFOX/FOLFIRI without molecularly-targeted agents) remains to be explained.
Aims and Methods: The purpose of this study was to clarify the impact of primary tumor location as a predictive factor in cytotoxic anti-cancer agent using CD-DST. Between Mar. 2008 and Apr. 2017, we obtained tumor specimens from 133 CRC patients (CC; n:87, Rectal Cancer; n:46) without preoperative chemotherapy. Written informed consent for measurement of individual chemosensitivity was obtained from all patients. Approval for the present study was obtained from the Tobu Chiiki Hospital Institutional Review Board (No: 02.03.29. #1).

CD-DST was performed and the growth inhibition rate (IR) was determined by incubation for 24 h with 5-FU and l-OHP (6.0 and 3.0 μg/ml, respectively) and 5-FU and SN-38 (6.0 and 0.2 μg/ml, respectively). The IR values under each condition and the relationship between the tumor side and the IR values were evaluated using linear regression analysis and the t-test, respectively. Cancers proximal or distal of the splenic flexure were classified as right-side or left-side, respectively.

Results: There was a strong correlation between the IRs (%) of the FOLFOX and FOLFIRI regimens ($y = 0.88x+14.98$, $R^2 = 0.74$) using linear regression analysis. The median of the IRs (%) with the FOLFOX and FOLFIRI regimen were 58.2 and 66.2, respectively.

Among all patients, there was no significant difference in the IRs (%) of the FOLFOX and FOLFIRI regimens for right-sided vs left-sided tumors. In the FOLFOX regimen, the IRs (%) of right-sided and left-sided tumors were 57.4 ± 2.5 and 58.5 ± 1.8, respectively ($p = 0.72$). In the FOLFIRI regimen, the IRs (%) of right-sided and left-sided tumors were 67.0 ± 2.3 and 65.8 ± 1.9, respectively ($p = 0.69$).

Moreover, in 87 CC patients, there was also no significant difference in the IRs (%) of the FOLFOX and FOLFIRI regimens for right-sided vs left-sided tumors. In the FOLFOX regimen, the IRs (%) of right-sided and left-sided tumors were 57.4 ± 2.5 and 61.6 ± 2.4, respectively ($p = 0.23$). In the FOLFIRI regimen, the IRs (%) of right-sided and left-sided tumors were 67.0 ± 2.3 and 69.1 ± 2.4, respectively ($p = 0.53$).

Of the133 patients, 42 patients received palliative chemotherapy after surgery. From the 42 patients, the same results were also obtained.

Conclusion: In this study, there was no impact of primary tumor location in cytotoxic anti-cancer agent regimens for CRC. In contrast, as previously reported, a better outcome for left-sided CC compared with right-sided CC depended on molecular tumor biology, especially when using molecularly-targeted agent regimens.

As such, our findings underscore the fact that molecularly-targeted agents rather than cytotoxic anti-cancer agents may result in a better outcome for left-sided tumors.

Disclosure: Nothing to disclose

P0428 RANDOMIZED COMPARISON OF SURVEILLANCE AFTER COLONOSCOPIC REMOVAL OF ADENOMATOUS POLYPS: ENDOCUFF-ASSISTED COLONOSCOPY VERSUS THE STANDARD COLONOSCOPY

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Introduction: Endocuff-assisted colonoscopy (EAC) not only enabled a higher adenoma detection rate (ADR), but also increased the mean number of adenomas detected per patient (MAP)[1)]. According to the National Polyp Study (NPS)[2)], an interval of at least 3 years is recommended before follow-up examination after colonoscopic removal of newly diagnosed adenomatous polyps. However, only few reports have described follow-up surveillance for patients who underwent EAC and complete endoscopic removal of all adenomas.

Aims and Methods: The aim of this study was to compare the performance of EAC and standard colonoscopy (SC) as surveillance colonoscopy techniques after complete adenoma removal during EAC. For this study, 134 patients who underwent total EAC and removal of all adenomas between March and September 2014 were enrolled, and they prospectively underwent follow-up colonoscopy at 3 years in accordance with the recommendation of the NPS. They were randomly assigned to undergo follow-up EAC ($n = 66$) and SC ($n = 67$). The primary end point was the detection of index lesions (defined as those ≥10 mm in diameter and/or with villous component of >20%, and/or high-grade adenoma or invasive cancer). The secondary end point was the detection of any adenoma.

Results: The detection rates of index lesions were 3.0% (2/66) in EAC and 3.0% (2/67) in SC. There was no significant difference found between the two in both groups. The polyp detection rates and ADRs were higher in the patients who underwent EAC than in those who underwent SC, but these differences were not statistically significant (60.6% vs. 47.8% [$p = 0.14$] and 57.6% vs. 44.8% [$p = 0.14$]). The mean number of polyps detected per patient and MAP were also higher in the patients who underwent EAC, but these differences were not statistically significant (1.21 ± 1.45 vs. 0.85 ± 1.15 [$p = 0.15$] and 1.06 ± 1.30 vs. 0.82 ± 1.06 [$p = 0.31$]). There was no adenocarcinoma in both groups. No significant differences were found in detected polyp size, morphology, and distribution were found in between the both groups. No major complication occurred.

Conclusion: Both EAC and SC detected adenomas with advanced pathological features and adenomas in equal proportions in when they were used for follow-up surveillance after 3 years for patients who underwent EAC and were complete adenoma removaled all adenomas detected adenomas with advanced pathological features and adenomas in equal proportion. Further studies are required to confirm the current present results.

Disclosure: Nothing to disclose

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P0429 INCOMPLETE RESECTION IS A MAJOR CAUSE OF POST-COLONOSCOPY COLORECTAL CANCER AFTER RESECTION OF A POLYP WITH INTRAMUCOSAL CARCINOMA

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Introduction: We aimed to determine the cause of and risk factors for post-colonoscopy colorectal cancer (pcCRC) in patients who underwent endoscopic resection of a polyp with intramucosal carcinoma (IMC).

Aims and Methods: Patients diagnosed with IMC in the period 1995–2005 were selected from the Netherlands Cancer Registry (NCR). Patients with a surgical resection of intramucosal carcinoma or hereditary CRC were excluded. pcCRC was defined as CRC diagnosed between 6 and 60 months after endoscopic resection of IMC. Additional data were collected in 31 hospitals from all pcCRC cases and a sample of 367 controls. Multivariate logistic regression analysis was performed to identify risk factors for pcCRC.

Results: Among 1,979 patients who underwent endoscopic resection of IMC, 48 (2.4%) were diagnosed with a pcCRC according to the NCR. Manual review of the available medical records confirmed pcCRC diagnosis in 27 patients, discarded pcCRC diagnosis in 9 patients and identified 2 additional pcCRC cases among a sample of controls. Of these 29 pcCRC patients, 14 (48%) were attributed to an incomplete endoscopic resection, 9 (31%) to inadequate colonoscopy, 4 (14%) to a missed lesion and 2 (7%) were new CRCs. Recurrence of IMC (OR 10.65 95% CI 4.48–25.30; $p < 0.01$) and a personal history of CRC (OR 5.82 95% CI 1.23- 27.45; $p = 0.03$) were independent risk factors for pcCRC.

Conclusion: The majority of pcCRCs after endoscopic resection of polyps with IMC can be attributed to incomplete resections, with recurrence of IMC and personal history of CRC as most important risk factors. This suggests that en-bloc resection of polyps suspected to contain IMC is justified to limit the risk of invasive recurrence.

Disclosure: Nothing to disclose

P0430 A COMPARATIVE STUDY BETWEEN COLORECTAL NEOPLASMS DETECTED AT THE INITIAL COLONOSCOPY AND THOSE DETECTED AT THE FOLLOW-UP COLONOSCOPIES

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Introduction: Initial colonoscopies for screening or diagnostic colonoscopy and follow-up colonocopies for surveillance were frequently performed in the daily practice. There have been few studies regarding the clinicopathological comparison between colorectal neoplasms detected at first-time colonoscopy and those detected at subsequent colonoscopies. We tried to compare the characteristics of colorectal neoplasms detected at initial and follow-up colonoscopies.

Aims and Methods: A total of 3345 patients (group A) were included in this study who underwent an initial colonoscopy (1232 asymptomatic patients for first screening, 1173 for positive fecal occult blood test of first round, and 940 symptomatic patients for diagnostic colonoscopy). Another total of 2092 patients (group B) were also included who underwent follow-up colonoscopies for surveillance (1014 with no polyps or diminutive polyps at baseline, 690 with adenoma and/or intramucosal cancer resected at baseline, and 388 with invasive cancer resected at baseline). Detected colorectal neoplasms more than 5mm in size between group A and B were compared with each other regarding their prevalences and the characteristics.

Results: The prevalences of patients with low-grade adenoma, those with high-grade adenoma or intramucosal cancer, and those with invasive cancer between group A and B were 14.0% (467/3345) and 17.0% (355/2092), 4.5% (152/3345) and 5.0% (104/2092), and 5.6% (187/3345) and 1.3% (28/2092), respectively. The prevalence of patients with invasive cancer was significantly lower in group B than that in group A ($p < 0.0001$), although the prevalence of those with low-grade adenoma was significantly higher in group B than that in group A ($p < 0.005$). There was no difference of the prevalence of patients with high-grade adenoma or intramucosal cancer between group A and B. 793 and 952 low-grade adenomas, and 184 and 116 high-grade adenomas or intramucosal cancers were detected in group A and B, and total of 977 and 1068 mucosal lesions between group A and B were compared with each other. The prevalences of the lesions between group A and B with regard to the clinicopathological factors were as follows. The locations of the lesions were in the right colon 40.4%, 52.6%, left colon and lectum 59.6%, 47.4%, the numbers of the lesions were single or double 83.5%, 59.0%, triple or more 16.5%, 41.0%, the sizes of the lesions were less than 10mm 63.5%, 82.2%, 10mm or more than 10mm 36.5%, 17.8%, the configulations of the lesions were polypoid 87.2%, 83.7%, non-polypoid 12.8%, 16.3%, and the histologies of the lesions were low-grade adenoma 81.2%, 89.1%, high-grade adenoma or intramucosal cancer 18.8%,

10.9%, respectively. The lesions detected in group A were characterized by their left-sided location ($p < 0.0001$), no multiplicity ($p < 0.0001$), larger size ($p < 0.0001$), polypoid appearance ($p < 0.05$), and more-advanced histology ($p < 0.0001$). In contrast the lesions detected in group B were characterized by their right-sided location, multiplicity, smaller size, non-polypoid appearance, and less-advanced histology.

Conclusion: The prevalence of patients with invasive cancer was significantly lower in those at follow-up colonoscopies than those at initial colonoscopy. In contrast the prevalence of patients with low-grade adenoma was significantly higher in those at follow-up colonoscopies than those at initial colonoscopy. Adenomas and intramucosal cancers detected between an initial and follow-up colonoscopies disclosed clearly different characters as to the location, number, size, configulation, and histology.

Disclosure: Nothing to disclose

P0431 RAID-LS: A NON-INVASIVE TOOL BASED ON A FAECAL BACTERIAL SIGNATURE FOR LYNCH SYNDROME SURVEILLANCE

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Introduction: Lynch syndrome carriers' surveillance is performed through endoscopic examinations and with intervals of no more than 2 years. Colonoscopy allows direct visualization of the entire colon but requires bowel preparation, sedation, there is risk of intestinal perforation, it is time consuming and it has high associated costs. These are some of the reasons for which there is low surveillance acceptance among patients.

Aims and Methods: The aims of this work were to compare a specific faecal bacterial signature of sporadic colorectal cancer patients (CRC) and inflammatory bowel disease patients (IBD) with Lynch carriers and develop a non-invasive tool, hereby named RAID-LS, based on these bacterial signatures, which enabled the detection of neoplasia in Lynch population.

A cohort consisting of 66 Lynch syndrome carriers who underwent a surveillance colonoscopy were recruited. A second cohort consisting of 301 control individuals was recruited through the regional CRC screening program or for presenting CRC compatible symptomatology. We performed the analysis of 9 CRC-specific bacterial markers (CRC1, 2, 3, 4, 5, 6, 7, 9, 10) and 4 associated to IBD (IBD1, 2, 3, 4) in stool samples. The RAID-LS was eventually defined using 3 of the analysed biomarkers.

Results: Comparison between those Lynch syndrome carriers who had had CRC and those with no CRC personal background did not show significant differences in the abundance of any of the analysed bacterial markers.

When Lynch with a normal colonoscopy (NC) were compared to control subjects with NC, non-advanced adenomas and advanced adenomas, significant differences were found in the abundance of 4 (CRC1, $p = 0.014$; CRC5, $p < 0.001$; CRC6, $p < 0.001$; CRC7, $p = 0.03$), 7 (CRC2, $p = 0.043$; CRC3, $p < 0.001$; CRC5, $p < 0.001$; CRC6, $p < 0.001$; IBD2, $p = 0.013$; IBD3, $p = 0.012$, IBD4, $p = 0.003$) and 9 bacterial markers (CRC2, $p = 0.010$; CRC3, $p < 0.001$; CRC5, $p < 0.001$; CRC6, $p < 0.001$; CRC7, $p < 0.001$; IBD1, $p = 0.013$; IBD2, $p = 0.046$; IBD3, $p = 0.003$; IBD4, $p = 0.005$), respectively. Interestingly, only CRC3 showed significant differences when NC Lynch were compared to control subjects with CRC ($p = 0.034$).

We designed the RAID-LS algorithm combining CRC1, CRC3 and IBD2 bacterial markers. This combination allowed the detection of neoplastic lesions in Lynch syndrome carriers with sensitivity, specificity, true and negative predictive values of 100%, 72%, 42% and 100%, respectively (AUC = 0.859, 95% CI (0.754–0.964)). These results leaded to a false-positive rate of only a 23%, reducing by 60% the number of colonoscopies.

Conclusion: Healthy Lynch syndrome carriers show a similar microbiota to that of patients with tumour lesions, suggesting that there is an inflammatory basal gut environment in Lynch similar to that of CRC.

RAID-LS efficiently detects precancerous lesions in Lynch carriers. The use of this tool would suppose a breakthrough for Lynch carriers, who will significantly improve their quality of life by expanding the intervals between colonoscopic surveillance.

Disclosure: Prof. Garcia-Gil, Dr. Aldeguer, Dr. Serra-Pagès, Dr. Serrano, Dr. Ramió-Pujol, Mr. Amoedo, Ms. Oliver are employees from GoodGut, company who has received private and public funding. The rest of the authors have nothing to disclose.

P0432 COMPARISON OF THREE LYMPH NODE STAGING SCHEMES FOR PREDICTING SURVIVAL IN PATIENTS WITH COLORECTAL CANCER: A LARGE POPULATION DATABASE AND CHINESE MULTICENTER VALIDATION

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Introduction: Several node staging schemes have been proposed for colorectal cancer (CRC) and multiple studies have been conducted to whether number-based scheme (pN), ratio-based scheme (rN) or log odds of positive lymph nodes scheme (LODDS) was associated with CRC survival. However, to the best of our knowledge, there was no study investigate which kind of node staging schemes predicted CRC survival to the best using predicting capacity and the optimal system remains controversial.

Aims and Methods: This study aims to compare 3 node staging schemes in predicting survival outcome in patients with colorectal cancer. Patients with CRC were identified from the Surveillance, Epidemiology, and End Results (SEER) database, and a Chinese multicenter cohort was used for independent validation. The prognostic performance of 3 node staging schemes predicating CRC casue-specific survival (CSS) was compared, involving pN, rN and LODDS. Prediction performance were assessed for overall performance using R^2, discriminatory capacity using Harrell's C statistic, time-dependent receiver operating characteristic (tdROC) at 1, 3, 5, 7, 10 year survival and clinical utility using decision curve analysis (DCA) at 1, 3, 5, 7, 10 year survival. Sensitivity analyses were performed when competing risk was considered or when overall survival (OS) was used. R^2 and Harrell's C statistic was assessed for each multivariate model after including sex, race, age, tumor location, T stage, M stage, grade, histology and size. Comparison in predicting OS was also performed in Chinese multicenter cohort using R^2, Harrell's C statistic and tdROC.

Results: There were 240,898 patients in the SEER database and 1316 in the Chinese multicenter cohort. LODDS scheme performed better in overall performance R^2 (LODDS vs. rN vs. pN: 19.4% vs. 17.6% vs. 9.4%), predictive accuracy with Harrell's C statistic (LODDS vs. rN vs. pN: 0.727 vs. 0.719 vs. 0.712) and ROC (LODDS vs. rN vs. pN, 1year: 74.6 vs. 76.1 vs. 77.3; 3year: 75.5 vs. 76.5 vs. 77.4; 1year: 74.9 vs. 75.6 vs. 76.4; 7year: 74.4 vs. 74.9 vs. 75.2; 1year: 73.6 vs. 73.9 vs. 73.9) than either pN or rN, for patients with colorectal cancer in SEER database. DCA also showed LODDS scheme had higher net benefit than either pN or rN (LODDS vs. rN vs. pN, 1year: 0.019 vs. 0.019 vs. 0.007; 3year: 0.116 vs. 0.118 vs. 0.052; 5year: 0.171 vs. 0.139 vs. 0.139; 7year: 0.200 vs. 0.184 vs. 0.184; 1year: 0.226 vs. 0.219 vs. 0.219) when threshold probability was set at 20%. Similar results could be attained in the sensitivity analysis, multivariate cox model and independent Chinese multicenter cohort.

Conclusion: LODDS performed better than rN, and pN in predicting CRC survival.

Disclosure: Nothing to disclose

Abstract No: P0432: Overall prognostic performance of node staging schemes for colorectal cancer using different analytic strategy

Analysis	R2	HarrelÍs C index	ROC at 1 year	ROC at 3 year	ROC at 5 year	ROC at 7 year	ROC at 10 year
Multivariate model							
pN	0.214	0.754 (0.753–0.755)	80.7	80.5	79.5	78.4	77.4
rN	0.239	0.768 (0.767–0.769)	81.8	81.9	80.9	79.7	78.5
LODDS	0.252	0.775 (0.774–0.776)	82.1	82.7	81.7	80.5	79.2
Chinese multicenter cohort							
pN	0.118	0.638 (0.616–0.661)	69.0	68.3	67.3	65.4	NA
rN	0.138	0.646 (0.624–0.668)	71.9	68.7	67.4	66.2	NA
LODDS	0.143	0.656 (0.630–0.682)	73.4	70.3	69.1	69.0	NA

P0433 ATTEMPTS AND LONG-TERM OUTCOMES OF LOCAL RESECTION FOLLOWED BY ADJUVANT CHEMORADIOTHERAPY FOR PATIENTS WITH HIGH-RISK PT1 RECTAL CANCER

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Introduction: We previously reported the risk for local recurrence was significantly higher in patients with rectal cancer than with colon cancer when treated with only endoscopic resection (ER) for pT1 colorectal cancer having high risk of lymph node metastasis. Especially, patients with high-risk pT1 rectal cancer should be recommended additional surgery after ER to prevent recurrence. However, some patients with high-risk pT1 rectal cancer refused additional surgery because of highly invasiveness including permanent stomas. Recently, we have experimentally performed adjuvant chemoradiotherapy (adj CRT) for only patients who had rejected additional surgery after local resection including ER or transanal local excision for pT1 rectal cancer in the rectum.

Aims and Methods: Our aim is to clarify long-term outcomes of local resection followed by adj CRT for patients with high-risk pT1 rectal cancer.

We retrospectively collected all data on patients with high-risk pT1 rectal cancer treated from January 2000 to December 2016 in our hospital. Patients were classified into 3 groups: patients undergoing only local resection (group A), patients undergoing initial or additional surgical resection with lymph node dissection (group B), and patients undergoing adj CRT after local resection for pT1 rectal cancer (group C). Adj CRT consisted of continuous infusion of 5-fluorouracil or oral administration of capecitabine, and concurrent radiation of 45Gy in total. We assessed to compare the recurrence rate (RR), 5-year disease-free survival (DFS), and 5-year overall survival (OS) between each groups.

Results: A total of 237 patients with pT1 rectal cancer were enrolled. Median follow-up period was 52.7 months (range, 12.2–180.2 months). Group A, B, and, C were 29, 169, and, 39 cases. RR in group A, B, and C was 20.7% (6 cases), 4.7% (8 cases), and 0%, respectively. In Group A, 3 cases developed local recurrence and the other 3 cases developed distant metastasis. In Group B, 2 cases developed local recurrence and the other 6 cases developed distant metastasis. RR in group A was significantly higher than group B and C ($p < 0.05$). 5-year DFS in group B (95.3%) and group C (96.3%) were significantly better comparing group A (70.8%) (A vs B, A vs C, $p < 0.05$). 5-year OS in group B (97.2%) and group C (96.2%) was also better comparing with group A (88.7%), however the difference was not significant among 3 groups. And, there were not significantly differences between group B and C in RR, DFS, and OS.

Conclusion: Long-term outcomes of adj CRT after local resection for patients with high-risk pT1 rectal cancer were similar to those of surgical resection. Adj CRT may be a treatment option if patients with high risk pT1 rectal cancer reject additional surgery.

Disclosure: Nothing to disclose

P0435 SCAR-BIOPSIES AFTER MALIGNANT COLORECTAL POLYPECTOMY OF UNCERTAIN RADICALITY

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Introduction: Approximately 40–60% of T1 colorectal carcinomas (T1 CRCs) are not recognized as such during endoscopy and often inadequately resected. This results in unclear resection margins at histology. Adjuvant surgery is often carried out, but residual malignancy is only found in 6–14% of cases. Biopsies from the polypectomy site are variably used in clinical practice to provide additional evidence for a local radical excision if they are negative for residual cancer. However, sensitivity of scar biopsies for residual cancer after polypectomy is unknown.

Aims and Methods: We aimed to evaluate the sensitivity of endoscopic biopsies < 6 weeks from the endoscopic polypectomy site for residual tumor. This concerns an interim report of an ongoing multicenter prospective cohort study since May 2016. Patients with 1) an endoscopically removed T1 CRC with unclear resection margins, or a resection margin less than 1 mm at histology, and 2) absence of additional conventional risk factors such as lymphovascular invasion, tumor budding, second tumor or oncological treatment were included. If patients were scheduled for adjuvant surgery or rescue endoscopic full thickness resection, patients were enrolled for protocol biopsies from the polypectomy site just before or during this procedure. The results of the biopsies were compared to findings of the resection specimen.

Results: In total, 81 patients have been prospectively included (mean age 66.9 years, 34% female). The T1 CRC was located in the recto-sigmoid in 67/81 (82%) of cases. Major segmental bowel resection was performed in 56 (69%) patients and bowel wall full thickness resection in 25 (31%) patients. In 68 (84%) patients the T1 CRC was not recognized as such during endoscopy. The reason for additional surgery was a positive resection margin (R1, $n = 34$ (42%)), a resection margin that was impossible to assess (Rx, $n = 32$ (40%)), and a tumor-free margin < 1 mm (R0 $<$ 1mm, $n = 15$ (19%)). At second look, visible tumor or adenomatous remnant was noticed in 3 and 6 patients respectively. 3 of them had malignancy in biopsies, two of them in the resection specimen. 4 patients without visible lesion still had tumor in the bowel wall in the resection specimen. In none of the patients with an endoscopically clean polypectomy site (scar or benign postpolypectomy ulcer only), tumor was found in biopsies. The resection specimen showed remaining cancer cells at the polypectomy site in 6/81 (7.4%) of these cases. This was located deeper in the bowel wall in 5/6 (83%) patients. In total 2 of 6 patients were detected by biopsies. This yielded a sensitivity of 33.3% (95% CI −4.4%–71.0%) and a specificity of 98.67% (95% CI 98.63%–98.70%). As all of these patients had visible remnants, the sensitivity of random biopsies from a scar of postpolypectomy ulcer without tumorous or adenomatous remnants was 0%.

Conclusion: The sensitivity of biopsies from the polypectomy site within 6 weeks is too low to safely exclude residual cancer. These biopsies should not be used to decide to refrain from additional surgery. As we did not find any residual cancer cells within the group of R0 resection but a margin < 1 mm, this argues against the value of this 1mm cut-off to predict local recurrence of cancer.

Disclosure: Nothing to disclose

P0436 ALCOHOL CONSUMPTION IS ASSOCIATED WITH THE RISK OF DEVELOPING COLORECTAL NEOPLASIA: PROPENSITY SCORE MATCHING ANALYSIS

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Introduction: Despite the well-known association between alcohol consumption and the development of colorectal neoplasm (CRN), the cumulative effect of alcohol consumption at the time of surveillance colonoscopy has not been investigated, and alcohol consumption was not included in the risk factors for the determination of the time interval of surveillance colonoscopy.

Aims and Methods: This study aimed to determine if alcohol consumption is associated with the development of CRN at the time of surveillance colonoscopy taking consideration with risk stratification of index colonoscopy. We retrospectively identified 1,448 patients who underwent index and subsequent surveillance colonoscopy during the study period. The association between significant alcohol consumption (males $>$ 30g/day, females $>$ 20g/day) and the cumulative occurrence of overall and advanced CRN at the time of surveillance colonoscopy was analyzed using propensity score matching (PSM) analysis.

Results: In the PSM analysis with 210 matched-pairs, the cumulative rate of overall CRN at 5 years after index colonoscopy was higher in the significant alcohol consumption group than in the control group (40% vs. 27.6%, $p = 0.004$). Significant alcohol consumption (adjusted hazard ratio [aHR]: 1.86, 95% CI:1.28–2.70, $p = 0.001$) was associated with the occurrence of overall CRN at surveillance colonoscopy with male (aHR:2.73, 95% CI:1.14–6.52, $p = 0.02$), hypertension (aHR:2.05, 95% CI:1.38–3.04, $p < 0.001$), and high-risk findings at index colonoscopy (aHR:2.26, 95% CI:1.38–3.72, $p = 0.001$). In subgroup analyses based on the risk categories of index colonoscopic findings, significant alcohol consumption was associated with the overall CRN occurrence at the time of surveillance colonoscopy in the normal (aHR:1.90, 95% CI:1.16–3.13, $p = 0.01$) and low-risk groups (aHR:2.13, 95% CI:0.98–4.62, $p = 0.06$). Moreover, Significant alcohol consumption was a risk factor for CRN occurrence at the distal colorectum (aHR: 2.01, 95% CI: 1.10–3.66, $p = 0.02$) and appeared to increase the risk of multiple CRNs (≥ 3) occurrence at surveillance colonoscopy with marginal significance in male (aHR: 2.64, 95% CI: 0.93–7.52, $p = 0.07$). However, there was no association between significant alcohol consumption and the development of advanced CRN on surveillance colonoscopy.

Conclusion: Significant alcohol consumption is associated with the risk of overall CRN occurrence, especially in patients in the normal or low-risk categories at index colonoscopy. In addition, significant alcohol consumption was associated with overall CRN occurrence in the distal colorectum and with more than 3 CRNs occurrence at surveillance colonoscopy. Alcohol consumption habits might be reflected in the determination of optimized time intervals for surveillance colonoscopy.

Disclosure: Nothing to disclose

P0437 LONG-TERM OUTCOMES AFTER ENDOSCOPIC VERSUS SURGICAL RESECTION OF T1 COLORECTAL CARCINOMA

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Introduction: The gold standard for treatment of T1 carcinoma used to be an oncological surgical resection including resection of draining lymph nodes. The number of endoscopic resections of T1 carcinoma will continue to increase in line with the increased detection. Increasing evidence showed that endoscopic resection is adequate for T1 carcinoma with a low risk for LMN. Long-term outcomes of patients with T1 colorectal carcinoma (CRC) treated by endoscopic resection (ER) or surgical resection have not been well established in Korea.

Aims and Methods: The aim of this study was to evaluate the long-term outcomes among patients with T1 CRC. This retrospective study included 386 patients with T1 CRC with initial endoscopy (n = 188) or surgery (n = 198) between 2000 and 2015 at Seoul St. Mary's Hospital. Patients who did not meet the curative criteria in the Japanese Society for Cancer of the Colon and Rectum guidelines (negative resection margin, no lymphovascular invasion, submucosal invasion depth < 1000 μm, well/moderately differentiated adenocarcinoma, grade 3 tumor budding) were defined as 'high risk', and were subdivided into 4 groups: ER with low risk (Group A: 71 patients), ER with high risk (Group B: 117 patients), surgery with low risk (Group A: 65 patients), surgery with high risk (Group B: 133 patients).

Results: During follow-up period, local recurrence or distant metastasis was developed in 8 (1.98%) patients (Group A: 0, Group B: 4, Group C: 0, Group D: 4). 5-year recurrence free survival rate was significantly lower in Group B (Group A: 100%, Group B: 85.0%, Group C: 98.5%, Group D: 95.6%, p = 0.02). However, there was no statistically significant difference in the 5-year overall survival rate among treatment methods (Group A: 100%, Group B: 94.2, Group C: 98.5%, Group D: 98.1%, p = 0.233). Among patients (n = 285) who underwent surgery, lymph node metastasis (LNM) was observed in 33 (11.6%) patients. In the multivariate analysis, lymphatic invasion and depth of submucosal invasion were independent risk factors of LNM.

Conclusion: Endoscopic resection of T1 CRC in patients with low risk is safe. ER for T1 CRC did not worsen the clinical outcomes of patients who required additional surgical resection.

Disclosure: Nothing to disclose

P0438 QUALITY OF LIFE AND WORRY ABOUT CANCER RECURRENCE IN T1 COLORECTAL CANCER PATIENTS TREATED WITH ENDOSCOPIC OR SURGICAL TUMOUR RESECTION

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Introduction: To optimise therapeutic decision-making in T1 colorectal cancer (T1 CRC) patients, it is important to elicit the patient's perspective next to considering medical outcomes. Because empirical data on patient-reported impact of different treatment options are lacking, we evaluated patients' quality of life, perceived time to recovery and worry about cancer recurrence after endoscopic or surgical treatment for T1 CRC.

Aims and Methods: In this cross-sectional study, we selected patients with histologically confirmed T1 CRC, who had participated in the Dutch Bowel Cancer Screening Programme and received endoscopic or surgical treatment between January 2014 and July 2017. Quality of life was measured using the EORTC QLQ-C30 and the EQ-5D-5L questionnaire. We used the Cancer Worry Scale to evaluate patients' worry about cancer recurrence. A question on perceived time to recovery after treatment was also included in the set of questionnaires sent to the patient.

Results: Of all 119 eligible patients, 92.4% responded to the questionnaire (endoscopy group: 55/62, surgery group: 55/57). Compared to the surgery group, perceived time to recovery was on average 3 months faster in endoscopically treated patients after adjustment for confounders (p = 0.001). The 2 treatment groups did not show any significant difference in global quality of life, functioning domains as well as symptom severity. Moreover, patients in the endoscopy group did not report significantly more worries about cancer recurrence than those in the surgery group.

Conclusion: From the patient's perspective, endoscopic treatment provides a quicker recovery than surgery, without provoking more cancer recurrence worries or any deterioration in quality of life. These results contribute to the shared therapeutic decision-making process of clinicians and T1 CRC patients.

Disclosure: Nothing to disclose

P0439 THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY IN FUNCTIONAL ANORECTAL DISORDERS: RESULTS FROM A LARGE OBSERVATIONAL COHORT STUDY

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Introduction: The aim of the study was to describe the results of 3-dimensional high-resolution anorectal manometry (3DHRAM) in a large cohort of patients with functional anorectal disorders.

Aims and Methods: In this single-centre retrospective study, all consecutive patients referred for investigation of faecal incontinence (FI) or dyssynergic defecation (DD) underwent 3DHRAM. The parameters analysed were usual manometric data, repartition of dyssynergic patterns, and the prevalence of a new 'muscular subtype classification' underlying dyssynergia, of anal sphincter defects and of pelvic floor disorders.

Results: Final analyses were performed in 1477 patients of mean age 54 ± 16 years; 825 were suffering from DD and 652 from FI. Among the patients, 86% met dyssynergia diagnostic criteria. Dyssynergic pattern II was the most frequently observed (56%) in women and in men suffering from FI, as well as in women with DD. Type I was the most frequently observed in men with DD (49%). Regarding the muscle type subgroups, combined puborectalis muscle involvement with external anal sphincter profile was the most frequently observed. The global prevalence of rectal intussusception and of excessive perineal descent were 13% and 21%, respectively. The type III dyssynergic pattern was more frequently associated with pelvic floor disorders than were other types ($p < 0.001$).

Conclusion: This large cohort study provides reference values of 3DHRAM in patients with functional anorectal disorders. Further studies will be necessary to assess the prevalence of pelvic floor disorders in healthy volunteers and to develop new scores and classifications including all of these new parameters.

Disclosure: VV, MB and CA have conflicts of interests. They previously have worked for Given Imaging as experts in order to teach 3DHRAM to other practitioners.

P0440 THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY CAN PREDICT RESPONSE TO BIOFEEDBACK THERAPY IN DEFECATION DISORDERS

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Introduction: Biofeedback therapy (BT) is a simple and effective technique for managing outlet constipation and faecal incontinence. Several clinical factors are known to predict BT response, but a 50% failure rate persists. Better selection of BT responsive patients is required. We aimed to determine whether the defecation disorder type per high-resolution manometry (HRM) was predictive of BT response.

Aims and Methods: We analyzed clinical, manometric and ultrasound endoscopic data from patients who underwent BT in our department between January 2015 and January 2016. Patients were classified into 4 groups per the following defecation disorder classification criteria: rectal pressure > 40 mmHg and anal paradoxical contraction (type I); rectal pressure < 40 mmHg and anal paradoxical contraction (type II); rectal pressure > 40 mmHg and incomplete anal relaxation (type III); and rectal pressure < 40 mmHg and incomplete anal relaxation (type IV). An experienced single operator conducted 10 weekly 20-minute sessions. Efficacy was evaluated with the visual analog scale.

Results: Of 92 patients, 47 (50.5%) responded to BT. Type IV and type II defecation disorders were predictive of success (p = 0.03) (OR = 5.03 [1.02; 24.92]) and failure (p = 0.05) (OR = 0.41 [0.17; 0.99]), respectively. The KESS score severity before BT (p = 0.03) (OR = 0.9 [0.81; 0.99]) was also predictive of failure.

Conclusion: The manometry types identified according to the defecation disorder classification criteria were predictive of BT response. Our data confirm the role of 3-dimensional HRM in the therapeutic management of anorectal functional disorders.

Disclosure: VV, MB and CA have conflicts of interests. They previously have worked for Medtronic as experts in order to teach 3DHRAM to other practitioners.

P0441 WHOLE AND REGIONAL ASSESSMENT OF CONTRACTILITY, TEMPERATURE AND PH PROFILE IN PATIENTS WITH FUNCTIONAL CONSTIPATION, IRRITABLE BOWEL SYNDROME WITH CONSTIPATION AND HEALTHY VOLUNTEERS USING WIRELESS MOTILITY CAPSULE

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Introduction: Constipation is a very common disorder with a wide spectrum, from functional constipation (FC) to irritable bowel syndrome with constipation (IBS-C). There are similitudes and differences between FC and IBS-C including changes in gut microbiota compared to healthy volunteers (HV). The wireless motility capsule (WMC) incorporates measurements of pressure, temperature and pH along the gastrointestinal (GI) tract. Whole and regional transit times, pressure pattern and pH have been described in several populations.

Aims and Methods: Aim: to describe whole and regional temperature, pressure pattern and pH profile values in patients with FC, IBS-C, and HV.

Methods: This is a prospective study conducted at 2 GI Motility Labs, in the INCMNSZ and IIMB-UV. We included patients fulfilling ROME III criteria for FC and IBS-C. HV were asymptomatic, no major comorbidities, no previous GI surgery. After a 12-hour fast, WMC was administered without having consumed antibiotics in the previous month, no bowel preparation and no fiber supplement administration were allowed 7 days before study. Subjects were instructed to wear a receiver and kept a diary until WMC was expulsed or for up to 120 hrs. Whole and regional transit time, pressure pattern and pH profile were evaluated. For detailed analysis, small bowel (SB) and colon were divided into quartiles (Q1-Q4) using specialized software (GIMS data viewer, Buffalo, NY). The variables are summarized with medians, frequencies and percentages. Non-parametric tests were used for comparisons.

Results: 52 subjects were included, 17 HV, median age 39 yo (25–54, 25th–75th), BMI 26.3 kg/m^2 (24–27.5), 8 IBS-C, median age 29.5 yo (24–41.5), BMI 25.9 kg/m^2 (21.2–28.7) and 27 FC median age, 41 yo (31–56), BMI 26.8 kg/m^2 (23.5–29.2). There was no difference in age distribution ($p = 0.35$) or BMI ($p = 0.52$). No changes were shown in whole and regional transit times and pressure pattern between groups ($p > 0.05$) (Table). FC had a lower SB pH profile, 6.66 (6.42–6.88, $p = 0.039$) compared to HV 6.87 (6.7–7.03) and IBS-C 7.03 (6.97–7.10) (Figure). Similarly, at ileum (distal quartile in SB), pH was lower in FC 7.18 (7.08–7.42, $p = 0.023$) vs HV 7.44 (7.19–7.66) and IBS-C 7.54 (7.47–7.66). At cecum (1st quartile at colon) FC had lower pH profile 6.02 (5.74–6.24) compared to IBS-C 6.31 (6.14–6.82; $p = 0.024$) but not different to HV.

Conclusion: FC presents a more acidic profile in the SB, ileum and cecum. This leads to the hypothesis that changes in pH may be due to differences in microbiota composition between study populations. It is necessary to evaluate these findings when comparing microbiota with intraluminal pH and symptom profile.

Disclosure: Nothing to disclose

P0442 LONG-TERM LINK BETWEEN THE SEVERITY OF FAECAL INCONTINENCE AND THE EXTENT OF THE OBSTETRICAL ANAL SPHINCTER DISRUPTION

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Introduction: Anal sphincter disruption, mainly from obstetrical origin, is frequent in patients suffering from fecal incontinence (FI). However, the link between the extent of the disruption and the severity of FI is not clear according to the time between the anal sphincter disruption and the apparition of FI. Our main objective was to assess, in the long term, the link between the anal sphincter disruption and the severity of FI.

Aims and Methods: In this retrospective study, all patients referred to our center for investigation of FI including an endo-anal ultrasonography (EUS) and a 3D High Resolution Anorectal Manometry were eligible. Clinical, manometric and EUS data were recorded, the Wexner score being assessed for the severity of FI.

Results: 250 patients (243 women), of mean age 59.97±14 years, were included. The mean duration of symptoms was 61.37±86.10 months. The repartition of anal sphincter disruption was as follows: isolated IAS disruption 30.4%, isolated EAS disruption in 8.4%, both IAS and EAS disruption in 60%. Considering manometric data, the voluntary contraction was lower in patients with EAS disruption and resting pressure was lower when an IAS was identified.

No significant link was observed between the extent of anal sphincter disruption and the severity of FI assessed by the Wexner score. BMI and urinary symptoms were not either linked to the severity of FI.

In our study, in multivariate analysis, menopause was the only independent factor linked to the FI severity.

Conclusion: In the long term, no link was identified between the extent of the disruption and the severity of FI, menopause being the only independent risk factor for the severity of FI.

These data confirm that, as suggested by the literature, the role of the extent of sphincter rupture occurs only in the immediate postpartum period. In the long term, this role is reduced due to the multifactorial nature of FI.

Disclosure: VV and CA have conflicts of interest. They previously have worked for Medtronic as experts in order to teach 3-dimensional high-resolution manometry to other practitioners.

P0443 POLYETHYLENE GLYCOL 3350 PLUS ELECTROLYTES FOR CHRONIC CONSTIPATION: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED MEDIUM-TERM STUDY WITH AN EXTENSIONAL 52 WEEKS OPEN-LABEL, LONG-TERM STUDY

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Introduction: Although polyethylene glycol 3350 plus electrolytes (PEG3350+E) is the most popular osmotic laxative in Europe, prospective long term (over 6 months) safety and efficacy clinical data has not been available to date. In Japan, the current standard cure of chronic constipation is magnesium oxide, PEG3350+E has not previously been used as treatment for chronic constipation.

Aims and Methods: We aimed to determine the efficacy and safety of PEG3350+E for the treatment of chronic constipation with an extensional long term study in Japan. We report a Phase 3 trial; a randomized, double-blind, placebo-controlled medium-term study (Confirmatory phase) with an extensional open-label, long-term (52 weeks) study (Extensional phase) in patients with chronic constipation (who satisfied Rome III criteria for functional constipation). In the Confirmatory phase, 156 patients were randomized to receive PEG3350+E (80) or placebo (76) orally for 2 weeks. In the Extensional phase, 153 patients moved from the Confirmatory phase and received PEG3350+E orally. Starting dose was 13.7g/day dissolved in 125mL of water; dose titration was allowed in both phases within the range of 13.7–41.4g/day, according to the patient's bowel condition. We monitored bowel function (including number of bowel movements, stool consistency) and adverse events. The primary end point of the Confirmatory phase was the increase from baseline (last week of run-in period: Week -1) in spontaneous bowel movements (SBMs) per week during Week 2 of treatment. Secondary endpoints included frequency of complete spontaneous bowel movements (CSBMs), proportion of responders (defined as 3 or more SBMs/CSBMs per week with an increase from baseline of at least 1 SBM/CSBM per week), the median day to first SBM, stool consistency.

Results: In the Confirmatory phase, the difference from baseline in frequency of SBMs in Week 2 was significantly increased with PEG3350+E (4.3 ± 2.9 [Mean ± SD]) compared with placebo (1.6 ± 2.0, $p < 0.001$). Similarly, the frequency of CSBMs and proportion of responders were significantly improved with PEG3350+E compared to placebo.

In the Extensional phase, PEG3350+E showed sustained improvement in bowel function. The difference from baseline in frequency of SBMs in Week 1 and Week 2 were 2.98 ± 2.27 and 4.34 ± 2.89 respectively. Thus, it showed an increasing trend until Week 2 and remained stable at 3.89–4.82 times from Week 2 through Week 52. The frequency of SBMs from Week 1 to Week 52 was significantly increased compared with baseline. The SBMs proportion of responders was 78.4% (95% CI: 71.26%–84.21%) in Week 1 and remained stable at 78.4%–94.0% from Week 1 to Week 52.

In the Confirmatory phase, the incidence of adverse events (AEs) of placebo and PEG3350+E were 19.7% (15/76 patients) and 20.0% (16/80 patients) in the PEG3350+E group, respectively. The incidence of adverse drug reactions (ADRs) of placebo and PEG3350+E were 5.3% (4/76 patients) and 7.5% (6/80 patients), respectively.

In the whole phase 3 trial, the incidence of AEs was 78.8 % (123/156 patients) and the incidence of ADRs was 21.2 % (33/156 patients). The most common ADRs were gastrointestinal disorders (abdominal pain: 4.5%, diarrhea: 3.8%, nausea: 3.2% and abdominal distension: 2.6%). The incidence of AEs did not increase through the whole phase 3 trial.

Conclusion: PEG3350+E resolves constipation compared to placebo in the medium term, is well tolerated and improves bowel functions when administered for 52 weeks in Japanese patients with chronic constipation.

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Disclosure: This study was supported by EA Pharma Co., Ltd. Atsushi Nakajima as the clinical trial advisor

P0444 CHOLESTYRAMINE AS AN ADJUNCT TO PERCUTANEOUS TIBIAL NERVE STIMULATION FOR THE MANAGEMENT OF FECAL INCONTINENCE

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Introduction: Patients with faecal incontinence (FI) who are refractory to Loperamide and biofeedback may respond to neuromodulation. Previous data suggests a possible benefit of Cholestyramine, an anion exchange resin, binds to bile in the gastrointestinal tract, for FI management. We report a single center experience of Cholestyramine in the treatment of FI.
Aims and Methods: We report 44 patients with FI refractory to lifestyle modification, Loperamide and biofeedback therapy. All patients had organic disorders excluded by serology and endoscopy, and also had intact anal sphincters on endoanal ultrasound. *Group A* patients received Cholestyramine (median dose 4.9g per day) along with Percutaneous tibial nerve stimulation (PTNS) for 12 weeks and *Group B* received PTNS alone. Bristol stool form scale (BSFS), weekly incontinence episodes, weekly stool frequency, median St Mark's faecal incontinence score and days per week with abdominal pain were assessed at baseline and 12 weeks after therapy. SeHCAT studies were undertaken in some patients during PTNS.
Results: Data is shown in the Table with group A patients showing greater improvement in stool form, bowel frequency, episodes of incontinence and incontinence score compared to Group B. Only Group A patients had reduced abdominal pain. A responder analysis (>50% episodes reduction) was greater in Group A than B (73% vs 48%). In total, 26 patients underwent SeHCAT testing, 13 in each group: in Group A 7/13 were positive of whom 6 responded to cholestyramine + PTNS, in Group B 5/13 were positive, none of whom responded to PTNS alone.
Conclusion: Cholestyramine is efficient adjunctive therapy to PTNS for FI management. A positive SeHCAT was seen in 46% of patients, and associated with an excellent response to Cholestyramine.
Disclosure: Nothing to disclose

P0445 EFFECT OF GREEN KIWIFRUIT ON TRANSIT AND TOLERANCE TO INTESTINAL GAS IN HUMANS

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Introduction: Previous studies have shown that green kiwifruit is a fiber-rich fruit that enhances colonic transit and may be effective for treatment of constipation in humans. However, non-soluble fibers are fermented by colonic bacteria increasing intestinal gas production and thereby may produce bloating and abdominal distension, a common complain of patients with functional gut disorders.
Aims and Methods: Our aim was to determine the effect of kiwifruit intake on gas production, transit, and tolerance to intestinal gas.
In 10 healthy individuals, transit and tolerance to intestinal gas was studied using a previously developed model of gas retention induced by lipids. A mixture of non-absorbable gases was infused into the jejunum at 12 mL/min for 2 h (total volume 1440 ml) with simultaneous duodenal lipid infusion (Intralipid 1 kcal/min). Intestinal gas clearance was continuously measured using a rectal cannula connected to a barostat. Abdominal symptoms, by a 0–6 score questionnaire and abdominal distension, by a metric tape, were measured at 10-min intervals during the gas infusion period. In each participant, 2 gas transit studies were performed in separate days and random order: 1) after 2 weeks on a low flatulogenic diet and daily intake of 2 kiwifruits (Green Kiwifruit, Zespri, New Zeland) and 2) after 2 weeks on the same low flatulogenic diet but without intake of kiwifruits. During the 2 weeks on low flatulogenic diet prior to the gas transit test, the number and consistency of stools, and abdominal symptoms were daily registered using specific diaries.
Results: During the 2 weeks with daily intake of 2 kiwifruits, participants reported a greater number of bowel movements (1.8±0.1) and a looser consistency of the stools (Bristol score 3.3±0.2) than during the 2 weeks off-kiwifruit (1.5±0.1 bowel movements/day; $p = 0.0009$ vs on-kiwifruit, and Bristol score 2.8±0.1; $p = 0.0716$ vs off-kiwifruit), without differences in the referred abdominal symptoms (abdominal pain score 0.1±0.1 and bloating score 0.1±0.0 on-kiwifruit; pain score 0.0±0.0 and bloating score 0.1±0.0 off-kiwifruit). During the gas transit studies, there were no differences in the volume of gas evacuated (1238±254 ml and 1172±290 ml on-kiwi and off-kiwi, respectively; $p = 0.4355$), in the subjective abdominal perception of symptoms (score 1.2±0.2 and 1.3±0.3 respectively; $p = 0.2367$) or in objective abdominal distension (girth increment 17±7 mm and 17±6 mm respectively; $p = 0.4704$).
Conclusion: Green kiwifruit increases the number of bowel movements and reduces the consistency of stools without increasing gas production or transit and tolerance to intestinal gas.
Disclosure: Nothing to disclose

P0446 CHANGES IN PSYCHOLOGICAL PROCESSES THROUGHOUT ANORECTAL BIOFEEDBACK THERAPY: CORRELATIONS WITH DYSSENERGIC DEFECATION AND FAECAL INCONTINENCE OUTCOMES

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Introduction: Anorectal biofeedback (BF) therapy has established efficacy for both fecal incontinence and dyssynergic defecation. The BF program involves education and advice on toileting behaviour and positioning, diaphragmatic breathing, manometric-based biofeedback aimed at normalising anorectal physiology, sensory retraining and balloon expulsion retraining. In addition to pretreatment clinical state [1], some psychological characteristics of patients have shown to predict BF efficacy [2]. Although psychological mechanisms must be involved in this learning process, there is little information on the psychological changes that occur through anorectal BF.
Aims and Methods: Our aims were to determine (1) what psychological traits change as a result of BF, and (2) whether changes in psychological traits correlate with changes in patient symptoms and quality of life, in order to better understand their role in treatment efficacy. 67 patients ($M_{age} = 57$, $SD = 17$, 93% female) presenting to the Neurogastroenterology Unit at the Royal North Shore Hospital (Sydney, Australia) with fecal incontinence (FI) ($n = 39$) or dyssenergic defecation ($n = 28$) underwent a 6-visit instrumented anorectal BF program. Measures of executive function, cognitive flexibility, perceived stress, emotion regulation and self-efficacy were recorded prior to and at the end of therapy. Patient reported outcomes were symptom severity (Fecal Incontinence Severity Index and Constipation Score) and quality of life (Fecal Incontinence QOL and Patient Assessment of Constipation QOL) for FI and dyssenergic defecation patients as appropriate. Spearman's correlations above 0.3 were considered clinically meaningful (and bolded in the Table).
Results: Patients' perceived stress, executive function, cognitive flexibility, self-efficacy, and adaptive health-focused emotion regulation significantly improved throughout BF (all $Zs \geq 2.13$, all $ps < 0.05$. Change in psychological traits correlated more strongly with changes in QoL, as opposed to symptom severity (see Table). Improvement in constipation QoL was moderately correlated with greater decrease in stress and executive function impairment; improvement in FI QoL correlated with greater reduction in self-blame and catastrophizing, and increases in cognitive flexibility and self-efficacy.
Conclusion: Psychological traits of emotion regulation, cognitive functioning and stress improve through BF and correlate with improvements in PRO. While we cannot conclude causal direction of the relationships, our results open the possibility of potential mechanisms in BF efficacy, with potentially different mechanisms for dyssenergic defecation and FI.

Table. Spearman's correlations between change in psychological traits with change in BF PROs. + $p < 0.10$ * $p < 0.05$ ** $p < 0.01$

Change in:	Fecal Incontinence Severity Index	Constipation Score	Fecal Incontinence QOL	Constipation QOL
Perceived stress	0.177	**0.428***	−0.119	**0.391**$^{+}$
Executive function impairment	0.201	−0.007	0.246	**0.366**$^{+}$
Cognitive flexibility	−0.297^{+}	0.031	**0.531****	−0.244
Emotion regulation: self-blame	**0.349***	−0.117	**−0.383***	0.093
Emotion regulation: acceptance	0.206	0.253	**−0.386***	0.166
Emotion regulation: positive refocus	−0.016	−0.138	0.256	**−0.404**$^{+}$
Emotion regulation: planning	−0.069	−0.124	0.002	**−0.391**$^{+}$
Emotion regulation: putting into perspective	0.007	−0.126	0.283	**−0.532****
Emotion regulation: catastrophizing	0.153	0.084	**−0.351**$^{+}$	0.306

Disclosure: This abstract was submitted for presentation at Digestive Diseases Week 2018.

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P0447 VALIDATION OF THE "FAILURE TO PROVIDE ADEQUATE RELIEF" (F-PAR) SCALE IN A SPECIALIST CLINICAL SETTUNG

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Introduction: Treatment of chronic idiopathic constipation is empiric, based on step-wise approach. If first-line conservative treatment (lifestyle advice and laxatives) do not relieve symptoms, secondary approaches with prokinetic or secretagogue drugs are used before considering hospital-based care (biofeedback, psychosocial support, transanal irrigation (TAI), surgery). Nevertheless, patients are often unsatisfied with care and fail to progress to adequate levels of therapy. The 5-point Failure to Provide Adequate Relief (F-PAR) scale was developed to facilitate the recognition of when to move from each step to the next. The aim of this study was to validate F-PAR in a tertiary clinic setting.
Aims and Methods: We studied 403 consecutive consultations of 331 patients (262 women, mean age 41) in our specialist clinic. All fulfilled Rome III/IV diagnostic criteria for chronic constipation. Immediately prior to clinical assessment by 1 of 2 experienced physicians, participants completed the F-PAR scale; patients were seen blind to the F-PAR result. Standard clinic assessment was undertaken to identify efficacy of the current management as the gold standard.
Results: Total of 403 consultations were accomplished, in 200 of which clinical assessment identified inadequate relief with current therapy (laxatives 81 patients, enema 22 patients, prucalopride 42 patients, lubiprostone 12 patients, transanal irrigation 20 patients, biofeedback 97 patients, surgery 3 patints or combination 127 patients). Neither duration nor type of treatment was correlated with relief. All the individual items of the F-PAR had specificity >96% but poor sensitivity (15–67%). Cumulatively, none of the subjects with 4 or more of 5 positive responses on the F-PAR had adequate relief with their current treatment.
Conclusion: We have shown that the F-PAR has excellent specificity, suggesting it is a useful confirmatory tests to confirm a clinical suspicion of inadequate relief. Good sensitivity is only seen if there are no positive F-PAR replies implying the F-PAR is only of screening value when there is high likelihood of treatment satisfaction. As such, the F-PAR may have a role in confirming efficacy of treatments in future trials of therapy for chronic constipation.
Disclosure: Nothing to disclose

P0448 RISK OF COLONIC DIVERTICULAR REBLEEDING ACCORDING TO ENDOSCOPIC APPEARANCE

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Introduction: Re-commencement of bleeding (rebleeding) of colonic diverticula after endoscopic hemostasis is a clinical problem.
Aims and Methods: This study aimed to examine whether endoscopic visibility of colonic diverticular bleeding affects the risk of rebleeding after endoscopic hemostasis. We performed a retrospective review of endoscopic images and medical charts of patients with colonic diverticular bleeding who underwent endoscopic hemostasis. Endoscopic visibility was classified into 2 types according to visibility of the source of bleeding; source invisibility due to bleeding or attached hematin (type 1), or endoscopically visible responsive vessels (type 2). Rebleeding rates within 1 year after initial hemostasis were examined.
Results: Of 93 patients with successful endoscopic hemostasis, 38 (41%) showed type 1 visibility, while the remaining presented type 2. All patients received hemostasis with clipping, rebleeding developed in 20 patients (22%). Type 1 visibility was more likely to be observed in patients with rebleeding (65% vs. 34%, $p = 0.013$). Multivariate analysis revealed that after endoscopic hemostasis, type 1 visibility (invisible source) was the only independent risk factor for colonic diverticular rebleeding (odds ratio, 3.05; 95% confidence interval, 1.03–9.59, $p = 0.044$). Kaplan-Meier curve showed the cumulative incidence of rebleeding was significantly higher in patients with type 1 visibility than those with type 2 visibility ($p = 0.0033$, log-rank test)
Conclusion: Hemostasis by clipping for colonic diverticular bleeding without definite observation of the source of bleeding may not be sufficiently effective. Other hemostatic methods, including band ligation, should be considered when the source of bleeding is unclear.
Disclosure: Nothing to disclose

P0449 THE "DICA" ENDOSCOPIC CLASSIFICATION FOR DIVERTICULAR DISEASE OF THE COLON SHOWS A SIGNIFICANT INTEROBSERVER AGREEMENT AMONG COMMUNITY ENDOSCOPISTS

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Introduction: A validated endoscopic classification of Diverticular disease (DD) of the colon, called DICA (Diverticular Inflammation and Complication Assessment), is currently available.
Aims and Methods: Our aim was to assess the agreement on this classification among an endoscopists community setting.
The DICA score for DD resulted in the sum of the scores for extension of diverticulosis, number of diverticula per district, presence and type of inflammation, and presence and type of complications: DICA 1 (up to 3 points); DICA 2 (from 4 to 7 points); DICA 3 (over 7 points). A total of 55 endoscopists,

subdivided between expert (31 raters, namely endoscopists using this classification in their practice) and not expert about DICA classification (24 raters), independently scored a set of DD endoscopic videos using DICA classification. The percentages of overall agreement on DICA score and a free-marginal multirater kappa (κ) coefficient were reported as statistical measures of inter-rater agreement.
Results: .1375 visualizations were performed. The overall agreement levels among the total group of raters were: DICA 1, 70.2%; DICA 2, 70.5%; DICA 3, 81.3%. The inter-rater agreement between the 55 evaluators varied as follows: DICA, 1 free-marginal $\kappa = 0.553$; DICA 2, free-marginal $\kappa = 0.558$; DICA 3, free-marginal $\kappa = 0.719$.
The overall agreement levels among the expert group of raters were: DICA 1, 78.8%; DICA 2, 80.2%; DICA 3, 88.5%. The inter-rater agreement between the 31 expert evaluators varied as follows: DICA 1, free-marginal $\kappa = 0.682$; DICA 2, free-marginal $\kappa = 0.712$; DICA, 3 free-marginal $\kappa = 0.828$
Conclusion: DICA score is a simple, reproducible, and easy-to-use endoscopic scoring system for diverticular disease of the colon. The inter-rater agreement in this study was strong with a significant improvement in the expert subgroup of raters.
Disclosure: Nothing to disclose

P0450 LONG-TERM EFFICACY OF RIFAXIMIN IN MANAGING SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON

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Introduction: Symptomatic Uncomplicated Diverticular Disease (SUDD) affects about 20% of patients having diverticulosis. However, there is no consensus about the best treatment in treating this disease and in preventing the disease's complications. Rifaximin, a not absorbable antibiotic, is currently advised as effective treatment in controlling symptoms and in preventing complications, but no long-term data are available.
Aims and Methods: Our aim was to assess the outcome of a cohort of SUDD patients treated with rifaximin during a retrospective follow-up study. The study group (group A) included 346 SUDD patients with a median (range) age of 61(49–83) years, of whom 216 (62.4%) were females. Patients were treated with rifaximin 800 mg/day for 7 days/month. The control group (group B) included 470 patients SUDD taking spasmolithics when needed, with a median (range) age of 59 (47–81) years, of whom 288 (61.3%) were females. Diagnosis of SUDD was performed by colonoscopy and by clinical accepted criteria. Follow-up visit was performed every 12 months or whenever patients consider it necessary. At each control visit, symptoms were assessed by the Global Symptomatic Score (GSS), assessing 4 main variables (left lower abdominal pain, bloating, diarrhea, constipation) graded as 0 = no symptom; 1 = mild, symptoms easily tolerated; 2 = moderate, symptoms sufficient to cause interference with usual daily activities; and 3 = severe, incapacitating symptoms with inability to perform normal activities).
Results: At baseline global symptomatic score (interquartile range) was 7 (5–8) in the study group and 6 (4–8) in the control one ($p = 0.243$). Either abdominal pain or bloating or bowel alteration were comparable between the 2 groups. At a median (range) follow-up of 8 (5–12) years global symptomatic score (interquartile range) was 3 (1–4) in the study group and 5 (3–7) in the control group ($p = 0.002$). With exception of abdominal pain, either bloating or bowel alteration were significantly reduced in the study group with respect to the control group.
The number of visit/patient/year were 2.4 patient/year in group A and 4.2 patients/year in group B ($p = 0.02$). Acute diverticulitis occurred in 9 patients (2.60%) in group A and in 21 patients (4.46%) in group B ($p = 0.01$). Surgery due to complication of the disease occurred in 4 patients (1.16%) in group A and 9 (1.91%) in group B ($p = 0.06$). Deaths due to disease were 0 in group A and 2 (0.42%) in group B ($p = 0.303$).
Conclusion: Rifaximin is effective in the symptomatic relief of symptomatic uncomplicated diverticular disease of the colon. In particular, symptomatic relief was due to a significant reduction in bloating and bowel alteration symptomatic score. Finally, rifaximin seems to be also effective in reducing the risk of disease's complications.
Disclosure: Nothing to disclose

P0451 DEMOGRAPHIC AND CLINICAL FACTORS ASSOCIATED WITH TREATMENT USE IN PATIENTS WITH DIVERTICULAR DISEASE: RESULTS FROM THE ITALIAN NATIONAL REGISTRY REMAD

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Introduction: Although diverticular disease is an extremely common condition, its effective treatment represents a difficult task in daily clinical practice. We have used the Italian national 'Registro Malattia Diverticolare' (REMAD) registry, an ongoing 5-year prospective, observational, multicenter, cohort study in 1206 consecutive patients with diverticular disease, to assess the prevalence of treatment use in the different clinical entities of this disorder and the demographic and clinical factors associated.
Aims and Methods: At the entry in the REMAD registry, patients were categorized in subgroups according to different clinical entities: diverticulosis, symptomatic uncomplicated diverticular disease (SUDD), previous diverticulitis (PD). Demographic, clinical and lifestyle factors and quality of life were registered (Carabotti et al., *UEG Journal* 2018 in press) as well as the use of 1 or more treatments for diverticular disease (including poorly absorbed antibiotics, like rifaximin, mesalazine, probiotics, prebiotics, fibers, and antispasmodics) in the last year. Logistic regression analysis was used to assess the association between demographic and clinical factors with treatment assumption.
Results: 500 of the 1206 subjects (41.5%) included in the study have taken at least 1 treatment for diverticular disease in the last year. Of these subjects, 166 belong to diverticulosis group (of a total of 702 subjects with diverticulosis, 23.6%), 165 to SUDD group (of a total of 295 subjects with SUDD, 55.9%), and 169 to PD group (of a total of 209 subjects with PD, 80.9%) ($p < 0.0001$ for all). In all groups, poorly absorbed antibiotics, particularly rifaximin, were the most common treatment, accounting for 87.3% in diverticulosis, 84.8% in SUDD and 75.7% in PD. In a multivariate analysis, the following factors resulted to be significantly associated with treatment use: female gender (OR = 1.6; 95% CI, 1.2–2.2), family history of colonic diverticula (OR = 1.5; 95% CI, 1.1–2.1), gastrointestinal comorbidity (OR = 1.9; 95% CI, 1.4–2.5) and impairment of quality of life, particularly the physical component summary (PCS) score (OR = 1.6; 95% CI, 1.2–2.2). Interestingly, older age (OR = 2.04; 95% CI, 1.1–3.7) and gastrointestinal comorbidity (OR = 2.1; 95% CI, 1.4–3.2) were the most relevant factors associated with the use of treatments in diverticulosis, while first-degree family history for colonic cancer (OR = 2.4; 95% CI, 1.0–5.7) and for diverticula (OR = 2.3; 95% CI, 1.1–4.9), the presence of gastrointestinal comorbidity (OR = 2.3; 95% CI, 1.3–4.3) and the impairment of PCS score (OR = 2.2; 95% CI, 1.2–4.2) were significantly associated with treatment use in SUDD.
Conclusion: Pharmacological approaches targeting enteric bacteria (with poorly absorbed antibiotics, like rifaximin) were the most common therapies in diverticular disease, due to their ability of controlling symptoms and also preventing complications. In addition, this nationwide registry study identified different demographic and clinical features associated with the use of pharmacological treatments in the distinct clinical entities of diverticular disease. The optimal regimen of therapy must be established in *ad hoc* studies. ClinicalTrial.gov Identifier: NCT03325829.
Disclosure: Nothing to disclose

P0452 ACUTE COLON DIVERTICULITIS HOSPITALIZATION TRENDS IN VENETO REGION (NORTHEAST ITALY)

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Introduction: Diverticular disease (DD) of the colon represents a common clinical condition affecting with high rate the population in developed countries. Several epidemiological studies have clearly shown that in the last decades the rates of hospital admissions for Acute Colon Diverticolitis (ACD), the most important complication of DD, is progressively increased.
Aims and Methods: Describe the hospitalization trend for ACD in Veneto region (North East Italy), including in-hospital mortality, and evaluate the impact of specialistic admission hospital units as Gastroenterologic (GE) units.
Data were obtained from the Veneto Region anonymous Hospital Discharge Record database from 2000 to 2017, in which diverticulitis of colon [ICD-9-CM code 562.11 and 562.13 (diverticulitis with and without mention of haemorrhage)] was the primary diagnosis.
Standardized Hospitalization Rate (SHR) per 5-year group (ref. pop. Veneto 2009) was calculated and expressed per 100,000 population.
To evaluate the impact of admission hospital units on the outcome of ACD management we analyzed in-hospital mortality, need for surgery (NFS) and lenght of stay (LOS).

Results: From 2000 to 2017 a total of 33,249 hospitalization for AD were registered with an increasing rate from 0.30 to 0.46 for 1,000 inhabitants (X^2 trend: 514.182 $p < 0.001$; mean increase of 2.6% per year, $p < 0.001$).
Mean age was 66.1±28.4, higher in female (70.1±29.8 vs. 60.5±24.9; $p < 0.05$) and the higher hospitalization rate (overall mean: 0.39) was in female (0.43 vs. 0.34; OR: 1.30; 95% CI:1.27–1.32; $p < 0.001$). SHR increased with age reaching the higher value in patients ≥85 years (162.43) with an increase of hospitalization over the study period for all class ages ($p < 0.001$).
Women showed an higher prevalence of hospitalization compared to men (OR: 1.30; 95% CI: 1.27–1.32; $p < 0.001$), and both genders presented an increasing trend, with a mean increase per year of 1.9% and 3.8% respectively ($p < 0.001$).
NFS was substantially stable (19.4%) while overall in-hospital mortality rate showed an important increase from 0.37 to 0.98 ($p = 0.037$). Also LOS decreased significantly (−18%) from 9.8 to 8 days ($p < 0.001$).
73% of patients were overall admitted by surgical units with a steady increase for admission in medical ones from 22% to 34% and in particular in GE units where admission rose from 7% to 22% of overall admission of Medical Area.
From the comparison between GE units and other medical area admissions, emerged that patients admitted in GE units do not have a significantly lower ($p > 0.05$) NFS rate (3.5% vs. 4.1%) and in-hospital mortality (0.3% vs. 1.4%), showing a significative lower LOS (7.1±2.2 vs. 11±3.6; $p < 0.001$).
Conclusion: Results suggest that ACD is an emerging heath-care problem related to the rising of age.
Through the years the NFS rate was stable with an increase of mortality.
In this scenary GE units seem to be more efficiently obtaining a significative reduction of the cost management of ACD.
Disclosure: Nothing to disclose

P0453 MAJOR GENETIC RISK VARIANTS IN DIVERTICULOSIS AND DIVERTICULITIS

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Introduction: Colonic diverticulosis is one of the most common gastroenterological disorders. Although diverticulosis is commonly benign, many individuals develop diverticulitis or other complications of diverticular disease. Diverticular disease is caused by a complex interaction of environmental and genetic factors. A recent genome wide study (Sigurdsson et al. *Nat Commun* 2017) identified gene variation in the Family with sequence similarity 155A (*FAM155A)*, Collagen-like tail subunit of asymmetric acetylcholinesterase (*COLQ)* and Rho GTPase-activating protein 15 (*ARGHGAP15)* genes, but was derived from population based-data, and the cohorts were not stratified into diverticulosis and diverticulitis.
Aims and Methods: The aim of our present study was to assess the effects of the detected risk variants in an endoscopically characterized cohort containing 1,275 patients referred for colonoscopy to 3 academic medical centers in Germany (Homburg and Köln) and Lithuania (Kaunas), and specifically dissect the association with the distinct phenotypes diverticulosis and diverticulitis. Presence of diverticulosis was assessed with colonoscopy in all patients, and diverticulitis additionally confirmed with ultrasound and/or computed tomography. Risk variants in *ARHGAP15* (rs4662344-T), *COLQ* (rs7609897-T) and *FAM155A* (rs67153654-A) were genotyped using Taqman assays in 778 patients with diverticulosis, 169 patients with diverticulitis and 462 controls of Caucasian descent and free of diverticulosis (as confirmed by colonoscopy). The associations of the risk variants with (i) colonoscopy-proven diverticulosis as compared to controls free of diverticulosis and (ii) patients with prior diverticulitis as compared to patients with diverticulosis and no prior diverticulitis were assessed in multivariate models including the established environmental risk factors age and body-mass index (BMI) (diverticulosis), as well as age, BMI, intake of nonsteroidal-antiinflammatory drugs (NSAIDs), smoking, and daily alcohol intake (diverticulitis).
Results: Median age of our patients was 64 years (interquartile range [IQR] 55–72). Overall, 47% ($n = 598$) were male. The variant in *COLQ* (rs7609897) deviated from Hardy-Weinberg equilibrium in controls and could not be included in the analysis. Median body mass index (BMI) was 27.6 kg/m^2 (IQR 24.8–31.2). In univariate analysis for diverticulosis age ($p < 0.001$) and BMI ($p < 0.001$) were significantly associated, and the presence of a risk variant in *ARHGAP15* was borderline significant ($p = 0.06$). Neither the risk variant *FAM155A* nor sex were associated with diverticulosis. In multivariate logistic regression analysis, age and BMI remained significant. In univariate analysis for diverticulitis, frequent NSAID intake ($p < 0.001$), age ($p < 0.001$), BMI ($p = 0.02$) and the risk variant in *FAM155A* ($p = 0.037$) where associated with diverticulitis, whereas daily alcohol intake, smoking and the risk variant in *ARHGAP15* were not. In multivariate logistic regression analysis, BMI ($p = 0.017$) and NSAID ($p < 0.001$) remained significant, and there was a trend for the *FAM155A* risk variant ($p = 0.10$).
Conclusion: A complex network of risk factors modulates diverticulosis and the development of diverticulitis. In addition to confirming previously known environmental risk factors in our cohort, a risk variant in *FAM155A* (rs67153654) might be associated with diverticulitis, but not diverticulosis.
Disclosure: Nothing to disclose

P0454 EVALUATION OF HIGH-RESOLUTION ANOSCOPY AS A SCREENING TOOL FOR ANAL INTRAEPITHELIAL NEOPLASIA (AIN): A COMPARISON TO THE GOLD STANDARD ANAL MAPPING BIOPSIES

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Introduction: Human papillomavirus-associated anal intraepithelial neoplasia (AIN) is a precursor of invasive anal carcinoma. High-resolution anoscopy (HRA) is recommended as a screening tool for AIN (1). However, the diagnostic accuracy of this method is unclear. In contrast, anal mapping biopsies (AMB) are not routinely performed and are not mentioned in the current guidelines. Whether they bring additional diagnostic benefit is unclear. To our knowledge, HRA has never been compared with systematic anal mapping biopsies before.
Aims and Methods: We aimed to evaluate HRA as a screening tool for AIN in comparison to anal mapping biopsies as the gold standard.
Retrospective analysis of a cohort of consecutive patients at risk for AIN, in whom both HRA and anal mapping biopsies had been performed. Histological findings of anal mapping biopsies performed on suspected HPV-associated lesions were compared with HRA findings. The comparison of HRA with mapping biopsies was carried out by inspection and description of lesions as a whole (lesion-based analysis) and for each field (field-based analysis). For the field-based analysis, the anal region of each patient was divided into 28 fields, which were assessed (HRA) and biopsied separately.
Results: 29 patients (20 male, 9 female) with anal mapping were analysed during 2 years. Of the 20 male patients, 11 were HIV positive and 14 practiced men sex with men (MSM). All women were HIV negative. HRA identified 23 lesions suspicious for AIN. 22 lesions (96%) were histologically confirmed as AIN. Anal mapping detected 27 AIN lesions. In HRA, the 22 confirmed lesions spread over 49 fields and 60 additional fields were detected by mapping biopsies (+122%). HRA shows in the lesion-based analysis a sensitivity of 84.6%, a specificity of 87.5%, a PPV of 95.7% and a NPV of 63.6%. For field-based analysis, HRA shows a sensitivity of 45%, a specificity of 98.6%, a PPV of 83.1% and a NPV of 92%.
Conclusion: This study shows that, although most AIN are detected with HRA, their extent is underestimated by 120%. It can be assumed that the repeatedly observed high recurrence rate (up to 60% in 2 years) after highgrade-AIN therapy is not only caused by overlooked lesions or due to their biological properties but also by underestimating their extent (2,3). This is relevant for therapy, especially when therapeutic interventions without resection and histological evaluation of the margins such as cryotherapy, CO_2 laser ablation, or RFA are used. In summary, the results of this study imply that anal mapping biopsies should be considered prior to local therapy, at least in high-risk patients with positive results in the HRA study.
Disclosure: Grant by Olympus, comperative study HRA vs. endoscopy for AIN diagnsotics

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P0455 DIAGNOSIS OF HIRSCHSPRUNG'S DISEASE IN CHILDREN - PRELIMINARY EVALUATION OF A NOVEL ENDOSCOPIC TECHNIQUE FOR RECTAL BIOPSY

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Introduction: The diagnosis of Hirschsprung's disease (HD) relies on anorectal manometry, barium enema and rectal biopsy. The role of endoscopic biopsy is not well-known for the diagnosis of HD in children.
Aims and Methods: In this study, we evaluated the safety and adequacy of biopsies procured by endoscopic mucosal resection (EMR) for the diagnosis of HD. All the children with suspected HD underwent anorectal manometry and barium enema. Children with absence of recto-anal inhibitory reflex and/ or radiological images suggestive of HD were included in the study. EMR was performed using the standard band ligation device at a distance of about 3 cm from dentate line along posterior wall of rectum. Submucosal lifting injection (saline + indigocarmine dye) was done in children < 3 years of age. All samples were assessed macroscopically and microscopically. Adequate sample was defined as - measuring >3 mm and including adequate submucosa for identification of ganglion cells.
Results: 6 children (median age, 5 years) underwent EMR using the band ligating device for the evaluation of HD. EMR was performed with and without submucosal lifting injection in 2 and 4 children, respectively. All the samples were adequate macroscopically (>3 mm). The mean volume of biopsy specimen was 0.11 ± 0.07 $cm^3$with inclusion of submucosa in all children. Ganglion cells were identified in 3 children and thereby, excluding the diagnosis of HD. There were no immediate or delayed complications.
Conclusion: Rectal biopsy using EMR with a band ligating device is feasible and provides adequate sample for the evaluation of HD in children.
Disclosure: Nothing to disclose

P0456 HEMORROITEQ STUDY: PROSPECTIVE EVALUATION OF FOUR NON-SURGICAL INSTRUMENTAL MODALITIES FOR THE TREATMENT OF PROLAPSED HEMORRHOIDAL DISEASE

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Introduction: Persistent symptomatic hemorrhoidal disease after general counseling measures requires instrumental intervention. The benefit of the association of phlebotonics is uncertain.
Aims and Methods: Comparative study on the efficacy and safety of 4 instrumental non-surgical modalities for treatment of prolapsed internal hemorrhoids (IH).
Prospective (2016–2018) randomized non-blinded sequential trial with four intervention arms: Rubber band ligation (B) vs. Sclerotherapy with foam Polidocanol (PLDf) vs. [Ligation + phlebotonics (B+P)] vs. [PLDf + P]. Inclusion of adult patients with IH (grade II-III) diagnosis with no previous instrumental treatment, after signed written consent. Demographic and clinical characterization. Assessment of outcomes: Safety (adverse events after intervention); efficacy (complete, partial or absent response) at week 4–8 (short-term) and weeks 12–24 and 44–52 (long-term). Reintervention if indicated, at the same timepoints. Statistics: Oneway ANOVA, Welsh and Levéne test; chi-square.
Results: 68 patients were included (37 males, mean age 54 ± 12.8 years) and distributed among the 4 treatment groups (19 vs.19 vs.17 vs.13), adjusted for age ($p = 0.92$) and gender ($p = 0, 86$).
Short-term analysis - all patients were evaluated for this analysis. 3 cases of self-limited pain only, were documentes. Efficacy was superior for B group [no case of lack of response and 12/19 cases of complete response ($p = 0.006$)].
Long-term analysis - 46 patients were assessed (5 dropouts, 17 still incomplete follow-ups). 100% and 43% re-interventions were preformed on the 2nd and 3rd timepoints without reported adverse events In this long-term evaluation there is no difference between the treatment modality and the efficacy, time made the outcomes similar between treatment groups: The efficacy of each treatment is provided in 75% complete response and 25% partial response, with numerical superiority for the PLDf + P group (87.5% and 12.5%, respectively).
Conclusion: Non-surgical instrumental IH therapy is safe and globally effective. B showed to have superior efficacy at week 4 to 8, after a single intervention. Efficacy over time and after re-interventions is similar for B and PLDf. Combined PLDf + P therapy seems to enhance sustained efficacy over time.
Disclosure: Nothing to disclose

P0457 HIGH-INTENSITY CONTRAST IMAGING ASSISTED HIGH-RESOLUTION ANOSCOPY FOR ANAL CARCINOMA SCREENING IN HIV-INFECTED PATIENTS

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Introduction: Human immunodeficiency virus (HIV) infection contributes to the occurrence of anal cancer in men who have sex with men (MSM), leading to a 30–100 fold higher anal carcinoma incidence in this patient group. Therefore convenient screening tools are mandatory to identify anal intraepithelial neoplasia (AIN) at early stages, which allow an early curative intervention.
Aims and Methods: In this pilot study we screened for anal carcinoma in HIV positive MSM, receiving stable antiretroviral therapy. Endoscopic high-intensity contrast (HIC) and the most recently introduced Blue Light Imaging technology (BLI) with optical magnification were applied during high-resolution anoscopy. The HIC/BLI equipped endoscope was advanced into the anal region of interest via a pre-inserted standard rectoscope. Conventional imaging in combination with aceto-enhancement, anal swaps as well as directed biopsies served as reference methods to identify AIN.
Results: Following preliminary inclusion of consecutive HIV patients, median (range) age 49.5 (37–61) years, CD4-count 633 (298–1076) cells/µl and HIV-RNA 0 (0–34) copies/ml, we were able to identify 1 patient with *condyloma acuminata* and low-grade AIN. HIC/BLI as well as aceto-enhancement both resulted in consistent findings and lead to the diagnosis of AIN. In addition magnified HIC/BLI revealed irregular superficial vascular network pattern within the identified AIN and condyloma lesions. In contrast, anal swaps and cytology, showing inconclusive results (PAP IIb) in 20% (1/5) and normal cytology in 80% (4/5), were not able to identify AIN in these patients.
Conclusion: HIC/BLI enhanced anoscopy provides an additional time-sparing method for the screening of anal carcinoma in HIV infected patients. High-definition imaging with the BLI technology also allows for identification of vascular patterns, which might help to characterize dysplastic anal lesions and might therefore allow for more targeted diagnosis and treatment.
Disclosure: Nothing to disclose

P0458 A EUROPEAN MULTICENTRE POST-AUTHORISATION STUDY OF ORAL TRISULPHATE SOLUTION AS A BOWEL CLEANSING PREPARATION: COMPLIANCE WITH INSTRUCTIONS OF USE, TOLERABILITY AND SAFETY IN REAL-LIFE SETTING

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Introduction: Oral Trisulphate Solution (OTS) is a low-volume bowel cleansing solution administered as 2 x 500 ml saline sulphate solution followed by 2 x 1 l water or clear liquids (for hydration). The aim of this study was to: assess misuse (defined as non-compliance with hydration); describe the safety profile overall and in case of misuse; and identify any immediate/acute adverse events (AEs) in special populations (the elderly and patients at risk of electrolyte shifts).
Aims and Methods: This was a prospective, non-interventional, multicentre, European Post Authorisation Safety Study (PASS) in patients receiving OTS in routine clinical practice (NCT02630680), requested by the European Medical Agency. Inclusion began on 12 October 2015 and ended on 20 January 2017. Consecutive patients who went for colonoscopy and were eligible for OTS were included at each participating centre, to achieve a target enrolment of 76 patients per site. Patients were instructed to record compliance and AEs on a leaflet. Compliance to hydration was calculated as a ratio of actual volume taken versus prescription 2 l. Non-compliance was defined as having taken $< 75\%$ of hydration. Missing volumes were imputed as not taken. Investigators assessed colon cleansing level on a 4-point scale.
Results: 1281 patients were recruited in 16 centres in the Czech Republic, Germany, the Netherlands and Poland. 1206 patients took OTS and provided safety information (safety population). 1177 patients reported their level of compliance (registry population). The most frequent indications for colonoscopy were screening (33%), a history of polyp or neoplasm (21.7%), and abdominal pain (13.2%). 94.5% of patients were compliant to hydration guidelines; 86.8% of patients were 100% compliant (Table). Compliance to osmotic OTS solution was 96.8%. Subgroup analyses (age, gender, dosing regimen) revealed no differences in compliance. Reported colon cleansing level was excellent-to-good in 1048/1196 patients (87.6%). 329 patients (27.3%) experienced 758 related treatment-emergent AEs (TEAEs), mostly gastrointestinal (82.9%). Most TEAEs were considered mild or moderate in intensity. TEAEs were similar in compliant versus non-compliant patients, and in elderly versus younger patients; however, significantly more TEAEs were noted in female than male patients. TEAEs were not associated with lower compliance. No AEs suggestive of dehydration were

noted in non-compliant patients. No acute AEs were observed in special populations. TEAEs did not differ in nature and intensity from the known safety profile overall and in special populations.
Conclusion: In this non-interventional study, treatment compliance to hydration guidelines was excellent or good in 94.5% of patients. The safety profile of OTS was good and similar to previous reports overall and in special populations.

Compliance to hydration guidelines: registry population (N = 1177)	n (%)
Compliant patients (volume taken ≥75%)	1112 (94.5)
Excellent (100%)	1022 (86.8)
Good (<100 and ≥75%)	90 (7.6)
Compliant patients to hydration guidelines by subgroups	**n (%) [95% CI]**
<65 years (n = 720)	689 (95.7) [93.9; 97.1]
≥65 years (n = 457)	423 (92.6) [89.8; 94.8]
Male (n = 606)	576 (95.0) [93.0; 96.6]
Female (n = 571)	536 (93.9) [91.6; 95.7]
Related TEAEs: safety population (N = 1206)	**n (%)**
Any related TEAEs [number of occurrences]	329 (27.3) [758]
Compliant patients (n = 1120)[95% CI]	304 (27.1) [24.6; 29.8]
Non-compliant patients (n = 86)[95% CI]	25 (29.1) [19.8; 39.9]
Male (n = 618) [95% CI]	110 (17.8) [14.9; 21.0]
Female (n = 588) [95% CI]	219 (37.2) [33.3; 41.3]

[Table: Patient compliance, and treatment-emergent adverse events]
Disclosure: JR has received honoraria/consultation fees from Ipsen, Polpharma, Takeda, Alfa Wasserman, Krka, Promed, and travel grants from Abbvie and Alfa Wassermann. MCWS and SS have no conflicts of interest to declare. AK and VP are employees of Ipsen. WF has received honoraria for speaking from Abbott, AbbVie Deutschland, Bio Merieux, Boehringer Ingelheim, Falk, Kibion, Norgine, Pfizer, and Reckitt Benckiser, and had advisory roles with Norgine and Pfizer.

P0459 OPTIMAL TIMING OF ADDING SIMETHICONE FOR BETTER BOWEL PREPARATION USING POLYETHYLENE GLYCOL PLUS ASCORBIC ACID; A DOUBLE- BLIND RANDOMIZED TRIAL

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Introduction: Colonic bubbles are common and obscure the colonic mucosa during colonoscopy with polyethylene glycol plus ascorbic acid (PEG-Asc). Antifoaming agent, simethicone was known to enhance colonic visualization during colonoscopy.
Aims and Methods: The aim of this study was to determine the optimal timing to add simethicone for improving bowel preparation during colonoscopy using PEG- Asc. This single-center, prospective, double-blind, randomized study enrolled the patients undergoing elective colonoscopy between January 2017 and January 2018. All patients were taken polyethylene glycol plus ascorbic acid (PEG-Asc) for bowel preparation. They were randomly assigned to 3 groups; received only PEG-Asc (Control) or adding simethicone in the morning on the day of colonoscopy (PEG-S1) or adding simethicone in the evening a day before colonoscopy (PEG-S2). The primary outcome measure colon cleansing quality using air bubble grades in 5 colonic segments (cecum, ascending, transverse, descending and rectosigmoid colon). The secondary outcomes were adenoma detection rates (ADR), polyp detection rates (PDR) and diminutive adenoma/polyp detection rates (diminutive ADR/PDR).
Results: 240 patients were randomly allocated to the 3 groups; 6 patients were withdrawn. Of 234 patients evaluated, 78 patients were control group, 79 patients were PEG-S1group and 77 patients were PEG-S2 group. Air bubble grades of all colonic segments were most significantly lowest in PEG-S2 group. There was no significant difference in the ADR and PDR among the 3 groups. However, diminutive PDR was significantly higher in PEG-S2 group compared with other 2 groups (Control: 11.5% vs PEG-S1: 8.9% vs PEG-S2: 23.4%, p = 0.038).
Conclusion: Bowel preparation with PEG-Asc plus simethicone eliminates air bubble effectively. Furthermore, adding simethicone at the optimal time could improve the quality of bowel preparation, especially enhancing diminutive PDR.
Disclosure: Nothing to disclose

P0460 PUBLIC ATTITUDES TO COLONOSCOPY: HOW MUCH BOWEL PREPARATION LIQUID MUST BE DRUNK BEFORE A COLONOSCOPY?

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Introduction: In European countries, public beliefs and attitudes to bowel preparation before colonoscopy are poorly understood. A survey was conducted to address the issue.
Aims and Methods: An online survey was conducted in 5 large European countries (UK, Germany, France, Spain, and Italy), among members of the general public who had not had a colonoscopy. 1 of 10 questions asked: Before a colonoscopy can be undertaken, the colon must be cleaned by the patient drinking a bowel preparation solution. How much of the bowel preparation liquid do you think a patient needs to drink prior to the procedure? The survey targeted 500 people aged 18–70 years from each country, and aimed to balance respondent groups for region, gender, age and occupation.
Results: Among 53,795 invited persons, 18,650 (35%) responded to the survey and 2,500 (5%) completed the survey who had never had a colonoscopy before across the 5 assessed EU countries. Among these, 13% respondents believed they had to drink maximally 1 half-litre bowel preparation liquid. 16 percent believed they must drink between 1 half and 1 litre, while 38% thought they must drink 1 whole litre. Fewer, 22%, expected to drink 2 litres, and only 12% believed they must drink more than 2 litres. Taken together, nearly 9 out of 10 potential colonoscopy patients expected to drink maximally 2 litres of bowel preparation liquid to accomplish their colon cleansing. The national levels were comparable except for Germany, where only 8 out of 10 respondents expected to drink maximally 2 litres.
Conclusion: The vast majority of people in UK, Germany, France, Spain, and Italy expect to drink 2 litres or less of a bowel preparation liquid before a colonoscopy. Such widespread public beliefs could potentially collide with clinical reality where patients must often drink 3 litres or more to adequately prepare their bowels. The new availability in Europe of highly effective low-volume bowel preparations such as the 1 L polyethylene glycol NER1006 can help close this perceptual gap whilst ensuring reliable cleansing success at a reduced fluid volume intake.
Disclosure: Amlani B, employee of Norgine; Radaelli F, speaker and advisory board member for Norgine, Boehringer Ingelheim; Bhandari P, nothing to disclose.

P0461 GENOMIC MEDICINE IN GASTROENTEROLOGY, PRESENT AND FUTURE: A NATIONWIDE SURVEY OF UK GASTROENTEROLOGY TRAINEES

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Introduction: Genomics and personalised medicine are increasingly relevant for patients with gastroenterological conditions. In the United Kingdom, the higher training curricula of other specialities (e.g. cardiology and oncology) have been revised with the addition of modular training in genomics. We aim to capture the current state of genomics training in gastroenterology in the UK to review current understanding, clinical experience and long-term training needs of trainees, and to assess their preparedness for future consultant practice.
Aims and Methods: A web-based nationwide survey of all UK Gastroenterology specialty trainees was carried out in November and December 2017, supported by the British Society of Gastroenterology national training committee.
Results: 100 trainees (representing 15.2% of the 658 UK gastroenterology trainees) across 17 of 18 regions responded to this survey, representing a full range of gastroenterology registrar training levels.
Only 9% and 16% of trainees believe that their local training programme adequately prepares them for future clinical practice utilising genomic medicine and personalised medicine respectively. Barriers identified (with percentage agreeing or strongly agreeing in parentheses) include the need for greater education of trainees (95%), inadequate clinical guidance to base interventions on the results of genomic testing (53%), concerns over misinterpretation by patients (43%) and overuse/misuse of testing by clinicians (34%).
When assessing current mainstream genetic and personalised tests, trainees felt prepared to perform *HFE* genotyping (98%), assess TPMT status (97%), and

interpret HLA subtyping for suspected coeliac disease (85%). However, only a minority of trainees felt prepared to perform the following investigations: polyposis screening (34%), hereditary pancreatitis screening (30%), testing for Lynch Syndrome (33%), and *KRAS* testing for colorectal cancer (20%). For their future clinical practice, 76% of trainees did not know what mainstreaming of genomics would entail, with only 6% of trainees having recruited patients for the UK 100,000 genomes project.

Most trainees would support having dedicated training days on genomic medicine (83%), formal training provisions for the mainstreaming of genomic testing (64%), an update to both the UK gastroenterology specialty training curriculum as well as the specialty examinations (57%), and better-defined pathways for referral to local genomic services (91%).

Conclusion: Most British gastroenterology trainees feel ill-equipped to practise genomic and personalised medicine as consultants, at a time of progressive mainstreaming of genomic practice in our specialty. We propose that the UK gastroenterology specialty curriculum requires specific revision to prepare trainees for genomics in their future clinical practice, and recommend that other European gastroenterology training programmes also assess their local genomics training requirements.

Disclosure: Nothing to disclose

Reference

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P0462 *FEAR-OF-CANCER*-RELATED PSYCHOLOGICAL BARRIERS TO COLONOSCOPY IN FECAL OCCULT BLOOD TEST (FOBT)-POSITIVE *COLONOSCOPY REFUSERS*

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Introduction: Up to 25% of fecal occult blood test (FOBT)-positive participants of colorectal cancer (CRC) screening programs fail to show up for colonoscopy. For many of them, the main obstacle is not lack of information, oppositional personality or denial, but rather a fear of finding out that they have cancer. The fear paralyzes their ability to start the work up. At the same time, they are completely aware of and frightened of the potential consequences of not undergoing the test. This unresolved emotional stress leads to feelings of anxiety and guilt, and often result in coping by self-explanations as to why the need for the test may not apply in their case, doing repeated FOBTs in the hope the results will be normal, and procrastination - the practice of performing less urgent tasks in preference to more urgent ones, to transfer attention away from it. Physicians often mistake coping mechanisms as patient resistance.

Motivational interview (MI) is a psychological intervention technique designed to facilitate a patient's awareness of the barriers, and aimed to challenge the patient to take steps toward the desired action. Our goal was to examine the efficacy of a brief MI-style telephone intervention in assisting patients to overcome this barrier.

Aims and Methods: Our study comprised 50 consecutive participants of the National CRC screening program who were reported FOBT-positive, and failed to show up for colonoscopy. Patients who completed colonoscopy within 48 months prior to FOBT were excluded.

Participants were randomized 3:1 to an intervention group (a single 5–10 minute telephone call session delivered by a medical psychologist specially trained in MI and problem-solving techniques), and a control group (control for attention; received a telephone call from administrator offering assistance in scheduling the test). The primary outcome was documentation of a colonoscopy, obtained by the 3-month follow-up chart review.

Results: 50 consecutive average CRC-risk patients aged 50–75 years were enrolled. 37 were enrolled for intervention and 13 for control.

The reported barriers for colonoscopy were (no. of patients):

Lack of information, 2
Denial, 1
Oppositional personality, 3
Fear of cancer-related stress, 31
Of these,
Repeated FOBT came back normal, 6
I have an alternative explanation for the result, 5
Would not fight the destiny, 5
Procastination, 15

14 of the 37 patients (38%) approached by the MI agreed to, and underwent colonoscopy. Advanced adenomata were found in 2 (14%), and multiple diminutive adenomata in 1 (7%).

Additional 10 patients (27%) agreed to schedule colonoscopy yet failed to complete the test within the study time-lines. 5 patients expressed significant emotional stress: 3 patients scheduled then cancelled the test, and another 2 stated that they have no emotional strength to fight the destiny.

13 patients (37%) persisted in their refusal for colonoscopy; 5 (38%) stated that their initial stress was relieved by a repeated FOBT and 3 (28%) replied that they would not fight the destiny.

None of the 13 patients in the control group agreed, neither completed colonoscopy within the study period.

Using Fisher's exact test for difference in colonoscopy completion ratio we found that patients approached by MI had a significantly higher probability to complete colonoscopy ($p = 0.007$).

Conclusion: Fear-of-cancer-related psychological barriers are an important obstacle to completion of work-up in FOBT-positive patients. MI is an efficient and valuable tool, and in our cohort helped 38% of patients to overcome this barrier.

Disclosure: This work was supported by Israel Cancer Association research grant

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P0463 PREVENTING COLON CANCER VS. EARLY DIAGNOSIS, WHAT IS BEST? A META-ANALYSIS OF THE U.S. PREVENTIVE SERVICES TASK FORCE EVIDENCE REPORT ON SCREENING TESTS

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Introduction: As of 2009, 19 out of 27 EU countries had a program for colorectal cancer (CRC) screening, with at least 3 countries currently using flexible sigmoidoscopy (FS). FS is the only cancer screening test proven to reduce all-cause mortality in randomized controlled trials. We hypothesize that this unique all-cause mortality reduction is attributable to colorectal cancer prevention rather than early detection.

Aims and Methods: Exploration of the relationship between mortality reduction and CRC prevention in randomized controlled trials of CRC screening. Study Design: Random effects meta-analysis with correlation of study outcomes using Pearson correlation coefficient followed by linear regression for statistically

Abstract No: P0463

Study/Subgroup	Screening		Usual Care		Weight	RR [95% CI]
	Deaths	Total	Deaths	Total		
FS Trials						
Schoen 2012 (PLCO,11.9y)	9390	77445	9627	77455	10.9%	0.976 [0.950, 1.002]
Segnan 2011 (SCORE,10.5y)	1202	17136	1233	17136	2.1%	0.975 [0.903, 1.052]
Atkin 2010 (UKFSST,11.2y)	6775	57099	13768	112939	10.6%	0.973 [0.947, 1.0002]
Holme 2014 (NORCAPP [50–54],11.2y)	427	6920	2387	37131	1.3%	0.960 [0.869, 1.061]
Holme 2014 (NORCAPP [55–64],11.2y)	1756	13652	5375	41089	4.4%	0.983 [0.935, 1.034]
Total (95% CI)	**19550**	**172252**	**32390**	**285750**	**29.3%**	**0.975 [0.958, 0.992]**
Heterogeneity: Tau 2 = < 0.0001; Chi2 = 0.22, df = 4 (p = 0.99); I2 = 0% Test for overall effect: Z = −2.88 (p = 0.0040)						
FOBT						
Shaukat 2013 (Minnesota,30.0y)	22076	31157	10944	15394	20.2%	0.997 [0.984, 1.009]
Scholefield 2012 (Nottingham,19.5y)	40681	76056	40550	75919	22.4%	1.001 [0.992, 1.011]
Lindholm 2008 (Goteborg,15.6y)	10591	34144	10432	34164	13.1%	1.016 [0.993, 1.039]
Kronborg 2004 (Funen,17.0y)	12205	30967	12248	30966	15.0%	0.996 [0.977, 1.016]
Total (95% CI)	**85553**	**172324**	**74174**	**156443**	**70.7%**	**1.001 [0.992, 1.010]**
Heterogeneity: Tau 2 = < 0.0001; Chi2 = 2.33, df = 3 (p = 0.51); I2 = 0% Test for overall effect: Z = 0.22 (p = 0.83)						

significant correlations. Setting or Dataset: Randomized controlled trials specified in the U.S. Preventive Services Task Force 2016 Evidence Report for Colorectal Cancer Screening. Patients: 786,769 normal risk males and females age 45 to 80 years. Interventions: CRC screening with FS or fecal occult blood test (FOBT). Main and Secondary Outcome Measures: All-cause mortality, CRC incidence, mortality attributed to CRC, quantitative comparison of these outcomes for different tests, and correlations of these outcomes.
Results: FS reduces all-cause mortality (relative risk [RR], 0.975; 95% CI, 0.958–0.992) and reduces CRC incidence (RR, 0.79; 95% CI, 0.74–0.84) at 10.5–11.9 years of follow-up, with an all-cause mortality reduction which shows a strong linear correlation with CRC incidence reduction (R, 0.95; 95% CI 0.42–0.99). FOBT does not reduce all-cause mortality (RR, 1.001; 95% CI, 0.992–1.010) nor CRC incidence (RR, 0.96; 95% CI, 0.89–1.02) but does reduce mortality attributed to CRC (RR, 0.84; 95% CI, 0.78–0.91) at 15.6–30.0 years.
Conclusion: All-cause mortality reduction displays a dose-response relationship with CRC prevention and regression analysis indicates that CRC prevention is the sole mechanism of action effecting all-cause mortality in these trials. Early detection of CRC does not appear to reduce all-cause mortality. These findings should inform updated recommendations for effective CRC screening in populations.*[All-Cause Mortality for Randomized Controlled Trials of Flexible Sigmoidoscopy and Fecal Occult Blood Test]*
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00-17:00
Oesophageal, Gastric and Duodenal Disorders I - Hall X1____

P0464 ANCILLARY D2-40 AND ELASTIN STAINS CAN IMPROVE INTEROBSERVER AGREEMENT AND DETECTION OF LYMPHOVASCULAR INVASION IN EARLY GASTRIC CANCER

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Introduction: The presence of lymphovascular invasion (LVI) is the most influential risk factor for lymph node metastasis (LNM) and has been recognized as a potential prognostic factor in patients with early gastric cancer. There is accumulating evidence that immunohistochemical (IHC) and elastin stains markedly increase the detection of LVI, and LVI detected by these ancillary stains has stronger correlation with LNM than that by hematoxylin-eosin (HE) stain alone [1]. However, interobserver variability of assessment for LVI could be expected [2], and little is known about that in gastric cancer.
Aims and Methods: The aim of this study was to investigate the interobserver agreement and detection of LVI between 2 pathologists by adding IHC and elastin stain to HE stain.
A total of 60 lesions were randomly selected from lesions which were resected using endoscopic submucosal dissection (ESD) and pathologically diagnosed as submucosal invasive cancer between April 2014 and December 2016. 2 pathologists (A: expert, B: trainee) who were blinded to the clinicopathological information reviewed the specimens. First, they independently assessed lymphatic vessel invasion (LI) and venous vessel invasion (VI) with HE slide alone. Second, they reviewed corresponding slides of IHC stain (D2-40) and elastin stain (Elastica van Gieson; EVG). Interobserver agreement of LI and VI was evaluated using κ coefficients, respectively.
Results: Interobserver agreement of LI and VI in HE slides was poor ($\kappa = 0.35$ for LI; $\kappa = 0.35$ for VI). After reviewing D2-40 and EVG slides, interobserver agreement was improved to good ($\kappa = 0.64$ for LI, and $\kappa = 0.64$ for VI). The detection rate of LI was 23.3% for pathologist A and 18.3% for pathologist B in HE slides. By adding D2-40 slides, the detection rate of LI elevated to 36.7% and 36.7%, respectively. The detection rate of VI was 10% and 6.7% in HE slides. The observation of EVG slides improved the detection rate to 25% and 25%, respectively. Among 40 patients who underwent additional gastrectomy with lymph node dissection after ESD, 3 patients had lymph node metastasis. Although 2 of 3 cases were assessed as LI negative by both 2 pathologists in HE slide, LI was detected in D2-40 slide.

	Staining	κ-Value
Lymphatic vessel invasion	HE	0.346
	D2-40	0.641
Venous vessel invasion	HE	0.348
	EVG	0.644

[Interobserver agreement of lymphatic and venous vessel invasion]
Conclusion: Additional D2-40 and EVG stains improved interobserver agreement between expert and trainee in the histological LVI diagnosis in early gastric cancer. Furthermore, trainee's detection rate increased similarly to the level of the expert.
Disclosure: Nothing to disclose

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P0465 LYMPHOVASCULAR INVASION IN EARLY GASTRIC CANCER: INTEROBSERVER AGREEMENT AMONG EXPERT PATHOLOGISTS

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Introduction: Lymphovascular invasion (LVI) in gastric cancer is the most intensive risk factor of lymph node metastasis and has the greatest influence in determining whether to perform radical gastrectomy with lymph node dissection. [1] Although the interobserver variability of judgment for LVI could be expected even among expert pathologists [2], little is known about the degree of the diagnostic agreement in gastric cancer. Our hypothesis is that the agreement on examination of the hematoxylin and eosin (HE) slides is poor, however the use of ancillary immunohistochemical and histochemical stains improve the interobserver agreement.
Aims and Methods: The aim of this study was to investigate the interobserver agreement in the diagnosis of LVI in gastric cancer among expert pathologists. We randomly selected a total of 60 patients with a postoperative diagnosis of submucosal invasive gastric cancer who underwent endoscopic submucosal dissection (ESD) at Shizuoka Cancer Center Hospital between April 2014 and December 2016. 2 experienced gastrointestinal pathologists (pathologist A and B) who were masked to clinical information independently reviewed the HE slides (one slide from each case). The ancillary staining (D2-40 and EVG) on the corresponding section were then examined. D2-40 was applied for the detection of lymphatic invasion and EVG was used for the detection of venous invasion. The diagnostic agreement was evaluated using κ statistics between 2 pathologists.
Results: The interobserver agreement was 0.59 (95% CI: 0.34–0.84; moderate) in HE and 0.89 (95% CI: 0.77–1.00; excellent) in HE + D2-40. The detection rate of lymphatic invasion in HE was 23.3% for pathologist A and 25.0% for pathologist B. After reviewing D2-40 slides, the detection rate of lymphatic invasion increased in both examiners (A, 36.7%; B, 35.0%). Regarding venous invasion, the interobserver agreement was 0.21 (95% CI: 0.00–0.81; poor) in HE and 0.67 (95% CI: 0.44–0.90; good) in HE + EVG. The detection rate of venous invasion was 10.0% for pathologist A and 3.3% for pathologist B in HE staining. However, the detection rate was also raised to 25% for pathologist A and 20% for pathologist B by adding EVG to HE slides. Among 40 patients who underwent additional surgical resection with lymph node dissection, there were ten cases which were diagnosed as negative for LVI in HE slides and positive for LVI in D2-40 and/or EVG. Lymph node metastasis was histologically confirmed in the dissected specimens in 2 of these 10 patients.
Conclusion: The ancillary staining (D2-40 and EVG) dramatically improved the interobserver agreement among expert pathologists in gastric cancer. The higher detection rate with D2-40 and EVG could lead efficient identification of high-risk patient of lymph node metastasis.
Disclosure: Nothing to disclose

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P0466 IDENTIFYING FGF18 AS A POTENTIAL ONCOGENE AND MIR-590-5P TARGET IN GASTRIC TUMORIGENESIS

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Introduction: Fibroblast growth factors (FGFs) and their receptors are significant components in signal transduction cascade and associated with fundamental cellular processes. FGF18 plays distinctively in modulating the activity of both tumor cells and tumor microenvironment.
Aims and Methods: This study aims to comprehensively investigate the expression and functional role of FGF18 in gastric cancer (GC) and elucidate its regulatory mechanisms. The expression of FGFs and FGFRs were detected among GC cell lines by expression microarray. The clinical relevance of FGF18 in GC was acquired and analyzed from online databases. To identify the biological function of FGF18 in GC cells, siRNAs against FGF18 were applied in the functional assays including cell proliferation, monolayer colony formation, cell invasion, cell-cycle distribution, and anti-tumor drug sensitivity. Expression Microarray was then employed in siFGF18 transfected cells and negative controls to identify the associated signaling pathways. The expression of the key factors in these pathways were validated by qRT-PCR, and the activities of related effectors were examined by Western blot and immunofluorescence. The miRNA that potentially binds to the 3'UTR of FGF18 was predicted by the miRNA database miRDB. The regulation of FGF18 by putative miRNA was confirmed by qRT-

PCR, Western blot, and dual luciferase activity assays. The *in vivo* functional roles of FGF18 and miRNA were demonstrated by the xenograft formation assay.
Results: FGF18 showed higher mRNA level than that of other FGF members in GC cell lines. The relative mRNA expression of FGF18 was upregulated in 7 out of 9 (77.8%) GC cell lines. In primary GC samples, FGF18 was overexpressed in genomically stable and chromosomal instability subtypes of GC and its overexpression was associated with poor survival in GC patients. FGF18 shows gene amplification in some primary samples but the increased copy number changes did not positively correlate with its mRNA upregulation. Knocking down FGF18 led to inhibition of cell proliferation, monolayer colony formation, and cell invasion ability. In addition, siFGF18 induced G1 phase cell-cycle arrest and increased anti-cancer drug sensitivity. The MEK-ERK signaling was suppressed in the siFGF18 transfectants. Expression microarray profiling analysis revealed that silencing FGF18 activated ATM pathway but quenched TGF-β signaling pathway. In ATM signaling, ATM, CTBP1 and TP53BP1 were upregulated in siFGF18 transfected cells. In TGF-β signaling pathway, TGFBR1, TGFBR2, ARRB2 and BAMB1 were downregulated in siFGF18 transfectants. After siFGF18 transfection, the phosphorylated ATM and downstream factor γH2AX were activated, while phosphorylated Smad2 and Smad3 were decreased. FGF18 was further confirmed to be a direct target of miR-590-5p. Their expressions showed a negative correlation in primary GC samples ($r = -0.278$, $p < 0.001$, $n = 367$). miR-590-5p suppressed the tumorigenic properties of GC cells. Re-overexpression of FGF18 partly reversed the tumor-suppressive effect of miR-590-5p.
Conclusion: FGF18 is overexpressed and plays a tumorigenic role in gastric carcinogenesis. The activation of FGF18 in GC is partly due to the silence of a tumor-suppressive miRNA, miR-590-5p. These findings comprehensively deciphered the regulatory mechanism between FGF18 signaling and miR-590-5p, which might imply a constructive therapeutic intervention in GC.
Disclosure: Nothing to disclose

P0467 ABERRANT EXPRESSION OF SPP1 THROUGH DOWNREGULATION OF HELIOS IN GASTRIC CANCER

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Introduction: Gastric cancer remains a cancer of high incidence and poor long-term survival in Taiwan, despite of the effort to eradicate *H. pylori* infection. Helios belongs to Ikaros family proteins, which perform as tumor suppressors because many studies reported that abnormal expressions of these proteins. Helios can express in regulatory T (Treg) cells and expression of Helios enhanced the suppressive function of Treg. Except the expression in T cells, in our previous study showed that higher expression of Helios in gastric cancer cells with better survival. These tumor suppressive pathways regulated by Helios shall be further examined.
Aims and Methods: To elucidate the Helios function in gastric cancer cells, we used IKZF2-targeting CRISPR-Cas9 system to knock-out Helios expression in AGS cell line. The CCK8-dependent proliferation assay, wound healing assay and invasion assay were performed. We further analyzed the genes expression between AGS and AGS-KO cells by next generation sequencing (NGS), and finally validated the gene expression in AGS and AGS-KO cells by QRT-PCR.
Results: The proliferation was inhibited, while the mobility and invasiveness were increased in Helios knockdown AGS cells compared to parental cells. The data of NGS indicated an increase of SPP1 expression upon depletion of Helios, and SPP1 mRNA was significantly higher expression in knockdown AGS cells. SPP1 has been shown to promote cancer progression and may be a therapeutic target.
Conclusion: Together, our finding illustrates the molecular pathway controlling SPP1 expression and the protective role of Helios in gastric cancer.
Disclosure: Nothing to disclose

P0468 METHYLOMICS ANALYSIS IDENTIFIES SPG20 AS A SENSITIVE NON-INVASIVE BIOMARKER FOR EARLY DETECTION OF GASTRIC CANCER

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Introduction: Gastric cancer is one of the second leading cause of cancer worldwide. Our previous studies showed that aberrant activation of JAK/STAT3 signaling confer epigenetic silencing of its target genes in gastric cancer. However, the clinical significance of aberrant epigenetic silencing of STAT3 targets in gastric cancer is not fully understood.
Aims and Methods: To identify STAT3 targets that are epigenetically silenced by activation of STAT3 in gastric cancer, Illumina 850K methylation microarray was performed in AGS gastric cancer cells and cells depleted with STAT3. Bisulphite pyrosequencing or methylation-specific PCR (MSP) was also performed to examine promoter methylation of the identified targets in tissue or serum/plasma samples from patients with gastric cancer ($n = 53$), IM ($n = 8$), gastritis ($n = 12$) and a panel of gastric epithelial cells including cancer cell lines. While epigenetic drug treatment by DNMT inhibitor together with qRT-PCR was used to examine the role of DNA methylation in the expression of the identified targets.
Results: Integrative methylation microarray and computational analysis identifies SPG20 as one of the STAT3 targets that showed promoter hypomethylation in STAT3 depleted AGS cells. To confirm our results, bisulphite pyrosequencing found that promoter region of SPG20 was hypermethylated in a panel of gastric cancer cell lines including AGS cells but not in GES immortalized gastric epithelial cells. As expected, SPG20 was downregulated in a panel of gastric cancer cell lines in which the expression can be restored by the treatment of DNMT inhibitor thus suggesting that SPG20 is epigenetically silenced by promoter methylation. To determine the clinical significance of SPG20 methylation in gastric cancer, we examined promoter methylation of SPG20 in 53 paired of gastric cancer patient samples, 8 samples of intestinal metaplasia (IM) and 12 samples of gastritis by bisulphite pyrosequencing. Interestingly, promoter methylation of SPG20 is significantly higher in cancer tissues than that of gastritis ($p < 0.01$) and adjacent normal ($p < 0.01$). Unexpectedly, there is no association between SPG20 methylation and tumor grade, stage and patient's survival suggesting that methylation of SPG20 may be an early event. To confirm this hypothesis, we performed methylation specific PCR (MSP) in cfDNA isolated from serum samples of gastric cancer ($n = 53$), IM ($n = 3$) and gastritis ($n = 9$). Interestingly, SPG20 methylation showed a progressive increase in tumor progression (SPG20 methylation% in gastritis = 37.5%, IM = 66.7%, cancer = 91.7%, $p < 0.05$).
Conclusion: Taken together, SPG20, a potential STAT3 target, is frequently hypermethylated in gastric cancer. Methylation of SPG20 may be a novel non-invasive biomarker for early detection of gastric cancer.
Disclosure: Nothing to disclose

P0469 2,4-DIAMINO-QUINAZOLINE, A SMALL-MOLECULE INHIBITOR OF WNT/β-CATENIN SIGNALING, REDUCES PROLIFERATION AND MIGRATION/INVASION BEHAVIOR OF GASTRIC CANCER

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Introduction: Gastric cancer is among the most treatment-refractory epithelial malignancies. Aberrant activation of Wnt/β-catenin signaling has been implicated in a variety of human cancers, including gastric cancer.
Aims and Methods: The purpose of this study is to develop optimized strategies for the use of Wnt/β-catenin signaling inhibitors to treat gastric adenocarcinomas. In this study, we tested the efficacy of 2,4-diamino-quinazoline for selective antagonistic effect on Wnt/β-catenin signaling response in gastric cancer cells
Results: Here we first found that the elevated lymphoid enhancer factor 1 (Lef1) expression was associated with TNM (tumor-node-metastasis) stage of gastric cancer. Then we screened for small-molecule compounds that acted against Wnt/β-catenin pathway and consequently suppressed the growth of gastric cancer cells. We identified a selective inhibitor of Wnt/β-catenin signaling, 2,4-diamino-quinazoline, which decreased the expression of Wnt/β-catenin target genes such as Axin2, Myc, and Lgr5, and resulted in the inhibition of gastric cancer cell proliferation through the apoptotic pathway. Additionally, 2,4-diamino-quinazoline also exhibited an inhibitory effect on the migration/invasion of gastric cancer cells. *In vivo* xenograft assay also showed that 2,4-diamino-quinazoline inhibited the growth of the grafted tumor when compared to the control.
Conclusion: Taken together, 2,4-diamino-quinazoline could have significant therapeutic activity against gastric cancer via suppressing Wnt/β-catenin signaling pathway.
Disclosure: Nothing to disclose

P0470 THE CYTOTOXIC EFFECT OF HYPERTHERMIA IN ADDITION TO CISPLATIN IS ENHANCED BY PRIOR HO-1 SILENCING IN OVARIAN BUT NOT GASTRIC CANCER CELLS

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Introduction: Hyperthermal intraperitoneal chemotherapy (HIPEC) is a treatment method to cure intraperitoneally spread gastric and ovarian cancer. Although a number of clinical trials report satisfactory results, data remains controversary. Heat shock proteins are known being responsible for cellular resistance to temperature. HO-1 is a heat shock protein, which is induced by hyperthermia.

Aims and Methods: The aim of our *in vitro* study was to clarify the response of gastric and ovarian cancer cells to hyperthermia and cisplatin, following the modulation of HO-1 expression.
AGS (gastric adenocarcinoma), OVCAR-3 (ovarian adenocarcinoma) cells were treated with different temperature regimens (normothermia: 37°C; and hyperthermia: 43^0C) either in isolation or combined with IC_{50} of cisplatin for one hour. Prior the treatment experimental groups of cells were HO-1 silenced by siRNA transfection. MTT was used to evaluate cells viability. Apoptosis was assessed by flow cytometry, using Annexin V-PE and 7ADD. Real-time cell analyzer was used to evaluate the changes of viable cell rates in real time manner. HO-1 expression was detected by QRT PCR and Western blot.
Results: Cisplatin increased *HO-1* expression by 3.73-fold in normothermia and 2.4-fold in hyperthermia for OVCAR-3 cells. Hyperthermia stimulated the increase of *HO-1* expression unsignificantly by 1.34-fold. *HO-1* expression was not affected neither by temperature, nor by cisplatin in AGS cells. In OVCAR-3 protein level, HO-1 expression was increased similarly as for RNA - by cisplatin and temperature. In AGS cells, temperature was the only trigger, increasing the level of HO-1 protein. The exposure of OVCAR-3 cells to cisplatin and temperature at 43°C resulted in drop of cells viability by 36% and *HO-1* silencing enhanced this effect by additional 20%. In AGS cells, HO-1 silencing reduced the viability by 16% at 37°C. HO-1 silencing in normothermia increased apoptosis rates in cisplatin treated OVCAR-3 and AGS cells by 2.07-fold and 2.63-fold. Silencing HO-1 in hyperthermia and treating with cisplatin, increased apoptosis rates by 3.09-fold and 6.84-fold in OVCAR-3 and AGS cells respectively. Real time cell analysis showed that exposure to cisplatin gradually decreased cell index of OVCAR-3 and AGS (HO-1 silenced) cells in normothermia. Hyperthermia enhanced this effect in OVCAR-3 cells, while AGS cell index stayed similar
Conclusion: Cytoprotective protein HO-1 is induced in cancer cells by different stressors in variable manner. In tumors with highly inducible *HO-1*, prior silencing of this gene could improve the cell response to hyperthermia and cisplatin.
Disclosure: Nothing to disclose

P0471 HEALTHY CHILDREN FROM 4 TO 12 YEARS OF AGE: FECAL CALPROTECTIN AND EOSINOPHIL-DERIVED NEUROTOXIN LEVELS

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Introduction: We have previously reported that young infants have higher concentrations of fecal Calprotectin (fCP) and Eosinophil-Derived Neurotoxin (fEDN) compared to adults. The highest concentrations for both biomarkers were found in infants less than 4 years of age. There was also a large variation in fCP and fEDN concentrations between individual children in the 0 to 4 years age group, which stabilized from 4 years of age onwards.
Aims and Methods: The objective of the current study was to investigate fCP and fEDN levels in healthy children 4 to 12 years of age.
Prospective study including 153 healthy children, 4 to 12 years old, from the general population. Fecal samples (n = 153) were collected, sent to the laboratory no later than 7 days after collection and stored at −20°C until analysis. The extraction procedure was performed with the *Faecal sample preparation kit* (Roche Diagnostics). Fecal CP and fEDN levels in the fecal samples were measured by EliA Calprotectin 2 and an EDN research assay developed on the ImmunoCAP platform, respectively (Thermo Fisher Scientific).
Results: The median (50th percentile) of fCP and fEDN concentrations in the 153 children were 20.31 mg/kg and 0.3 mg/kg respectively. The 95th Percentile of fCP and fEDN concentrations were 104.85 mg/kg and 2.01 mg/kg. We did not find a statistically significant association between the median fCP concentration and age ($p = 0.31$) or gender ($p = 0.97$), or for the median fEDN concentration and age ($p = 0.08$) or gender ($p = 0.059$). However we found a statistically significant association between the 95th percentile of fCP and fEDN concentrations with age ($p < 0.001$), and this association was stronger at younger ages and decreased at around 80 months of age. We developed a nomogram showing that the lower 95th percentile of fCP and fEDN concentrations were 108.5 and 1.7 mg/kg, respectively, in the age group 4 to ≤6 years, and 66.2 and 1.1 mg/kg, respectively, in the age group >6 to 12 years.
Although the median concentrations for fCP were lower than the 50 mg/kg cutoff value proposed for adults, there was a percentage (21%) of children with fCP concentrations above 50 mg/kg. Therefore, the 95th percentiles of fCP concentrations for the age range of 4 to 12 years were higher than the cutoff value for adults. However, in agreement with our previous study, the fCP concentrations were lower, and showed less variability, in the age group of 4 to 12 years compared to the fCP concentrations in children below the age of 4 years (*JPGN* 2017 Oct;65(4):394–398).
Conclusion: Based on the results and a developed nomogram, 2 different age groups for evaluation of fCP and fEDN in children aged 4 to 12 years are suggested: from 4 to ≤6 years, and from >6 to 12 years. We also suggest reference values for fCP and fEDN representing the lower value of the 95th percentile for each age group: 108.5 and 1.7 mg/kg, respectively, in the age group 4 to ≤6 years, and 66.2 and 1.1 mg/kg, respectively, in the age group >6 to 12 years. For fCP, the suggested reference values are higher than the 50 mg/kg cutoff value proposed for adults.
Disclosure: Helena Ekoff and Niclas Rydell are employed at Thermo Fisher Scientific. The remaining authors report no conflicts of interests.

P0472 EFFECTIVENESS OF REBAMIPIDE IN THE PREVENTION OF ESOPHAGEAL STRICTURE FORMATION IN ADVANCED CORROSIVE ESOPHAGITIS: A PROSPECTIVE RANDOMIZED CONTROL STUDY

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Introduction: Corrosive esophagitis causes significant morbidity with grades 2b and 3 esophagitis developing strictures in 70–100% of cases. According to the Philippine National Poison Management and Control Center 2009 report, each year 23% of 500 poisoned patients referred to them are due to caustic ingestion (1). While information on the effect and outcome of esophageal corrosive injury have been well documented, there is no clear evidence on the management of caustic esophageal injury, in particular, the prevention of esophageal stricture. However, animal studies show that suppressing inflammation and fibrosis can prevent stricture formation (2). Rebamipide, an anti-ulcer agent, has been shown to stimulate prostaglandin generation, increases epidermal growth factor expression, increases blood flow, and scavenges active oxygen radicals thereby reducing inflammation (3). Moreover, based on animal studies rebamipide has been shown to reduce the inflammation and decrease the mucosal permeability associated with acute reflux esophagitis (4-5).
Aims and Methods: This study aims to determine the effectiveness of rebamipide in preventing stricture formation in advanced corrosive esophagitis.
We conducted a prospective, assessor-blinded, randomized control study. Proper approval from the Institutional Review Board and written informed consent from the patients were obtained. 37 adult patients with grades 2B to 3B corrosive esophagitis admitted in our institution were included. They were randomly allocated into 2 groups. First group (n = 18) received conventional proton pump inhibitor (PPI) therapy with rebamipide (PPI+rebamipide group) while second group (n = 19) received only conventional PPI therapy (PPI group), both for 3 weeks duration. Endoscopists blinded to group allocations and damage severity before treatment performed upper endoscopy (EGD) on Days 21 and 60. Presence of dysphagia, number, length and stricture location were recorded. Descriptive statistics, Independent sample T-test, Mann-Whitney U test and Chi-square test were the analysis used. Null hypothesis was rejected at 0.05 α-level of significance. STATA 15.0 was used for data analysis.
Results: 34 patients were included in the final analysis. Dysphagia and esophageal stricture at Day 60 were significantly greater with PPI group versus PPI+rebamipide group (47% vs 5.88%, $p = 0.017$). Although the median length of esophageal stricture in the PPI group vs PPI+Rebamipide group at Day 60 is significantly shorter (5 cm vs 8 cm; $p = 0.034$), there were still significantly more patients with stricture formation in the PPI group (8 vs 1; $p = 0.017$). Presence of gastric stricture was not significantly different between the 2 groups both at Day 21 (23.53% vs 17.65%; $p = 1.00$) and Day 60 (29.41% vs 35.29%; $p = 0.714$). For both dysphagia and esophageal strictures, our data suggests that our number needed to treat to prevent 1 incident of these are at 3.40 patients at day 21 and 2.43 at Day 60.
Conclusion: PPI with rebamipide is effective in preventing dysphagia and esophageal stricture formation among patients with advanced corrosive esophagitis compared to PPI alone. However, this was not effective in preventing gastric stricture formation.
Disclosure: Nothing to disclose

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P0474 EFFECT OF MYD88 DEFICIENCY ON INTESTINAL INFLAMMATION AND MICROBIOTA IN COLITIS MICE

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Introduction: MyD88 is a key signaling adaptor for TLRs and involved in intestinal microbiota-host interaction associated innate and adaptive immune. This study aims at investigating the effect of MyD88 on colonic inflammation and gut flora.
Aims and Methods: MyD88 knockout mice and their wild-type littermates were kept under the same environment except for treated with normal drinking water (WT and MyD88 KO groups) or 3% DSS solution (WT-DSS and MyD88-DSS groups) for 7 days. Disease activity index (DAI) and histological score of colitis (HS) inflammatory cytokines were evaluated to determine the colonic inflammation severity. TGF-β1, EGF, COX-2 and tight-junction (T-J) protein mRNA was measured by qPCR to access epithelial restoration. NF-κB activation was evaluated by Western-blotting and measured by Grey-scale value. Proximal colonic mucosa was used to analyze gut mucosal flora using high-throughput sequencing analysis targeting V4-V5 regions of the bacterial 16S rRNA gene. Statistical analysis was performed using one-way ANOVA analysis and the Post Hoc LSD test or Tamhane's T2 test.
Results: Colonic NF-κB activation was significantly inhibited in MyD88-DSS group as compared to WT-DSS group, suggesting the inhibitory effect of MyD88 deletion on NF-κB activation. However, deletion of MyD88 failed to improve DAI and HS in DSS-colitis mice as compared to WT-DSS group. Besides, the difference of colonic IL-1β,TNF α and IFN γ mRNA expression didn't reach significance in MyD88 deficient mice with or without DSS challenge. TGF-β1, EGF, COX-2 and T-J protein mRNA was not significantly different among 4 groups, suggesting relatively normal epithelial reconstruction ability in WT-DSS, MyD88 KO and MyD88-DSS groups as compared to WT group. Colonic mucosal microbiome analysis shown that the alpha diversity was not significantly different among 4 groups in terms of diversity index (Shannon and inverse Simpson) and bacterial culture abundance (Chao). At phylum level, the proportion of *Proteobacteria* dramatically elevated to 41.9% in MyD88 KO mice as compared to WT, WT-DSS and MyD88-DSS groups (7.0%, 16.1% and 22.3%, respectively), within which pathegenic bacteria such as *Pseudomonadales*, *Burkholderiales* and *Enterobacteriales* were predominantly increased at order level in MyD88 KO mice. The percentage of probiotics such as *Lactobacillales* was decreased in MyD88 KO group (31.5%) and further dropped to 11.2% and 4.1% in WT-DSS or MyD88-DSS groups as compared to WT (55.5%).
Conclusion: Deficiency of MyD88 inhibited NF-κB activation but not colonic inflammation in mice with colitis possibly due to MyD88 deletion associated pathegenic-riched and probiotics-exhauseted gut microbiota.
Disclosure: Nothing to disclose

P0475 PILOT STUDY ON THE EFFECTIVENESS OF THE COMBINATION OF HYALURONIC ACID, COINDRITIN SULFATE AND POLOXAMER 407 IN SCAR HEALING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF THE ESOPHAGUS IN PORCINE IN-VIVO MODEL

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Introduction: Hyaluronic acid + chondroitin sulfate + poloxamer 407 (HA+CS) has shown efficacy in the repair of microscopically-damaged esophageal epithelium caused by gastroesophageal reflux (GER). However, there are no studies that show efficacy in the repair of macroscopic damage of the mucosa and/or submucosa.
Aims and Methods: Primary Objective: To assess the efficacy of HA+CS in healing scar due to deep submucosal injury after endoscopic submucosal dissection (ESD) of the esophagus in porcine models.
Secondary Objective: To evaluate the efficacy of HA+CS in the prevention of esophageal stenosis secondary to ESD. This was a randomized, experimental, endoscopist- and pathologist-blinded pilot study. Dissection of ¾ of the middle-distal esophagus circumference was performed on 6 anesthetized pigs (female Landrace-Large Whites). In 3 pigs (C1, C4 and C5) 10 ml of HA+CS (1 sachet) was injected on the surface of the eschar, infiltrating it with a syringe on the submucosa of the eschar edges. This was followed by treatment with HA+CS 3 sachets per day + Omeprazole 20 mg/12h po). The other 3 pigs received only the standard treatment, Omeprazole 20 mg/12h po, to avoid potential additional damage from GER. The pigs were kept on a liquid diet for the first 24 hours and then started on a regular diet. After 15 days, an endoscopic evaluation was conducted to assess the degree of stenosis and healing grade using the modified Manchester scale for the clinical evaluation of scars. Finally, histological analysis was conducted by 2 pathologists, following necropsy.
Results: The average weight at the beginning of the study for the HA+CS group vs control group was 44.63 kg and 44.43 kg respectively, and 36.48 kg vs 41.80 kg respectively at the end of the treatment.
There were no differences in the mean size of eschars (9.9 mm in the HA+CS group vs 8.82 mm in control group) or in their location (15.66 mm from the gastroesophageal junction in the HA+CS group vs 11.66 mm in the control group). All the eschars covered more than 50% of the circumference. Stenosis presented in 100% of the cases. In 2 (33.3%) cases, the endoscope could be passed through the stricture (C2 and C6). The score on the modified Manchester scale was 4.3 for the HA+CS group and 3.3 for the control group. Complications: perforation with paraesophageal collection in C4. Histological analysis: Higher inflammatory infiltrate with predominance of neutrophils, lymphocytes, macrophages (acute inflammatory reaction) in the control pigs vs. the pigs treated with HA+CS, in which chronic inflammatory infiltrate (lymphocytes) predominated. In the control group, neovascularization consisted of small to medium vessels and the reorganization of the connective tissue process was in its beginning phase, whereas in the HA+CS group the blood vessels were large and vertically arranged and reorganization of the connective tissue was more advanced, as evidenced by the presence of fibroblasts well organized in parallel lines. 1 of the HA+CS-treated pigs showed re-epithelialization on 1 border (C1).
Conclusion: The histological results suggest that HA+CS promotes the repair of esophageal mucosa after ESD, although a clinically significant difference to control treatment was not shown, as all the pigs developed stenosis. More studies are required, with a larger sample size, to evaluate the efficacy of HA+CS in the repair of macroscopic damage of the mucosa.
Disclosure: This study has been funded by Norgine and has received collaboration from Pentax and SimMedical Canarias

P0476 PANCOLITIS INCREASES THE MORTALITY RISK OF CYTOMEGALOVIRUS COLITIS IN PATIENTS WITHOUT INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE COHORT STUDY

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Introduction: Cytomegalovirus (CMV) colitis typically presents in immunocompromised and inflammatory bowel disease (IBD) patients. Several studies have been conducted on the endoscopic findings of CMV colitis in IBD patients; however, those of CMV colitis in non-IBD patients and their relationship with in-hospital mortality are unclear.
Aims and Methods: We aimed to describe the endoscopic presentation in these patients and to determine the endoscopic predictor of in-hospital mortality. Patients with CMV colitis diagnosed using histology between April 2002 and December 2016 at the Linkou Chang Gung Memorial Hospital, Taiwan, were retrospectively enrolled. Patients diagnosed with IBD during follow-up were excluded. Patient data, including underlying diseases, endoscopic presentation, laboratory data, clinical course, complications and clinical outcomes were collected. The independent risk factors for in-hospital mortality were analysed with logistic regression. The difference of overall survival was compared with Kaplan-Meier survival curve and log rank test. All statistical calculations were performed using SPSS software, version 21 (IBM, Armonk, New York).
Results: 69 patients were enrolled, and 8 IBD patients were excluded. Within the 61 non-IBD patients, 31 were diagnosed by colonoscopy and others by sigmoidoscopy. Ulceration (77%) was the most common endoscopic finding, followed by a cobble stone appearance (19.7%), colitis with/without erosions (9.8%), pseudomembrane (9.8%) and tumour/polyp-like lesions (8.2%). Among the patients who underwent full-length colonoscopy, 35.3% presented with right-sided colitis, 23.5% with left-sided colitis and 32.4% with pancolitis. Pancolitis was identified as a negative predictor of in-hospital mortality (odds ratio, 6.8; 95% confidence interval, 1.233-37.497; $p = 0.028$) and overall survival (log rank $p = 0.018$).
Conclusion: Colonoscopy is recommended for precise CMV colitis diagnosis and outcome prediction in non-IBD patients.
Disclosure: Nothing to disclose

P0477 CLOSTRIDIUM DIFFICILE ISOLATION AND CHARACTERISATION - RESULTS OF A PILOT STUDY

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Introduction: *Clostridum difficile* (CD) infection can lead to severe infectious colitis. Different bacterial toxins and diminished host immune response contribute to symptomatic disease. Inflammatory bowel diseases (IBD), ulcerative colitis, and Crohn's disease are chronic diseases causing a prolonged inflammation of gastrointestinal tract. In these patients colonisation with CD is often confirmed but its role is inconclusive.
Aims and Methods: The aim of the study was to compare CD colonization and selected inflammatory parameters in patients with IBD and other diseases in

hospitalized patients. We obtained fecal samples from 161 randomly selected patients, hospitalized at Department of Gastroenterology during the period between 1/12/2015 - 1/5/2016. Total DNA was isolated from feces and CD was detected using the real time PCR amplification of specific 16S RNA gene and toxigenic strains were confirmed by the amplification of *tcd*B gene. After collecting patient's basic information, inflammatory parameters (neutrophil granulocytes, leukocytes, CRP, erythrocyte sedimentation, albumins, ferritin, and iron) and therapy (pre-and hospital antibiotics, corticosteroids, biological therapy) we divided isolates in 2 groups: IBD group and control group.
Results: The final analysis included 151 samples, (male 75, female 76), 48 (31.8%) from IBD patients and 103 (68.2 %) from control group. In IBD group 23/48 samples (47.9%) were positive for CD; 7 of which (7/48, 14.6%) were *TcdB*+. In the control group 42/103 (40.8%) were positive for CD, 11 of which (11/103, 10.7%) were *TcdB*+. Between the 2 groups, significant differences were confirmed only in the use of corticosteroids and biological therapy prior to hospitalization, $p < 0.001$. Regarding the use of antibiotics prior to hospitalization, differences between the 2 groups were not confirmed, $p = 0.72$. There were no significant differences observed in inflammatory parameters within IBD patients (CD positive compared to CD negative).
Conclusion: The results of our study suggest that IBD patients and patients from the control group were colonized with CD in comparable proportions. The majority of strains were nontoxigenic, which will not cause CD infections, but could be regarded as a marker for disturbed gut microbiota.
Disclosure: Nothing to disclose

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P0478 UNIVERSAL ANTIBIOTIC PROPHYLAXIS MAY BE UNNECESSARY IN ACUTE VARICEAL BLEEDING: A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction: Randomized controlled trials conducted from the 1990s to early 2000s showed efficacy of antibiotic prophylaxis in acute variceal bleeding. Over the past decades, however, endoscopic and systemic therapy for variceal bleeding has improved remarkably, and the necessity of antibiotic prophylaxis could have decreased.
Aims and Methods: In this study, we aimed to evaluate the efficacy of antibiotic prophylaxis with our most recent data. We retrospectively studied clinical characteristics, treatment and outcomes of 150 patients (116 men, median age: 62 years) with acute variceal bleeding, who were admitted to our hospital between January 2012 and December 2016. Those who had obvious infection or aspiration pneumonia at admission were excluded. Patients were classified into 2 groups according to presence or absence of antibiotic prophylaxis. Rates of obvious bacterial infection, suspicious infection, in-hospital mortality, in-hospital rebleeding, and readmission within 30 days were compared between the 2 groups. Multivariate analysis was also performed to evaluate the efficacy of antibiotic prophylaxis.
Results: The median Child-Pugh score was 8. Immediate endoscopy was performed in 148 patients, and active bleeding was observed in 60 patients. Endoscopic variceal ligation was performed in 111 patients. Hemostasis was achieved in 148 patients. 2 patients died of uncontrolled bleeding (1 with and 1 without endoscopy). 46 patients (30.7%) received antibiotic prophylaxis. The rates of obvious bacterial infection, suspicious infection, in-hospital mortality, in-hospital rebleeding, and readmission within 30 days were not different significantly between the 2 groups. In the multivariate analyses, antibiotic prophylaxis was not associated with any of these outcomes. Instead, high serum creatinine levels at admission (greater than 1.2 mg/dL) were significantly associated with obvious bacterial infection (adjusted odds ratio 12.5, 95% CI 1.24–126), and higher Child-Pugh score (per point) was associated with mortality (adjusted odds ratio 3.57, 95% CI 1.25–10.2).
Conclusion: Universal antibiotic prophylaxis may be unnecessary in acute variceal bleeding. Impaired renal function at admission was a risk factor for bacterial infection and might be applied to a risk stratification approach for antibiotic prophylaxis.
Disclosure: Nothing to disclose

P0479 AIMS65 IS THE MOST ACCURATE RISK-SCORING SYSTEM FOR PREDICTING PROGNOSIS OF PATIENTS WITH DUODENAL ULCER BLEEDING

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Introduction: In spite of the advance of endoscopic hemostasis for upper gastrointestinal bleeding, treating duodenal ulcer bleeding is sometimes difficult and does not yield good prognosis.
Aims and Methods: In this study, we evaluated and compared various risk-scoring systems for upper gastrointestinal bleeding to predict outcomes of patients who underwent endoscopic treatment for duodenal ulcer bleeding.
Bleeding from peptic ulcer was diagnosed in 1,147 patients (892 patients with gastric and 255 with duodenal ulcer) among 7,106 patients who underwent emergent esophagogastroduodenoscopy for upper gastrointestinal bleeding at our hospital from July 2007 to June 2017. We retrospectively reviewed clinical records of the 1,147 patients and compared their prognosis after endoscopic therapy between gastric and duodenal ulcer patients. In the 255 patients with duodenal ulcer, we evaluated the following risk-scoring system; Glasgow Blatchford, AIMS65, admission Rockall and full Rockall scores, to predict in-hospital mortality by analyzing their area under the receiver operating characteristic curve (AUROC).
Results: The mortality rate of patients with duodenal ulcer bleeding was 6.7% (17/255), which were significantly higher than that of those with gastric ulcer bleeding (0.67%, 6/892) ($p < 0.001$). In the duodenal ulcer patients, risk scores were significantly higher in patients with in-hospital mortality than those without in all of the scoring systems, and AUROC of AIMS65 (0.83) was highest among them (Table).
With more than 2 points of AIMS65 score as a cut-off value, sensitivity and specificity to predict in-hospital mortality of patients with duodenal ulcer bleeding were 0.882 and 0.597, respectively.
Conclusion: The prognosis of patients with duodenal ulcer bleeding was poorer than that of patients with gastric ulcer. The AIMS65 score may be useful to predict the outcome after endoscopic treatment for duodenal ulcer bleeding, especially in the situation at deciding the indication of endoscopic hemostasis because this scoring system can be calculated without endoscopic findings.

Scoring system	AUROC (95%CI)	Cut-off score	Sensitivity (%)	Specificity (%)
Glasgow Blatchford	0.74 (0.61–0.86)	≧13	64.7	71.0
AIMS65	0.83 (0.74–0.92)	≧2	88.2	59.7
Admission Rockall	0.76 (0.66–0.87)	≧3	82.4	55.5
Full Rockall	0.82 (0.74–0.91)	≧6	82.4	66.0

[AUROC and sensitivity and specificity of each risk-scoring system to predict in-hospital mortality in patients with duodenal ulcer bleeding.]
Disclosure: Nothing to disclose

P0480 EFFECTS OF ASPIRIN ON MORTALITY AND RE-BLEEDING IN PATIENTS WITH NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Guidelines recommend resuming aspirin soon after control of bleeding in patients with cardiovascular disease who develop non-variceal upper gastrointestinal bleeding (NVUGIB).
Aims and Methods: Our primary aim was to synthesize the evidence comparing mortality and re-bleeding rates in patients who resume aspirin compared to those who do not after NVUGIB. Our secondary aim was to determine whether being on aspirin upon presentation with NVUGIB is associated with worse outcomes compared to not being on it.
We conducted a systematic review of randomized controlled trials (RCTs) and prospective observational studies. We ran a comprehensive sensitive search covering major electronic databases, clinical trial registries and grey literature. 2 teams of 2 reviewers screened titles and abstracts of identified citations independently and in duplicate for eligibility using pre-selected criteria. We retrieved full texts of citations judged potentially eligible by at least 1 reviewer. The 2 teams screened full texts independently and in duplicate, resolved disagreements, abstracted clinical characteristics of included studies and assessed their risk of bias using standardized forms. We used meta-analysis to pool data for mortality and re-bleeding outcomes.
Results: Of 9827 citations, we assessed 254 full-texts for eligibility. 1 RCT and 3 observational studies address the primary question; all assess low dose aspirin, but timing of its resumption varied. None compare different timings of aspirin resumption. The RCT suggests that early aspirin resumption may reduce mortality; HR = 0.20; 95% CI [0.06–0.63]; moderate certainty of evidence.

Meta-analysis of 3 observational studies suggests that aspirin resumption may reduce mortality: pooled HR = 0.79; 95% CI [0.50–1.25]; very low certainty of evidence. We assessed if the relative effect of resuming aspirin is modified by whether people were using it for secondary or primary prophylaxis. In those on aspirin for secondary prophylaxis, resuming aspirin may reduce mortality to a larger extent (HR = 0.56; 95% CI [0.31–1.00]) compared to those taking it for primary prophylaxis (HR = 4.07; 95% CI [0.54–30.74]), but studies were characterized by high heterogeneity (p = 0.06 for subgroup effect). The RCT suggests that aspirin resumption may increase re-bleeding; HR = 1.90; 95% CI [0.60–6.00]; moderate certainty of evidence, while meta-analysis of 2 observational studies suggests it may reduce re-bleeding: pooled HR = 0.82; 95% CI [0.35–1.91]; very low certainty of evidence.
7 observational studies address the secondary question. Meta-analysis of 5 studies suggests that being on aspirin upon NVUGIB admission is not associated with all-cause mortality: pooled HR = 1.02; 95% CI [0.70–1.51]; very low certainty of evidence. Meta-analysis of 2 studies shows no increased re-bleeding risk: pooled HR = 1.23; 95% CI [0.44–3.42]; very low certainty of evidence.
Conclusion: Evidence supporting a protective effect for aspirin resumption soon after NVUGIB is of very low certainty based on observational studies and moderate certainty based on 1 RCT. The available evidence is not informative as to the optimal timing of aspirin resumption. High quality RCTs are needed to address the best timing of aspirin resumption in patients with NVUGIB.
Disclosure: Nothing to disclose

P0481 OPTIMAL ENDOSCOPY TIMING ACCORDING TO THE SEVERITY OF UNDERLYING LIVER DISEASE IN PATIENTS WITH ACUTE VARICEAL BLEEDING

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Introduction: Current guidelines recommend endoscopic therapy to be performed within 12 hours for acute variceal bleeding (AVB). However, the optimal timing of endoscopic therapy for AVB remains unclear.
Aims and Methods: The aim of this study was to examine the relationship between the endoscopy timing and clinical outcomes in AVB, with emphasis on liver function and endoscopy timing. From January 2010 to June 2017, cirrhotic patients with varices confirmed as the source of bleeding by endoscopy were evaluated. The primary outcome was a composite of 6-week rebleeding and mortality. We stratified patients according to the model for end-stage liver disease (MELD) score and analyzed the association between the endoscopy timing and primary composite outcome.
Results: In 411 patients, the overall composite outcome rate was 30.9% (n = 127) at 6 week. Patients who underwent urgent endoscopy (≤12 hours) had a significantly higher composite outcome than patients who underwent non-urgent endoscopy (>12 hours) (34.4% vs. 19.1%; p = 0.005). Low-risk patients who underwent urgent endoscopy were more likely to reach the composite outcome (adjusted OR, 0.84 per 4 hours; 95% CI, 0.73–0.98; p = 0.027). However, time to endoscopy was not a significant predictor of composite outcome in high-risk patients. These findings persisted even after adjustment for baseline characteristics between the urgent and non-urgent groups.
Conclusion: Urgent endoscopy is significantly associated with a poorer outcome in patients with AVB, especially in low-risk patients. Our result provides a treatment strategy according to the severity of underlying liver disease in patients with AVB.
Disclosure: Nothing to disclose

P0482 FORREST CLASSIFICATION DOES NOT PROPERLY ASSESS REBLEDING RISK OR MORTALITY IN HIGH-RISK UPPER GI BLEEDING

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Introduction: Forrest classification has been the most endoscopic used 1 in upper GI bleeding. The 6 stages risk assessment establishes the higher risk in Forrest Ia patients, being the least Forrest III stage.
Aims and Methods: The aim of our research was to determine in a prospective upper GI bleeding patients whether this classification differentiates between patients with stage Forrest IIa and Forrest I, regarding rebleeding risk, because it has been previously suggested that a visible vessel might entail a higher risk of rebleeding.
Upper GI bleeding from Virgen de las Nieves University Hospital is a prospectively collected dadabase from January 2013. For this study, patients up to January 2017 were included. For every patient 150 clinical and biochemical variables are recorded. Variables were compared with SPSS 17 software (SPSS Inc. Chicago, ILL) by means of the Chi-square test.
Results: 414 patients were included (65.5% males) with non variceal upper GI bleeding. Mean age was 65.07 years (range 17–95).
The main upper GI bleeding etiologies were duodenal ulcer in 29%, gastric ulcer in 22%, acute gastric erosions in 13%, Mallory-Weiss and esophageal ulcers in 8%. 34 patients died (8.2%) and 69% had a relevant comorbidity. An endoscopic therapy with 2 methods (injection plus clipping or argon plasma coagulation) was applied to every patient.
Mortality did not significantly differ between Forrest Ib patients and Forrest IIa (19.6% vs. 20.8%). Regarding rebleeding, despite the proportion of rebleeding patients with Forrest IIa ulcers almost doubled Forrest Ib (20% vs. 10.9%), the statistic test did not reach statistical significance, neither did regarding the need for surgery (16% vs 6.5%, p = n.s.). Moreover, when mortality rates in patients with Forrest IIa and Ib were compared we found no significant differences, an a trend toward a higher mortality in Forrest IIa patients was higher (15.4% Ia vs. 21.7% IIa). A similar absence of statistical differences was observed for the rest of outcomes studied: rebleeding (23.1% Ia vs. 16.7% IIa) and need for surgery (23.1% Ia vs. 12.5% IIa).
Conclusion: Our study shows that that Forrest classification seems an inadequate predicting tool for rebleeding in its actual formulation. In view of our results, Forrest IIa patients should probably be considered of a higher risk than Forrest Ib, and closer to Forrest Ia. We might hypothesize that the presence of a visible vessel implies a higher risk than an oozing bleed, that usually originates in small capillaries, more easily coagulated through endoscopy and even natural mechanisms.
Disclosure: Nothing to disclose

P0483 RISK FACTORS OF POOR PROGNOSIS AND IMPAIRMENT OF ACTIVITIES OF DAILY LIVING IN PATIENTS WITH HEMORRHAGIC GASTRODUODENAL ULCERS

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Introduction: Although most of hemorrhagic gastroduodenal ulcers (HGU) can be safely treated with endoscopic procedures, some patients with HGU could have poor prognosis owing to comorbidities and medications for anticoagulation. In this study, risk factors of poor prognosis including mortality and impairment of activities of daily living (ADL) in patients with HGU were examined. In particular, prognosis of elderly HGU patients (≥ 75 years old) was evaluated in comparison to that of non-elderly (< 75 years old) patients.
Aims and Methods: The medical records of 589 patients with endoscopically confirmed HGU (430 men, 159 women; mean age 66.7 years; range 25–95 years) were retrospectively reviewed. Clinical backgrounds and outcomes were compared between patients < 75 years old (n = 394) and ≥ 75 years old (n = 195). The primary outcomes are overall mortality, mortality within 30 days after occurrence of hemorrhage, and impairment of ADL. Impairment of ADL was defined as admission to care facilities after hospital discharge or requirement of home modification for rehabilitation at home. Evaluated clinical factors were endoscopic features, need for interventional endoscopic procedures, comorbidities, symptoms, medications, vital signs, and blood test results.
Results: There were significant differences in overall mortality (3.8% vs. 7.6%), hospitalization period (16.2 ± 29.3 days vs. 22.8 ± 28.0 days), and impairment of ADL (1.3% vs. 6.7%) between patients < 75 years old and those ≥ 75 years old. Multivariate analysis revealed that independently significant risk factors for overall mortality were age (≥ 75 years) (odds ratio (OR) 2.25, 95% confidence interval (CI), 1.06–4.74), and renal disease (OR 3.38, 95% CI, 1.42–8.01). Risk factors of mortality within 30 days after hemorrhage were age (≥ 75 years) (OR 3.40, 95% CI, 1.21–9.56), need for interventional endoscopic procedures (OR 3.91, 95% CI, 1.08–14.1), and renal disease (OR 4.3, 95% CI, 1.40–13.2). Finally, risk factors of impairment of ADL were use of proton pump inhibitors prior to hemorrhage (OR 5.83, 95% CI, 2.1–16.2), heart disease (OR 3.06, 95% CI, 1.11–8.3), and age (≥ 75 years) (OR 5.07, 95% CI, 1.73–14.9).
Conclusion: High mortality and impairment of ADL were more likely to be observed in elderly HGU patients compared to non-elderly patients. In particular, concomitance of renal disease and heart disease was a risk of poor prognosis in those subjects. Prophylactic approaches for HGU and early improvement of ADL after HGU occurrence are particularly important in elderly patients with comorbidities.
Disclosure: Nothing to disclose

P0484 PALBI - THE PLATELET-ALBUMIN-BILIRUBIN SCORE - A BETTER PREDICTOR OF OUTCOME OF ACUTE VARICEAL BLEEDING

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Introduction: The albumin-bilirubin (ALBI) score eliminates the need for subjective variables required in the Child-Turcotte-Pugh (CTP) classification and has been validated as a prognostic indicator for patients with HCC. Incorporating platelet count to reflect portal hypertension in the PALBI score improved

validity in predicting outcome of patients with HCC undergoing resection and ablation.
Aims and Methods: We aimed to evaluate the PALBI score compared to the CTP class for predicting the outcome of acute variceal bleeding. Data of 1517 patients presenting with acute variceal bleeding were analyzed. The CTP class and PALBI score were calculated, and were correlated to mortality. PALBI score was calculated as = (2.02*Log10 bilirubin) +(−0.37*(Log10bilirubin)^2) +(−0.04*albumin) +(−3.48*Log10 platelets)+(1.01*(Log10 platelets)^2).[2] Areas under the receiving-operator characteristics curve (AUROC) were calculated for survival.
Results: Mean age was 52 years old; 77.5% were males. There were 69 CTP-A patients (4.5%), 434 (29.2%) CTP B and 1014 (66.8%) CTP C; 6 patients (0.39%), PALBI grade 1, 43 patients (2.8%) PALBI grade 2, 957 patients (63%) PALBI grade 3 and 542 patients (33.6%) PALBI grade 4. All CTP-A and PALBI-1 patients survived. 332 Patients died during the admission (21.9%). Bleeding related mortality occurred in 11% of CTP-B, 28% of CTP-C, and in 9.3% of PALBI-2, 14.1% of PALBI-3 and 35.6% of PALBI-4 patients. The AUROC for PALBI score was more significant in comparison to ALBI, MELD and CTP scores (0.871, 0.803, 0.689 and 0.668, respectively).
Conclusion: PALBI better predicts early mortality of patients with acute variceal bleeding than CTP score.
Disclosure: Nothing to disclose

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P0485 UPPER GASTROINTESTINAL BLEEDING NOT ASSOCIATED TO PORTAL HYPERTENSION: ASPECTS OF EPIDEMIOLOGY AND MANAGEMENT IN A SOUTHERN SPANISH AREA

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Introduction: The aim of the research was to evaluate different epidemiologic and management aspects of Upper Gastrointestinal Bleeding not associated to Portal Hypertension (UGBNPH) in Puerta del Mar Hospital, Cádiz (Andalucía, Spain).
Aims and Methods: Retrospective research including every patient admitted to Gastroenterology Department of Puerta del Mar Hospital (Cádiz), between January 2016 and December 2016, because of UGBNPH.
We analysed different variables: gender, age, cardiovascular risk factors such Arterial Hypertension (AHT), Diabetes Mellitus (DM) and Dyslipidemia (DLP); concomitant treatment with Proton Pump Inhibitors (PPIs), Antiplatelets, Antithrombotics, Nonsteroideal Anti-Inflammatory Drugs (NSAIDs) and Antidepressants; clinical and endoscopic findings; red blood cells and iron requirement, and *Helicobacter pylori* investigation. We also analysed short and medium term survival rates and recurrence rate in 1-year period.
Results: We included 75 patients admitted because of UGBNPH (56% men), with an average age of 69 years old (men 66, women 74).
We did not find significant differences by gender when analyzing AHT (53.3%), DM (28%) and DLP (34.7%), neither when analyzing PPIs treatament (men 33.3%; women 36.4%). The amount of patients with Antiplatelet (29.3%) and Antithrombotic (29.3%) concomitant treatment was similar. However, we found a higher quantity of UGBNPH events in men with Antiplatelet treatment (33.3%) and women with Antithrombotic treatment (36.4%). We also noticed more UGBNPH events in women who used NSAIDs (30.3%) and Antidepressant (24.2%), compared to men.
Clinical debut was predominantly as Melena (68%). Regarding Endoscopic findings, we found more frecuently Duodenal Ulcer among men (33.3%) and Gastric Ulcer among women (45.5%).
61.3% of patients needed red blood cell transfussion during their admission, with 4 packed red blood cells as average. We only began iron therapy in 22.7% of patients admitted. *Helicobacter pylori* investigation was made in 37.3% with high positivity rates (78.6%), especially among men (93.3%).
Short-term survival rate was similar (men 95.2%; women 94%), however medium-term survival rate (1 year after admission) was higher in men (88.1% vs women 78.8%). Recurrence rate in 1-year period was 14.1%, with no differences when analyzing genders or etiology of UGBNPH event.
Conclusion: Upper Gastrointestinal Bleeding not asocciated to Portal Hypertension is a frequent entity in our environment. Men using Antiplatelets and women using Antithrombotics are higher bleeding risk groups. In our experience, Duodenal Ulcer in men and Gastric Ulcer in women are more usual. Almost two-thirds of patients required red blood cells transfusion during admission, however we began iron therapy in a lower percentage. We did not investigate enough *Helicobacter pylori* infection. Finally, short-term prognosis was favorable, but recurrence is not unusual.
Disclosure: Nothing to disclose

P0486 UPPER GASTROINTESTINAL BLEEDING ASSOCIATED TO PORTAL HYPERTENSION: ASPECTS OF EPIDEMIOLOGY AND MANAGEMENT IN A SOUTHERN SPANISH AREA

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Introduction: The aim of the research was to evaluate different epidemiologic and management aspects of Upper Gastrointestinal Bleeding associated to Portal Hypertension (UGBPH) in Puerta del Mar Hospital, Cádiz (Andalucía, Spain).
Aims and Methods: Retrospective research including every cirrhotic patient admitted to Gastroenterology Department of Puerta del Mar Hospital (Cádiz), between January 2016 and December 2016, because of UGBPH.
We analysed different variables: gender, age, cardiovascular risk factors such Arterial Hypertension (AHT), Diabetes Mellitus (DM) and Dyslipidemia (DLP); concomitant treatment with Proton Pump Inhibitors (PPIs), Antiplatelets, Antithrombotics, Nonsteroideal Anti-Inflammatory Drugs (NSAIDs) and Antidepressants; clinical and endoscopic findings; red blood cells and iron requirement. We also analysed short and medium term survival rates and recurrence rate in 1-year period.
Results: We included 30 patients admitted because of UGBPH (73.3% men), with a younger average age among men (men 54 years old, women 73). We did not find significant differences by gender when analyzing DM (33.3%), with higher frecuence of AHT among women (62.5% vs 27.3%) and DLP among men (22.7% vs 0%).
We did not find significant differences by gender when analyzing concomitant treatment with PPIs (43.3%), Antiplatelets (6.7%), Antithrombotics (3.3%), NSAIDs (0%) and Antidepressants (23.2%).
Clinical debut as Hematemesis (66.7%) and Melena (63.3%) was similar in frecuence. Regarding Endoscopic findings, in both genders, we found more usually Esophageal Variceal bleeding as etiology (70%) compared to Portal Hypertension Gastropathy bleeding (33.3%).
87.5% of admitted women needed red blood cell transfusion (vs 59.1% of admitted men), with 2.9 packed red blood cells as average (vs 4 packed red blood cells in men). We only began iron therapy in 20% of patients admitted.
Short-term survival rate was 90% (men 86.4%; women 100%) and medium-term survival rate (1 year after admission) was 80%. Bleeding recurrence rate in 1-year period was higher among women (50%) compared to men (36.8%) and related more often to Portal Hypertension Gastropathy (53.8%).
Conclusion: In our research, when analyzing Upper Gastrointestinal Bleeding associated to Portal Hypertension, cirrhotic men of medium age was the more commonly affected demographic group. Esophageal Variceal bleeding is the most usual etiology in both genders, however Portal Hypertension Gastropathy bleeding has the highest recurrence rate. Regarding high red blood cells transfusion requirement, we should consider the use of iron therapy in more cases. Finally, short-term prognosis is favorable in our population.
Disclosure: Nothing to disclose

P0487 PREDICTOR OF MORTALITY IN UPPER GASTROINTESTINAL BLEEDING IN PATIENTS ALREADY HOSPITALIZED FOR ANOTHER CONDITION: A PROSPECTIVE STUDY

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Introduction: Upper gastrointestinal bleeding (UGIB) is one of the main causes of hospital admission and urgent endoscopy in Gastroenterology departments and represents a true emergency, associated with significant morbidity, mortality and healthcare costs. Several predictors of in-hospital mortality have been identified. 1 of these risk factors in patients with nonvariceal UGIB is a previous hospital admission because of a different medical problem, with reported mortality rates as high as 26% (1). Nonetheless, the reasons for increased mortality in this subgroup of patients have not been consistently identified. Recent data from Canada and Italy (2, 3) shed some light on the issue, showing that the mortality rate for in-patient (IP) bleeding was significantly higher than that of outpatient (OP) bleeding and identifying some predictors of outcomes. However, only 1 study is prospective and none includes patients with variceal bleeding.
Aims and Methods: The aim of our study is to compare outpatients (OPs) presenting with UGIB to those who started GI bleeding while IPs as well as to identify predictors of mayor outcomes: rebleeding and in-hospital mortality.
This was a prospective cohort study on consecutive patients with UGIB (variceal and non variceal) treated in "Virgen de las Nieves" University Hospital from 2013 to 2017 (from January 2013 to December 2017). All patients underwent upper endoscopy, and information regarding clinical and biochemical data, procedures, and outcomes for 6 months after admission were collected. Clinical outcomes documented were in-hospital mortality and rebleeding. Descriptive inferential and multivariate logistic regression models were carried out.
Results: 540 patients with a diagnosis of upper gastrointestinal bleeding were included, 481 IPs and 59 OPs. IPs differed from OPs in 30 days death rate (42.1% vs 7.8%; $p < 0.001$), rebleeding (29.3% vs. 15.3%; $p = 0.014$), AIMS65≥2 (25.6% vs. 13.7%;$p = 0.043$), ASA score (ASA disease acuity class of 3–4 86.4% vs. 65.5; $p = 0.001$), comorbidities (86.4% vs 73.6%; $p = 0.037$), antiplatelets drugs (39% vs. 21.4%; $p = 0.005$), active bleeding in endoscopy (55.9% vs. 26.4%; $p < 0.001$), endoscopic treatment (71.2% vs. 35.8%, $p < 0.001$), blood units transfusions (5.42 vs. 2.48; $p < 0.001$); days of hospital stay (23.69 vs. 6.91; $p > 0.001$), blood pressure (104.44 vs. 112.64; $p = 0.010$),

creatinine (1.44 vs. 1.19; p = 0.034) and albumin levels (2.76 vs. 3.22; p < 0.001). Independent predictors for mortality in IPs were ASA ≥3 (OR 7.8; 95% CI 2.089–29.143, p = 0.002) and need for endoscopic intervention (OR 2.00; 95% CI 1.063–3.746, p = 0.032).

Conclusion: In this study, we demonstrate that IPs have higher morbidity and mortality rates, and that ASA class is clearly a predictor of mortality in patients with UGIB (non-variceal and variceal). These results are in concordance with previous reports in non variceal bleeding population (2,3). More, we showed that those are also valuable for the whole group of bleeders. Guidelines on optimal management of IPs who develop UGIB have been derived essentially from studies on OPs bleeding, whereas few data are available that focus on in-hospital bleeding and its management. It is obvious that IPs have poorer outcomes, and better understanding of the reasons is essential to develop a specific management. More studies in this sense are needed.

Disclosure: Nothing to disclose

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P0488 RISKS OF UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WHO FAILED INITIAL *HELICOBACTER PYLORI* ERADICATION THERAPY: A PROPENSITY SCORE MATCHING STUDY

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Introduction: Upper gastrointestinal bleeding (UGIB) is a leading cause of hospitalization which is still associated with significant mortality. Although *Helicobacter pylori* (HP) eradication and the use of gastroprotective agents could lower the risk of UGIB, the actual bleeding risk in patients who had received HP therapy remains unclear, particularly those who failed initial HP eradication.

Aims and Methods: This was a propensity score matched cohort study to determine the risk of UGIB in HP-infected patients who had received a course of clarithromycin-containing triple therapy for HP eradication between Jan 2003 and Dec 2012. Patients were identified from the territory-wide electronic health database of the Hong Kong Hospital Authority. The follow-up period commenced from 60 days after the HP therapy until the occurrence of UGIB, death or the end of the study (30 Jun 2016). The primary outcome was the occurrence of non-variceal UGIB. Failed initial HP eradication was identified by the need of repeat HP eradication therapy including repeated first-line therapy, a second-line or third-line therapy. Covariates included baseline characteristics, baseline medical conditions and concurrent medications. As medication usages could change over time, the follow-up period was split into intervals of 3-month and drug usage was defined in each interval as more than 7 days use. To reduce the indications bias for gastroprotective agents, the last 6-week before the index date of events or censoring were excluded when retrieving proton pump inhibitors (PPI) and histamine type-2 receptor antagonists (H2RA) prescription records. Propensity score (PS) matching was used to select controls for each failed eradication patient by the ratio of 1:5. Cox proportional hazards model was used to adjust the confounders, in which medications were included as time varying variables. Hazards ratios (HR) and corresponding 95% confidence intervals (CI) were presented.

Results: 70,869 patients who had received HP eradication therapy were included in PS matching, with 5,593 patients in the failed initial eradication group and 27,965 patients as controls. The median follow-up duration was 7.3 (interquartile range, 4.8–10.1) years. The overall incidence rate of non-variceal UGIB was 4.10 per 1000 person-year (failed group 5.48 vs successful group 3.90; log-rank test p < 0.001). Multivariate Cox regression analysis showed that patients in the failed group had higher risk of UGIB (HR 1.31; 95%CI 1.11–1.55, p = 0.001). Other risk factors for UGIB included older age, male sex, history of UGIB or ulcer, diabetes, cirrhosis, renal disease and stroke (Table). Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), anticoagulants, corticosteroids, selective serotonin reuptake inhibitors (SSRI) also increased the UGIB risk but PPI and H2RA reduced the bleeding risk.

Conclusion: Patients who failed initial HP eradication still have higher UGIB risk, testifying the benefits of early HP eradication in preventing UGI complications. Both PPI and H2RA could further lower the risk of UGIB in HP eradicated subjects.

Variables	HR (95%CI)	P	Variables	HR (95%CI)	P
Age (in year)	1.06 (1.06–1.07)	< 0.001	PPI	0.74 (0.60–0.92)	0.006
Male	1.43 (1.26–1.63)	< 0.001	H2RA	0.57 (0.48–0.69)	< 0.001
Failed initial HP eradication	1.31 (1.11–1.55)	0.001	Aspirin	1.28 (1.03–1.60)	0.024
History of UGIB or ulcer	3.04 (2.65–3.49)	< 0.001	NSAIDs	1.76 (1.33–2.32)	< 0.001
Diabetes mellitus	1.43 (1.17–1.75)	< 0.001	Anticoagulants	1.80 (1.22–2.66)	0.003
Cirrhosis	3.08 (1.85–5.15)	< 0.001	Corticosteroids	2.06 (1.46–2.89)	< 0.001
Renal disease	1.56 (1.15–2.11)	0.004	SSRI	1.68 (1.23–2.30)	0.001
Stroke	1.28 (1.02–1.62)	0.033			

[Multivariate analysis for risk of UGIB in patients who had received HP therapy]

Disclosure: Nothing to disclose

P0489 MORTALITY RATE AND RISK FACTORS FOR GASTROINTESTINAL BLEEDING IN ELDERLY PATIENTS

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Introduction: Gastrointestinal bleeding (GIB) is among the top 10 reasons of gastroenterology referrals and is burdened by a high mortality rate. Little is known regarding GIB in elderly patients suffering from multimorbidity. We aimed to describe the prevalence, outcomes, and possible risk factors of GIB in a large cohort of elderly patients admitted in several internal medicine wards across Italy.

Aims and Methods: The REgistro POliterapie SIMI (REPOSI) is an Italian registry set up in 2008 with the aim of activating a network of internal medicine and geriatric wards in order to recruit, monitor, and prospectively study elderly patients, with particular regard to multimorbidity, polytherapy, and clinical outcomes. Data collection is still ongoing. A total of 101 internal medicine wards took part in the study. For the purpose of this study, we have identified all possible diagnoses of GIB (upper and lower), describing the length of stay (LOS), mortality rate, and possible risk factors of GIB, including drugs (i.e., anti-platelet agents, anticoagulants, selective serotonin reuptake inhibitors), smoking habit, alcohol abuse, obesity, index of comorbidity (through the Cumulative Illness Rating Scale [CIRS]), and common chronic diseases (i.e., diabetes mellitus, chronic heart failure, liver cirrhosis, and chronic obstructive pulmonary disease). Odds ratio, 95% confidence interval, and statistical significance were evaluated for all variables.

Results: The REPOSI registry includes 4486 (6-year time span). Among these, at least a diagnosis of GIB was reported in 120 patients (mean age 79±7, F:M 0.9:1), with a crude prevalence of 2.7%. Upper GIB occurred in 72 patients (mean age 79±7, F:M 0.8:1), lower GIB in 51 patients (mean age 79±7, F:M 0.9:1), and both upper/lower GIB in 3 patients. The pooled LOS of patients with GIB was 11.7±8.1 days. 4 patients with GIB died in hospital (3.3%) and eight died within the next 3 months (7.2%). Notably, the use of acetylsalicylic acid (ASA) and anticoagulants (either vitamin K antagonists and direct oral anticoagulants) was not associated with GIB (p = ns). Multivariate analysis for all the possible risk factors of GIB is shown in Table. Non-ASA anti-platelet agents (OR 2.77), CIRS index of comorbidity > 3 (OR 2.38), anaemia (OR 2.81), and liver cirrhosis (OR 5.87) were statistically associated with GIB (p < 0.01).

Conclusion: We here show for the first time that a high index of comorbidity (> 3) is associated with high odds for GIB. GIB carries both an in-hospital and 3-month high mortality rate. The use of non-ASA anti-platelet agents should be discussed and carefully evaluated in elderly patients.

Disclosure: Nothing to disclose

P0490 MAST CELLS INFILTRATION AND SPACIAL RELATIONSHIP TO MUCOSAL AFFERENT NERVES IN PATIENTS WITH REFLUX DISEASE

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Introduction: Oesophageal mucosal afferent nerve fibres lie more superficially in non-erosive reflux disease (NERD) patients, compared to erosive reflux disease (ERD) and Barrett's oesophagus [1]; possibly underlying the relative oesophageal hypersensitivity observed in NERD. A close spatial relationship between afferent nerves and mast cells (MCs) is implicated in colonic hypersensitivity observed in IBS patients [2].

Aims and Methods: This study aimed to quantify oesophageal mucosa MCs infiltration and their spacial relationship with afferent nerves in reflux disease patients.
Distal oesophageal biopsies from 10 patients with 'true' NERD and 11 patients with ERD were stained for CGRP and toluidine blue. The position of CGRP positive nerve fibres was determined as number of cell layers from the lumen. Similarly, the number of MCs per high power field (HPF: x50 magnification) and their position in the epithelium was recorded.
Results: The median age was 55.5 years (range: 28–75, 6M:4F) for NERD patients and 54 years (range: 31–73, 8M:3F) for ERD. The median density of MCs/HPF was 0.17 (CI: 0.08–0.5) for NERD vs 0.50 (CI: 0.5–0.8) for ERD ($p = 0.01$). There was no correlation between oesophageal acid exposure and density of MCs infiltration in NERD ($r = 0.09$). The MCs were more superficially located in NERD patients (17.5 cell layers) compared to ERD (23 cell layers), $p = 0.01$. There was no correlation between the position of the MCs and the nerve fibres amongst both groups ($r^2 = 0.2$, $p = 0.05$).
Conclusion: Although there are differences between the density of MCs infiltration and position of the MCs in the epithelium between NERD and ERD, we could not find a good correlation between the position of nerves and the position of the MCs. Therefore, the spacial relationship of the MCs and the mucosal afferent nerves in NERD appears to be different to IBS with possible pathophysiological implications.
Disclosure: Nothing to disclose

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P0491 THE EFFECT OF A SINGLE AND REPEATED DOSES OF MEMANTINE ON GASTRIC MYOELECTRIC ACTIVITY IN EXPERIMENTAL PIGS

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Introduction: Memantine, currently available for the treatment of Alzheimer's disease, is an uncompetitive antagonist of the N-methyl-D-aspartate type of glutamate receptors. Under normal physiologic conditions, these unstimulated receptor ion channels are blocked by magnesium ions, which are displaced after agonist-induced depolarization. In humans, memantine administration is associated with different gastrointestinal dysmotility side effects (vomiting, diarrhoea, constipation, motor-mediated abdominal pain), thus limiting its clinical use. Mechanism of these motility disorders has not been clarified yet. Pigs can be used in various preclinical experiments due to their relatively very similar gastrointestinal functions compared to humans.
Aims and Methods: The aim of this study was to evaluate the impact of a single and repeated doses of memantine on porcine gastric myoelectric activity evaluated by means of electrogastrography (EGG). 6 adult female experimental pigs (*Sus scrofa f. domestica*, mean weight 41.7±5.0 kg) entered the study for 2 times. The first EGG was recorded after a single intragastric dose of memantine (20 mg). In the second part, EGG was accomplished after 7-day intragastric administration (20 mg per day). All EGG recordings were performed under general anaesthesia. Basal (15 minutes) and study recordings (120 minutes) were accomplished using an EGG stand (MMS, Enschede, the Netherlands). Running spectral analysis based on Fourier transform was used. Results were expressed as dominant frequency of gastric slow waves (DF) and power analysis (areas of amplitudes).
Results: Single dose of memantine significantly increased DF, from basic values (1.65±1.05 cycles per min.) to 2.86 cpm after 30 min. ($p = 0.008$), lasting till 75 min. ($p = 0.014$). Basal power (median 452; inter-quartile range 280–1312 μV^2) raised after 15 min. (median 827; IQR 224–2769; $p = 0.386$; NS), lasting next 30 min. Repetitively administrated memantine caused important gastric arrhythmia. Basal DF after single and repeated administration was not different, however, a DF increase in the second part was more prominent (up to 3.18±2.16 after 15 and 30 min., $p < 0.001$). In comparison with a single dose, basal power was significantly higher after repetitively administrated memantine (median 3940; IQR 695–15023 μV^2; $p < 0.001$). Next dose of 20 mg memantine in the second part induced a prominent drop of power after 15 min. (median 541; IQR 328–2280 μV^2; $p < 0.001$), lasting till 120 min. ($p < 0.001$).
Conclusion: Both single and repeated doses of memantine increased DF. Severe gastric arrhythmia and long-lasting low power after repeated administration might explain possible gastric dysmotility side effects in the chronic use of memantine.

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Disclosure: Nothing to disclose

P0492 RELATIONSHIP BETWEEN ABUSE AND GASTROINTESTINAL SYMPTOMS IN NON PATIENTS WOMEN

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Introduction: It has been shown in severely abused 'non-patient' women population that a history of severe, combined physical and sexual abuse is associated with a higher number of GI symptoms (1).
Aims and Methods: To assess in healthy women, referring to lawyers for non-specific legal assistance excluding abuse (controls lawyers LC) compared to severely abused women (V) the prevalence of somatic symptoms and the association with the time of perpetration, type, and severity of abuse. 67 women, (18–58 yrs), receiving shelter in anti-violence associations and 46 lawyers controls (29–80 yrs) were invited to fill out an anonymous questionnaire with a medical and an abuse section. The severity of abuse was expressed as the 0–6 Abuse Severity Measure (ASM) (2). The association between abuse characteristics and the number of symptoms, was assessed by Poisson regression model.
Results: In controls lawyers (LC) 65% of woman suffered from physical and or sexual abuse in childhood and or adulthood vs 100% of severely abused women (V). Most women suffered from childhood and adulthood sexual and physical abuse. In 78% of LC the ASM was < 2 vs 36% of V (ASM$\geq$ 4 in 54%). Controls lawyers women reported a mean of 4.9 GI symptoms (median 4; IQR 2–8) vs 4.6 of severely abused women (median 4; IQR 2–7). Controls lawyers women with an ASM $\geq$2 reported significantly more GI symptoms (median 6.5; IQR 3–11 vs median 3; IQR 1–7) ($p = 0.002$ vs < 2). Severely abused women with an ASM $\geq$5 reported significantly more GI symptoms, than controls lawyers women (median 6; IQR 4–8 vs median 4.5; IQR 2–8 ($p = 0.000$). In both groups women having suffered from both sexual and physical abuse reported a higher number of GI symptoms than those reporting only one type of abuse.
Conclusion: Symptoms in abused 'non-patient' women mainly concern the abdomen and the GI tract. A history of severe, combined physical and sexual abuse, is associated with a higher number of GI symptoms
Disclosure: Nothing to disclose

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P0493 MOTOR ACTIVITY OF ESOPHAGUS AND STOMACH IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS: AN OBSERVATIONAL STUDY

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Introduction: Patients with Amyotrophic Lateral Sclerosis (ALS) may be affected by severe dysphagia, emerging in more than 80% of patients during the advanced phases of the disease and can affect all stages of swallowing with the need to resort to enteral nutrition via Percutaneous Endoscopic Gastrostomy. Previous studies have reported oro-pharyngeal dysfunction, but little is known about alterations of esophageal and gastric motor activity.
Aims and Methods: To assess motor function of esophagus and stomach, 12 ALS patients with bulbar or spinal presentation (6F; 63±12 yrs) underwent: (1) High Resolution Manometry with esophageal pressure topography, using a water-perfused catheter with 24 open tips 1 cm spaced (o.d.4.7mm) (EB Neuro S.p.A. Firenze), according to the Chicago III method and classification[1]; (2) evaluation of gastric emptying by ultrasonographic serial measurements of gastric antral volume in basal fasting conditions, and at the end and thereafter for 180 min from ingestion of a standardized 525 kcal solid-liquid meal. In 7 patients reporting dysphagia, the oropharyngeal stages of swallowing were evaluated by a fibrolaringoscopy procedure. The stage and progression of the disease were evaluated by ALS Functional Rating Scale (ALS FRS-R) and the Medical Research Council Score (MRC). The operators were blinded about the ALS clinical onset.
Results: Clinical presentation was bulbar in 5 patients (5F) and spinal in 7 patients (6M). The time interval between the onset of ALS symptoms and the enrollment was 23.2±18.8 months. The progression was slow in 8 cases and fast in 4 cases. ALS FRS was 39.6±5.1; the upper limbs MRC was 69.7±13.5, the lower limbs MRC was 59.8±20.4 and the total MRC was 129.4±26.5. Fibrolaryngoscopy identified dysphagia as oral, pharyngeal and mixed oropharyngeal respectively in 3, 1 and 3 patients. Resting pressure of the lower esophageal sphincter was normal in all patients except in 1 showing a reduced value; esophagel peristalsis was normal in 6 patients and ineffective in 8 patients (3/6 bulbar presentation; 5/7 spinal presentation). Delayed gastric emptying was detected in 2/5 bulbar presenting patients and in 4/7 spinal presenting patients. The oropharyngeal dysphagia was not related to manometric pattern, delayed gastric emptying was present in 4/7 of the dysphagic patients.
Conclusion: Statistical analysis cannot be performed because of the small study group, however these data suggest that patients with ALS may have defects in the esophageal peristalsis and delayed gastric emptying, and probably these defects are more frequent in spinal presentation than in bulbar one. The frequent association between oral and/or pharyngeal dysphagia with delayed gastric emptying suggests a possible involvement of the vagus nerve in these patients, as reported in a recent study.[2]
Disclosure: Nothing to disclose

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2. Ruoppolo G, *Front Neurol*. 2016;7:212.

P0494 DOPAMINE ANTAGONISM DOES NOT MODULATE ESOPHAGEAL SENSITIVITY IN HEALTH

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Introduction: Dopamine, a predominant catecholamine neurotransmitter, controls a wide range of functions such as emotion, cognition and positive reinforcement. Dopamine also plays an important role in the regulation of food intake and the gastrointestinal function. In animal models, dopamine-2 (D2) receptors have been implicated in the pathogenesis of visceral hypersensitivity (Nozu, NMO 2016) and itopride, a D2-antagonist and cholinesterase inhibitor, is able to decrease esophageal acid exposure and to improve reflux symptoms (Kim, *WJG* 2005; Scarpellini *APT* 2011). However, the role of dopamine in the control of esophageal sensitivity in man has not been studied.

Aims and Methods: We hypothesize that chlorpromazine, a D2-antagonist, decreases esophageal sensitivity in healthy volunteers (HV).

After IV administration of chlorpromazine (IV infusion 10mg) and placebo (0.9% NaCl), esophageal multimodal sensitivity was quantified in 13 HV (7m/6f, age 25y [19–40]) in a single-blind, randomized, cross-over study. After an overnight fast, a custom made probe with a balloon was positioned in the distal esophagus. Thermal, mechanical, electrical and chemical sensitivity were tested, in that order. Perception scores were evaluated using Visual Analogue Scales (VAS) and stimulus intensities were evaluated for first perception, pain perception threshold (PPT) and pain toleration threshold (PTT). General mood was assessed by the Positive and Negative Affect Schedule (PANAS) and the State-Trait Anxiety Inventory (STAI-state) questionnaires before and after the stimulations. Results were analyzed using two-tailed paired t-tests or Wilcoxon matched-pairs signed-rank test. A p-value of < 0.05 was considered significant.

Results: There was no difference in esophageal sensitivity to either 1 of the stimulations when comparing placebo to chlorpromazine. STAI scores were similar in both conditions and no differences were found between placebo and chlorpromazine after the stimulation. We did however find significantly lower positive affect scores after the stimulations in the chlorpromazine condition compared to before the stimulations (23.00 [19.50–28.50] vs. 29.00 [25.00–34.00], $p = 0.0002$). Positive affect was also significantly lower in the chlorpromazine condition compared to the placebo condition after the stimulations (23.00 [19.50–28.50] vs. 28.00 [25.00–33.00], $p = 0.004$).

Conclusion: Although positive affect scores after the stimulation procedure were lower when chlorpromazine was administered, chlorpromazine did not affect esophageal sensitivity to thermal, mechanical, electrical and chemical stimulation in HV. Therefore, we conclude that antagonism of the D2-receptor is not likely to be a therapeutic target for the modulation of esophageal pain perception.

Disclosure: Nothing to disclose

Reference

1. Nozu, *NMO* 2016 Kim, *WJG* 2005 Scarpellini *APT* 2011.

P0495 ANALYSIS OF FULL-LAYER MUCOSAL HISTOLOGY IN ACHALASIA

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Introduction: The mucosal histology in achalasia has only been investigated using superficial biopsy or surgically resected esophageal specimens in end-stage cases.

Aims and Methods: The present study aims to elucidate mucosal histological findings of achalasia and to determine if in fact these changes occur in the early stage of the disease. Endoscopy was performed to determine the pinstripe pattern (PSP) (an early achalasia indicator), dilation and thickening of the mucosa (advanced achalasia indicators). Peroral endoscopic myotomy was then performed, and the mucosal entry site was created using cap-fitted endoscopic mucosal resection to access the full-layer mucosa and the submucosa.

Results: Mucosal histology was compared between 35 patients with achalasia and 15 controls. Histological esophagitis with findings of inflammatory cell infiltration and dilated intercellular spaces was far more frequently observed in patients with achalasia than in controls (82.9% vs. 13.3%, $p < 0.001$; 77.1% vs. 46.7%, $p = 0.049$). Atrophy of muscularis mucosae (MM) and epithelial waves were only observed in achalasia (39.4% vs. 0%, $p = 0.004$; 25.7% vs. 0%, $p = 0.043$). Fibrosis was more common in achalasia, but without statistical significance (34.3% vs. 20.0%, $p = 0.502$). In achalasia with endoscopic dilation and thickening of the mucosa, atrophy of MM was observed histologically, and in patients involving endoscopic PSP, the histological epithelial waves were visible.

Conclusion: Histological findings of esophagitis were observed both in early and advanced achalasia. PSP corresponds to the epithelial waves observed histologically in achalasia, whereas endoscopic findings in advanced achalasia correspond to the atrophy of MM. Appropriate management is necessary during the early stage of achalasia to prevent progression to advanced achalasia with severe histological changes.

Disclosure: Nothing to disclose

P0496 HIGH-RESOLUTION OESOPHAGEAL MANOMETRY WITH A SOLID TEST MEAL IMPROVES DIAGNOSTIC SENSITIVITY AND SPECIFICITY FOR EVALUATION OF OESOPHAGEAL DYSMOTILITY: VALIDATION STUDY IN A MULTIRACIAL ASIAN COHORT

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Introduction: The Chicago Classification (CC) for oesophageal motility disorders is based on ten 5mLs single water swallows (SWS). The addition of a solid test meal (STM) was shown to improve diagnostic sensitivity for patients with oesophageal symptoms and a normal gastroscopy in a European cohort. We further validate the feasibility and tolerability of an adjunctive STM in the routine evaluation of patients presenting with oesophageal symptoms in a multiracial Asian cohort.

Aims and Methods: Prospective study of patients referred for esophageal HRM between October 2014 to April 2018 after a normal gastroscopy. Single water swallows (SWS) based on 10 5mLs water and STM studies with 200g plain rice were performed in the upright seated position. Diagnosis of major and minor esophageal motility disorders were based on CC version 3.0 for SWS and modified for STM as appropriate. Symptoms reported during HRM were analyzed for concomitant esophageal manometric abnormalities. A positive symptom associated dysfunction [SAD] referred to a symptom event occurring within 10seconds of concomitant esophageal dysmotility on HRM.

Results: 363 patients (163 [45%] male; mean age 50.5 ± 17.0 years; 244 [67.2%] Chinese; 66 [18.2%] Malays; 27 [7.4%] Indians; 26 [7.2%] others) underwent HRM with SWS. 2 patients with achalasia were evaluated with SWS only. 361 patients (dysphagia [n = 154 (42.7%)], reflux [n = 145 (40.2%)] and atypical chest pain [n = 62 (17.2%)] were evaluated with SWS and STM. More patients were

Abstract No: P0496: Overview of manometry findings on single water swallows (SWS) and solid test meal (STM)

	Group 1 Dysphagia (SWS n = 156/STM N = 154)	Group 2 Reflux (n = 145)	Group 3 Atypical chest pain (n = 62)	Total (SWS[n = 363], STM[n = 361])
Age (mean,SD)	53.3±18.0	46.9±15.6	50.9±15.6	50.3±16.9
Achalasia/Esophaogastric junction outflow obtruction on SWS. N (%)	33 (21.1)	2 (1.4)	2 (3.2)	37 (10.2)
Achalasia/Esophagogastric junction outflow obstruction on STM. N (%)	37 (24.0)	4 (2.8)	3 (4.8)	44 (12.2) p = 0.41 compared with SWS
Oesophageal spasm on SWS	2 (1.3)	1 (0.7)	0 (0)	3 (0.8)
Oesophageal spasm on STM	4 (2.6)	6 (4.1)	1 (1.6)	11 (3.0) p = 0.03 compared with SWS
Jackhammer oesophagus on SWS	1 (0.6)	2 (1.4)	5 (8.1)	8 (2.2)
Jackhammer oesophagus on STM	17 (11.0)	3 (2.1)	9 (14.5)	29 (8.0) p < 0.005 compared with SWS
Ineffective oesophageal motility on SWS	27 (17.3)	33 (22.8)	6 (9.7)	66 (18.2)
Ineffective oesophageal motility on STM	12 (7.8)	5 (3.4)	4 (6.5)	21 (5.8) p < 0.005 compared to SWS

diagnosed with esophageal spasm during STM (n = 11 [3.0%] compared to SWS (n = 3 [0.8%], p = 0.03) and jackhammer esophagus (n = 29 [8.0%]) during STM compared to SWS (n = 8 [2.2%], p = 0.0003). Similarly, more patients were diagnosed with esophagogastric-junction outflow obstruction (EGJOO) during STM (n = 15 [4.2%]) compared with SWS (n = 9 [2.5%], p = 0.22) Diagnostic sensitivity of HRM with inclusion of STM was improved, with a higher overall prevalence of a major motility disorder with STM (n = 91/361 [25.2%]) compared to SWS (n = 63/363 (17.4%) [p = 0.0141]. Conversely, more patients were diagnosed with a minor motility disorder on SWS (n = 66 (18.2%) compared to STM (n = 21 [5.8%], p < 0.0001). None of the patients experienced symptoms during SWS compared to 69 [19.1%] patients who had a positive SAD with STM (p < 0.0001). The STM was tolerated by all subjects.
Conclusion: Addition of STM to routine esophageal manometry was well tolerated in Asians. STM improved diagnostic sensitivity and specificity of clinically relevant esophageal dysfunction and symptom reproducibility in a multiracial Asian cohort.
Disclosure: Nothing to disclose

P0497 EFFECT OF EGJ BARRIER AND PERISTALTIC DYSFUNCTION ON ESOPHAGEAL CLEARANCE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: The relationship between esophageal chemical clearance and abnormal high-resolution manometry (HRM) findings in GERD patients has not been fully investigated in terms of both EGJ barrier and motility function.
Aims and Methods: The main aim of this study was to determine the effect of EGJ barrier and peristaltic dysfunction on esophageal clearance in patients with GERD. 53 patients with PPI-refractory GERD symptoms who underwent both HRM and MII-pH tests were recruited. 2 cases of EGJ outflow obstruction were excluded, 51 remaining cases including 4 cases of major motility disorders, 20 cases of minor motility disorders and 27 cases of normal motility were included. Esophageal chemical clearance was evaluated by post reflux swallow-induced peristaltic wave (PSPW) index and mean acid clearance time (MACT) in MII-pH test and compared among different groups of peristalsis and EGJ morphology on HRM. Prediction models were developed to assess the strength of esophageal clearance parameters in GERD diagnosis by calculating the area under the curve (AUC) at receiver-operating-characteristic (ROC) analysis.
Results: The median values of PSPW index for major disorder of peristalsis, minor disorder of peristalsis, and normal peristalsis were 9.4 (1.9–14.7)%, 12.7 (8.6–20.0)% and 16.7 (7.7–30.2)%, respectively. The median values of MACT were 172.5 (145.0–1268.8) seconds, 78.5 (22.7–165.5) seconds, and 46.0 (22.0–132.0) seconds, respectively. The MACT in the major disorder group was significantly higher than in the minor disorder group and the normal motility group (p < 0.05) while PSPW index did not show any significant difference among groups. On the other hand, there was no difference in PSPW index and MACT among 3 EGJ morphology types. At ROC analysis, median MACT and mean nocturnal baseline impedanc (MNBI) showed good prediction of GERD with AUC being 0.78 (p = 0.001) and 0.84 (p < 0.001), respectively.
Conclusion: Major disorder of peristalsis is a cause of chemical clearance dysfunction while minor disorder of peristalsis and EGJ morphology type do not play an important role. MACT could be used as a promising index to evaluate chemical clearance in GERD.
Disclosure: Nothing to disclose

P0498 LONG-TERM OUTCOMES OF PER ORAL ENDOSCOPIC MYOTOMY IN CHILDREN

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Introduction: Achalasia cardia (AC) is rare in children and optimum endoscopic management options are not known. Per oral endoscopic myotomy (POEM) is a novel treatment modality for AC with excellent results in adult patients. However, the long-term outcomes of POEM and incidence of gastroesophageal reflux disease (GERD) have not been evaluated in children.
Aims and Methods: In this study, we aim to evaluate the outcomes of POEM in children and adolescents with AC.
We analyzed the data of all the children (≤ 18 years) with AC who presented to our hospital from September, 2013 to January 2018. The following outcome parameters were assessed- technical success, clinical success and adverse events. GERD was assessed with 24-hour pH-impedance study and esophagogastroduodenoscopy.
Results: A total of 43 children (boys-22, girls-21) with mean age, 14.5 ± 3.41 years (4–18) underwent POEM during the study period. The subtypes of achalasia according to Chicago classification were - type I- 11, type II- 29, III- 2 and unclassified-1. 18 children (41.9%) had history of prior treatment including - pneumatic dilatation (15), laparoscopic Heller's myotomy (1) and both dilatation and Heller's myotomy (2). POEM was successfully performed in all the children. Mean total length of myotomy was 10.09 ± 2.53 cm (5–15). Median procedure time was 48 minutes (18–240). Operative time was significantly less in cases where new triangular knife with water jet was used as compared to those in whom old triangular knife was used (mean, 42.72±14.92 vs 97.05±47.30 min, p < 0.05). Intra-operative adverse events occurred in 11 (25.6%) children including retroperitoneal CO2 7, capnoperitoneum 3 and mucosal injury 1. At a median follow-up of 540 days (66–1594), the clinical success was 95.3% (39/41). Clinical success at 1, 2, 3, and 4-years follow-up was 96.42% (27/28), 100% (18/18), 92.3% (12/13), and 83.3% (5/6) respectively. GERD was evident in 55% (11/20) and 53.8% (7/13) children as assessed by endoscopy and 24-hour pH study, respectively.
Conclusion: POEM is safe and effective for the management of achalasia in children. However, GERD is a potential concern and evident in over half of the children. Randomized comparison with Heller's myotomy combined with fundoplication is warranted in future trials.
Disclosure: Nothing to disclose

P0499 AGING AND INCREASED PSYCHOLOGICAL STRESS ARE USEFUL PREDICTORS OF SLOWER GASTRIC EMPTYING FOR PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE - A HOSPITAL-BASED INVESTIGATION IN THE ASIA-PACIFIC REGION

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Introduction: Asian populations have relatively lower prevalence and singular symptom presentation of gastroesophageal reflux disease (GERD) in comparison with those of Western descent. Increased gastric retention as a result of slower gastric emptying (GE) is a pathophysiological factor of GERD. In Asia, previous study suggested elderly have slower GE compared with younger subjects. However, there are scant studies ascertaining potential relation between gastroduodenal motor function and GERD in the Asian countries.
Aims and Methods: Our aim is to examine the relevant implication of slower GE in GERD by the design of a hospital-based, single institution, cross-sectional survey in Taiwan. We recruited 152 patients (87 men, range: 18~69 years old, mean age: 40.4 ± 12.4 years) of GERD, diagnosed by symptom presentations and endoscopy examinations. They completed the scintigraphic measurement of solid phase GE. The presence of dyspetic and/or atypical GERD symptoms, psychological stress including Spielberger Trait Anxiety Inventory (TAI), Beck's Depression Inventory (BDI), and Social Readjustment Rating Scale (SSRS) are recorded by self-report questionnaire. The status of *Helicobacter pylori* infection, blood level of pepsinogen I and I/II ratio are assessed.
Results: 47% and 28 % of the patients have slower GE rate, depending on the defined cut-off values with half emptying time ($t_{1/2}$) ≥ mean plus 2 standard deviation (SD) and 3 SD, respectively. Multiple logistic regression analysis indicates that older age (adjusted OR = 1.037, p < 0.05) and BDI score (adjusted OR = 1.052, p < 0.05) are independently related to slower GE. Subgroup analysis according to the status of GE discloses that patients with slower GE and higher BDI score tend to present with non-erosive reflux disease (NERD) whereas higher BMI level and male gender in patients with normal GE predict the presence of erosive reflux disease (ERD). Severe ERD (Grade C & D, n = 12) tend to be older among the 88 ERD patients (p = 0.054).
Conclusion: A subset of Asian patients with GERD have slower GE and that are associated with aging and higher psychological stress. The presence of slower GE specifies distinctive clinical implications of the GERD.
Disclosure: Nothing to disclose

Abstract N

P0500 PERORAL ENDOSCOPIC MYOTOMY (POEM) IS EQUALLY EFFECTIVE AND DOES NOT LEAD TO INCREASED ACID REFLUX IN OBESE AS COMPARED TO NON-OBESE PATIENTS WITH ACHALASIA

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Introduction: Laparoscopic Heller's myotomy (LHM) is a technically difficult procedure in obese achalasia patients with sub-optimal outcomes and increased rates of gastro-oesophageal reflux disease (GERD). Per oral endoscopic myotomy (POEM) is emerging as a less invasive alternative to LHM in such patients. The impact of obesity on the outcomes and post-treatment GERD after POEM are not well known. Hence our study aims were to compare the outcomes and rates of abnormal oesophageal acid exposure after POEM in obese versus non-obese patients with achalasia.

Aims and Methods: Records of achalasia patients who underwent POEM between April 2014 and June 2017 were reviewed. Patients who underwent pre-treatment timed barium oesophagram (TBE), high-resolution oesophageal manometry (HREM) along with 2 month post-treatment TBE, HREM and a 24-hour oesophageal pH study were included. Patients were categorized into 2 groups, obese (BMI≥30 kg/m2) or non-obese (BMI < 30 kg/m2). Patient demographics, type of achalasia, prior interventions, pre-treatment and 2 month post-treatment TBE, HREM, Eckardt's scores and pH study findings were compared between the 2 groups. Eckhardt's symptom score of < 3 was considered as successful palliation of symptoms.

Results: Among a total of 134 patients who underwent POEM, 100 patients (Obese = 46; Non-obese = 54) met the study criteria. There were no significant differences in the age, gender, ASA class, achalasia subtype, prior interventions, procedure time, length of stay (LOS) and complication rates between the 2 groups. Post treatment Eckardt's scores, HREM parameters and TBE parameters improved significantly in both groups. Eckardt's scores improved from an average of 7 to 0 ($p < 0.001$) in both the groups. However there was no significant difference in pre-post change in values of these parameters between the 2 groups. DeMeester score was abnormal in 57.5% in non-obese versus 43.9% in obese group ($p = 0.22$). Similarly there was no difference in number of patients who reported having GERD symptoms in non-obese versus obese patients (15.8% vs. 21.1%, $p = 0.55$).

Conclusion: POEM is an equally safe and effective treatment option for both obese and non-obese achalasia patients. Interestingly, POEM does not lead to increased GERD in obese as compared to non-obese patients. POEM might emerge as the preferred approach for myotomy in obese achalasia patients as compared to LHM in future.*[Pre and Post POEM findings in Eckhardt's score, HREM, TBE and 24-hr oesophageal Ph study findings.]*

Disclosure: This Abstract is accepted to be presented at Digestive Disease week (DDW) meeting in Washington DC, USA in June/2018.

P0501 ROLE OF HIGH-RESOLUTION MANOMETRY IN THE DIAGNOSTIC AND THERAPEUTIC APPROACH OF POST FUNDOPLICATION DYSPHAGIA

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Introduction: Laparoscopic fundoplication is the gold standard of non-pharmacological treatment of gastroesophageal reflux disease (GERD). Despite good symptomatic control, a significant percentage of patients develop dysphagia at follow-up. High-resolution manometry (HRM) is indicated in the evaluation of these patients, but its impact is not well established.

Aims and Methods: We performed a retrospective study evaluating GERD patients who developed persistent post fundoplication dysphagia. Demographic, clinical and HRM data were evaluated whenever possible in the pre and postoperative period. The analysis of HRM data was performed according to the Chicago III classification.

Results: We included 27 patients, 63% women, with a median age of 58 years (range: 46–64). Nissen fundoplication was the most frequently performed surgical procedure (85%). Patients presented with dysphagia after a median period of 7 months (range: 1–43), more frequently for solid food (59%). 12 patients (44%) had preoperatively HRM, with abnormal findings in half of the cases (ineffective motility n = 4, hypercontractile esophagus n = 2). Significant manometric changes were observed in the postoperative HRM in 16 patients (59%). The main findings were esophagogastric junction outflow obstruction (n = 9, 33%) and absence of contractility (n = 3, 11%). Compared to the preoperative period, there was a significant increase in the resting pressure of the lower esophageal sphincter (8.1 mmHg vs. 20 mmHg, $p = 0.043$). There were no significant differences in the integrated relaxation pressure ($p = 0.686$) and in the distal contractile integral ($p = 0.109$). In patients with available pre and postoperative HRM, the manometric diagnosis was changed in 83% (10/12). In the follow-up, 15% of the patients were submitted to endoscopic dilatation and 41% underwent revision surgery, with clinical success of 25% and 75%, respectively.

Conclusion: HRM in post-fundoplication dysphagia is associated with relevant changes in a considerable percentage of patients, allowing a tailored management approach. Also, this study reflects the need for additional metrics to better identify patients at higher risk for postoperative dysphagia, and potentially benefiting from a different initial therapeutic strategy.

Disclosure: Nothing to disclose

P0502 THERAPEUTIC OUTCOMES FOLLOWING ENDOTHERAPY FOR REFRACTORY GASTROPARESIS

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Introduction: The relative merits of endotherapy for refractory gastroparesis remain unclear.

We assessed the symptomatic response of patients undergoing non-surgical pyloric intervention at a specialist tertiary centre.

Aims and Methods: 57 patients (21 male, mean age 47, 16–81) with medical refractory gastroparesis (29 idiopathic, 5 diabetic, 23 post-gastric transposition) underwent 117 endoscopic treatments from Sep 2013-Sep 2017: either 100IU units of Botox injected into 4 quadrants of the pylorus (N = 66), balloon dilatation to 15–20 mm (EBD, N = 13) or combination therapy (N = 38). Patients with gastric malignancy, pyloric surgery or no follow-up were excluded. Symptoms were assessed immediately prior to each procedure and at first follow-up using a retrospective scoring system based on the presence (1 point) or absence (0 points) of Vomiting, Nausea, Bloating or Early satiety. This formulated a composite symptom score (SS) out of 4; positive response was defined by improvement in SS of at least 1. Statistical analysis was performed using Wilcoxon Signed-Rank Test and Fischer's Test.
Results: There were no immediate or late complications. Mean symptom score (SS) improved per-patient from 2.1 points at baseline to 1.2 post initial endotherapy ($p < 0.01$) at median follow up of 2.1 months. 20 patients required further endotherapy (median 2.5 treatments; range 2–12); mean SS was 1.0 at latest follow-up.
Per-procedure, mean reduction in SS was 0.8 points ($p < 0.01$) with overall positive response rate of 67%. By symptom, vomiting was most responsive to endotherapy (86% pre v 32% post). By treatment type, Botox alone (N = 66) had the highest overall response (78%) compared to EBD (38%, p = 0.02) or combination therapy (66%, p = 0.3). Response to Botox was greater in patients under 40 (83% v 61%, p = 0.04) and females (81% v 33%, p = 0.002). By indication, diabetic GP(N = 17) were most likely to respond (76%).
Sub-group analysis showed procedures for gastroparesis (diabetic/ idiopathic, N = 75) responded significantly more to Botox (mean SS reduction 1, $p < 0.01$) than EBD (mean SS reduction 0.2, $p > 0.1$) or combination therapy (mean SS reduction 0.44, p = 0.12). Procedures for gastric transposition (N = 42) showed significant SS reduction post combination therapy (2.1 v 1.2, p = 0.01) but not post EBD (1.9 v 1.6, $p > 0.1$) or Botox (1.7 v 1.1, p = 0.08).
Conclusion: Endotherapy is a safe and effective treatment for refractory gastroparesis. We found Botox monotherapy significantly improved symptoms in diabetic or idiopathic gastroparesis, especially younger females; conversely, combination therapy was preferable for delayed gastric emptying post gastric transposition. Careful patient selection may augment therapeutic response.
Disclosure: Nothing to disclose

P0503 CLINICAL IMPACT OF LOWER ESOPHAGEAL SPHINCTER FUNCTION ON THE SYMPTOM ASSESSMENT OF NON-EROSIVE REFLUX DISEASE

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Introduction: Gastroesophageal reflux disesase is diagnozed based on the symptoms such as acid regurgitation or heartburn through transient lower esophageal sphincter (LES) relaxation. Non-erosive reflux disease (NERD) is recognized as hard to treat and less effective with proton pump inhibitor (PPI) compared with erosive reflux disease. Therefore, the diagnosis of NERD deserves functional testing as well as symptom association. The aim of the study was to evaluate the association between lower esophageal sphincter function and symptom and to assess the reponse to treatment with PPI.
Aims and Methods: A total of 80 patients with NERD were enrolled. All patients underwent esophageal manometry and symptom assessment using symptom index and symptom sensitivity index. All patients received a standard dose of PPI for 4 weeks, and then investigated symptom assessment by questionnaire.
Results: The patients were divided into 2 groups by LES function: normal LES relaxation group (LES relaxation % ≥90%) and abnormal LES relaxation group (LES relaxation % < 90%). Clinical and manometric findings were compared and investigated the reponse to PPI. 18 patients (22.5%) were included in the normal LES group whereas 62 patients (77.5%) in LES relaxation abnormality group. There was significant difference in sex (p = 0.007), major symptom (p = 0.024), symptom index (p = 0.032), symptom sensitivity index (p = 0.045), abnormal upper esophageal sphincter function (p = 0.032), and PPI response (p = 0.014) between the 2 groups. In a linear logistic regression model, only LES relaxation abnormality was associated with poor PPI response (p = 0.015).
Conclusion: LES relaxation abnormality was associated with patients' symptom, especially acid regurgitation. Furthermore, LES relaxation abnormality served as a predictor of poor PPI response.
Disclosure: Nothing to disclose

P0505 LACK OF IMPROVEMENT OF IMPAIRED CHEMICAL CLEARANCE CHARACTERIZES PPI-REFRACTORY REFLUX-RELATED HEARTBURN IN NON-EROSIVE REFLUX DISEASE PATIENTS

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Introduction: Heartburn is the most specific symptom of reflux disease, highly responsive to proton pump inhibitor (PPI) therapy. However, some patients do not respond to PPIs, but the mechanisms of refractoriness have not been fully elucidated. Impedance-pH monitoring, allowing a comprehensive off- and on-therapy assessment of reflux, represents a valuable test to investigate PPI-refractoriness.
Aims and Methods: We aimed to clarify the mechanisms of PPI-refractory reflux-related heartburn, as investigated with impedance-pH monitoring**.** In this prospective, multicenter, pathophysiological study, 64 patients complaining of heartburn with a negative upper gastrointestinal endoscopy, performed after 4-week PPI withdrawal, and with proven GERD at off-PPI impedance-pH monitoring, entered the study. 32 individuals had PPI-refractory heartburn (i.e. < 50% of symptom relief after 8-week high-dosage PPI therapy), and 32 had PPI-responsive heartburn. Mechanisms of heartburn refractoriness to high-dosage PPI were investigated by means of on-therapy impedance-pH monitoring and compared with off-PPI findings. Blindly and manually assessment of impedance-pH tracings comprised conventional reflux testing parameters, including esophageal acid exposure time (AET), number of reflux episodes and symptoms association analysis (symptom index, SI, and symptom association probability, SAP), and novel impedance-detected features, including the post-reflux swallow-induced peristaltic wave (PSPW) index and mean nocturnal baseline impedance (MNBI).
Results: The 2 groups were well comparable for gender, age, BMI, rates of hiatal hernia and of abnormal off-PPI impedance-pH variables (p = ns), as shown in the Table. On PPI, median esophageal AET did not differ between the 2 groups. Moreover, AET was abnormal in 6/32 (19%) of PPI-refractory patients. The total number of refluxes, weakly acidic refluxes and bolus exposure were significantly higher, while PSPW index and MNBI were significantly lower in PPI-refractory cases ($p < 0.05$). At multivariate logistic regression analysis, only PSPW index was an independent risk factor for PPI refractoriness (OR 1.082, 95% CI 1.022–1.146, p = 0.007). Comparing off- and on-PPI parameters, median PSPW index did not change in PPI-refractory patients (24% vs. 26%, p = 0.327), but increased significantly in PPI-responsive cases (29% vs. 46%, $p < 0.001$).
Conclusion: Lack of improvement of impaired chemical clearance represents a major biomarker of PPI-refractory reflux-related heartburn. Add-on therapies aimed to improve chemical clearance by stimulation of timely post-reflux salivary swallowing could benefit patients with PPI-refractory reflux-related heartburn.

	PPI-refractory N = 32	PPI-responsive N = 32	P value
Male Gender, n (%)	16/32 (50%)	18/32 (56%)	0.802
Age (years) (median) (IQR)	48 (44–56)	56 (47–62)	0.070
BMI (median) (IQR)	25 (23–27)	25 (24–27)	0.535
Endoscopic Hiatal Hernia, n (%)	24/32 (75%)	16/32 (50%)	0.071
Abnormal AET, n (%)	29/32 (91%)	24/32 (75%)	0.185
Abnormal PSPW index, n (%)	32/32 (100%)	32/32 (100%)	0.999
Abnormal MNBI, n (%)	26/32 (81%)	28/32 (88%)	0.731
Positive SAP, n (%)	21/32 (66%)	13/32 (41%)	0.080
Positive SI, n (%)	23/32 (72%)	15/32 (47%)	0.075

[Baseline demographic characteristics and reflux testing off-therapy features of 32 patients with PPI-refractory and 32 patients with PPI-responsive en]
Disclosure: Nothing to disclose

P0506 ESOPHAGEAL INTRALUMINAL MICROBIOTA IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE AND HEALTHY CONTROLS

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Introduction: Prevalence of gastroesophageal reflux disease (GERD) ranges 18–46%. In the last few years, the esophageal microbiota has been suggested to have a role in esophageal diseases (1). Identifying microbiota in the esophagus offers new approaches to understanding bacterial roles as pathogenetic factors in GERD, Barrett's esophagus, and esophageal adenocarcinoma (2).
Aims and Methods: We aimed to compare the esophageal intraluminal microbiota of patients of GERD and healthy controls using the 16S ribosomal RNA (rRNA) sequencing. A total of 22 patients were enrolled in this study: 16 patients with GERD and 6 healthy controls. All patients were performed esophageal fluids collection procedure using the specially designed esophageal perfusion catheter equipped with 2 inflatable intraesophageal balloons. mRNA expression was

analyzed by qRT-PCR. Bacterial DNA was purified from the esophageal fluids samples and analysed by next generation sequencing - metagenomic analysis.
Results: We found that microbial communities of esophageal fluid samples are different in healthy volunteers and patients with GERD. *Bacteroidetes* (25.8%), *Firmicutes* (25.5%), *Actinobacteria* (15.4%), *Proteobacteria* (11.7%) *Fusobacterium* (8.8%) were the most prevalent phylum represented in healthy volunteers. In patient with GERD the most prevalent phylum also were *Bacteroidetes* (34.2%), *Firmicutes* (27.3%), *Actinobacteria* (15.4%), *Proteobacteria* (3.5%). However, relative abundance of *Proteobacteria* of esophageal fluid samples in healthy volunteers was greater in comparison with patients with GERD (11.7% vs 3.5, $p = 0.047$). Proportion Bacterial families *Acetobacteraceae, Bacillaceae, Bdellovibrionaceae, Clostridiales Insertae Sedis XI, Fusobacteriaceae, Moraxellaceae, Pasteurellaceae and Rhodocyclaceae* also was higher in healthy volunteers ($p < 0.05$).
Conclusion: Our study showed difference in the esophageal intraluminal microbiota between the patient with GERD and healthy controls. Phylum-level and family-level analysis of esophageal fluids samples revealed that the bacterial communities differed among groups. We found that in healthy controls *Proteobacteria* was present in greater numbers in comparison with patients with GERD. However, a study with larger sample size is needed to further explore difference of esophageal microbiota.
Disclosure: All authors have declared no conflicts of interest

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P0507 MACROPHAGE FUNCTIONAL ACTIVITY CHANGES IN DIFFERENT CLINICAL VARIANTS OF GASTROESOPHAGEAL REFLUX DISEASE DEPENDING ON REFLUXATE PH VALUES

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Introduction: Esophageal exposure to gastric refluxate is a primary determinant of gastroesophageal reflux disease (GERD) disease severity. The refluxate provokes active esophageal mucosa inflammation with moderate immune cells infiltration, which includes macrophages. Considering the concept of macrophage functional activity changes depending on their phenotype (M1/M2) and its strong correlation with systemic Th1/Th2 immune response, macrophages greatly influence esophageal mucosa inflammation and affect GERD clinical variants.
Aims and Methods: Pooled analysis of macrophage and monocyte functional activity in exposure to different pH refluxates of patients with different clinical variants of GERD. Patients with non-erosive reflux disease (NERD; $n = 26$; 41.2±3.6 y.o.), erosive reflux disease (ERD; $n = 25$; 41.9±3.1 y.o.), and Barrett's esophagus (BE; $n = 19$; 43.7±4.2 y.o.) were included in the study. Macrophage functional activity was assessed cumulatively by *in vitro* model of local patients' refluxate exposure on macrophages and by monocyte/macrophage phenotype changes in systemic circulation. *In vitro* model included adding refluxates of patients ($n = 70$) with different pH (4.6–8.1) to peritoneal macrophages of C57/BL6 mice ($n = 70$) culturing in standard conditions for 36 hours. Monocytes were isolated from systemic circulation and derived to macrophages (MDM) in standard conditions. Assessment of macrophage and monocyte/MDM functionality included analysis of secretory activity (Th1/Th2 cytokine production in culture medium, Antigenix, USA), receptor characteristics - typical M1/M2 macrophage CD markers (CD25, CD80 and CD163, CD206, respectively) performed by flow cytometry (FC500, Beckman Coulter). Mean pH values of refluxates were assessed for all patients' groups.
Results: Upper range pH values were typical for ERD patients (6.53±0.41) vs 5.52±0.24 and 5.44±0.32 in BE and NERD, respectively. Analysis of cytokine production revealed the prevalence of Th1 and Th1/Th2 bivalent (IL-2, IL-6) cytokines as compared to Th2. The most significant changes in all patient groups were observed in such Th1 cytokines as IL-8, IL-12, INF-g; Th2 - IL-4, IL-5, IL-10. The production of IL-8 and IL-4 dominated in all groups. IL-8 level was 1.4-times increased in BE as compared to ERD (60.3±0.4 pg/ml vs 44.2±0.4 pg/ml, $p < 0.05$); IL-4 production was 2-fold elevated in BE as compared to NERD (13.3±0.7 pg/ml vs 6.8±0.6 pg/ml, $p < 0.05$). For pooled secretory function analysis Th1/Th2 cytokine production index was used. Th1/Th2 cytokine index varied among groups: 4.9 vs 5.7 vs 7.2 in ERD, BE and NERD, respectively. Expression analysis of surface M1/M2 macrophage receptors revealed the predominance of M1 macrophage phenotype in all groups and in all monocytes/MDM isolated from the patients' blood. The expression of CD25 (M1) and CD163 (M2) changed more significantly. The highest values of M1/M2 markers expression indices were noted in BE for both macrophages (2.96) and monocytes (2.56), the lowest - for ERD (2.08 for macrophages, 1.98 for monocytes). These data reflect the same trend as the analysis of macrophage secretory activity in the groups.
Conclusion: The pooled assessment of macrophage functional activity in different clinical variants of GERD, inclusive of pH of the refluxate, revealed characteristic changes of macrophage functional activity in groups. Progressive decrease of pooled Th1/Th2 cytokine production indices and M1/M2 surface CD markers expression indices on macrophages and monocytes are associated with higher pH refluxate values and are typical for ERD patients.
Disclosure: Nothing to disclose

P0508 THE VALIDATION OF PEPTEST, A NEW NON-INVASIVE TECHNOLOGY FOR THE DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE IN CHINA

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Introduction: At present the diagnosis of GERD uses syndrome-based diagnoses which often lacks specificity and are invasive. The disadvantage of endoscopy lies in its low detection rate, only 2.95% to 4.1% as NERD is the most frequent diagnosis. In recent years, Peptest™, a new non-invasive rapid diagnostic test, detecting and measuring pepsin in expectorated saliva as a marker of a prior reflux event, has been used in the western world to complement questionnaires and to assist office-based diagnosis. To validate the clinical benefits of Peptest™ in China; a multi-center clinical study involving a large number of patients and healthy controls has been conducted.
Aims and Methods: 1031 subjects aged between 18 to 75 years were recruited from 9 hospitals (2 Beijing and 7 Shanghai), including 323 asymptomatic healthy control subjects and 708 patients. According to their endoscopy results, patients were divided into 2 subtypes, Erosive Esophagitis (EE) and Non-Erosive Reflux Disease (NERD). All subjects were asked to provide 1 saliva sample 1 hour following the main meal of the day and patients were encouraged to provide an additional sample when their gastroesophageal reflux symptoms occurred, Table 1. All saliva samples were collected following the standard collection procedure in Peptest™ collection tubes and analysed for the presence of pepsin by lateral flow technology. A faint test line indicating a low pepsin concentration in the saliva of less than 75ng/ml was defined as weak positive and treated as negative, differentiating between physiological and pathological reflux (greater than 75ng/ml).
Results: Higher levels of pepsin were found in the EE and NERD patient groups with over 78% pepsin positivity (553 patients pepsin positive and 155 negative) compared to the control group with only 40% pepsin positivity. The overall sensitivity was 78% and specificity 60%. The positive predictive value (PPV), the fraction of those who were pepsin positive and actually have the disease was 81% and the negative predictive value (NPV) 55%. The likelihood ratio of positive patients presenting with reflux disease was 1.94 with an Observed Proportionate Agreement (accuracy) of 72.36%.
Conclusion: Pepsin a biomarker for reflux and Peptest™ which contains 2 unique anti-human pepsin monoclonal antibodies to detect and capture pepsin enables the rapid detection of pepsin in clinical samples. This easy-to-use non-invasive and rapid test improves the accuracy of reflux diagnosis complementing the use of questionnaires, invasive diagnostic tests and office based reflux diagnosis to better tailor appropriate treatments. The study also revealed that the prevalence of reflux disease in the Chinese population was much higher than previously reported.

	EE patients	NERD patients	Healthy controls
Postprandial sample	220	488	323
Post-symptom sample	214	478	N/A

[Sample distribution]
Disclosure: Nothing to disclose

P0509 EROSIVE ESOPHAGITIS - NEW APPROACHES TO DIAGNOSIS

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Introduction: At present time, the spread of the gastroesophageal reflux disease and its morbidity is still on a considerably high level, which compels to searching for new approaches to diagnosis and treatment.
Aims and Methods: To study the incidence of the virus persistence of the herpes febrilis (HSV), cytomegalovirus (CMV) and human herpes virus type 4 (EBV) in the esophageal mucosa of patients with an erosive form of gastroesophageal reflux disease.
75 patients with erosive esophagitis (detected via esophagogastroduodenoscopy) were included in this research, the mean age of the patients: 53 ± 14.7 years, males - 55 years, females - 20 years. During the endoscopic examination all patients underwent a biopsy of the esophageal mucosa from the visual defect (2 cm from the gastro-esophageal junction) for immunohistological analysis (IHC test).
Results: According to the results of the IHC test, 32 patients (42.7%) had a virus infection. The degree of incidence of the virus infection in patients with an erosive esophagitis was the following: 21 patients (40.4%) had herpes febrilis (HSV), 19 patients (36.5%) had cytomegalovirus (CMV) and 12 (23%) patients had human herpes virus type 4 (EBV). 18 patients (56.3%) had a combination of several virus types, from 2 to 3 types simultaneously.
Conclusion: Chronic virus infection of the esophageal mucosa is widespread amongst patients with an erosive form of gastroesophageal reflux disease. In the majority of cases, several virus types are present.
Disclosure: Nothing to disclose

P0510 MOTOR ABNORMALITIES IN EROSIVE GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: The Chicago Classification of esophageal motility disorders is not designed to evaluate motor function in gastroesophageal reflux disease (GERD)[1]. The aim of the study is to assess manometrical abnormalities in erosive GERD.
Aims and Methods: 127 patients (75 women, age 28–78 years) with esophagitis LA Grade B,C,D. Esophageal high resolution manometry (HRM), 24-h esophageal impedance-pH monitoring were performed in all patients after upper endoscopy. Esophagogastric junction contractile integral (EGJ-CI) was calculated during 3 respiratory cycles using the distal contractile integral (DCI) box. The calculated 'DCI' was then divided by the duration of the 3 respiratory cycles [2].
Results: According to esophageal impedance-pH monitoring pathological acid exposure time (AET > 6%) [2] was detected only in 115 (90.5%) patients, so the remaining 12 (9.5%) were excluded from further evaluation. Among 115 GERD-patients HRM revealed ineffective esophageal motility (IEM) in 44 (38.3%), absent contractility in 6 (5.2%), fragmented peristalsis in 2 (1.7%), normal esophageal motility in 63 (54.8%) patients. Esophageal manometry also assessed esophagogastric junction (EGJ) morphology [2]: type I was detected in 71 (62%), type II in 24 (20.7%), type III (≥3 cm separation between the LES and CD) in 20 (17.3%) patients. Basal LES pressure (median (5th–95th percentile)) in GERD patients was 10.7 (4.4–15.3) mm Hg, median EGJ-CI was 21.3 (10.4–38.6) mm Hg. Among 44 patients with IEM multiple rapid swallows revealed contraction reserve (post-MRS contraction has greater vigor than the preceding test swallows) in 12 (27.3%) patients, while 6 patients (100%) with absent contractility demonstrated absent post-MRS contraction.
Conclusion: Manometrical abnormalities in GERD include low basal LES pressure and low EGJ-CI (in comparison to normal values) [3], hiatal hernia, esophageal body hypomotility, absence of contraction reserve.
Disclosure: Nothing to disclose

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P0511 HEALTH-RELATED QUALITY OF LIFE IMPACT AMONG GASTROESOPHAGEAL REFLUX DISEASE PHENOTYPES IN ECUADORIAN PROTON PUMP INHIBITOR NON-RESPONDERS: A PROSPECTIVE COHORT

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Introduction: More than 50% of Gastroesophageal Reflux Disease (GERD) patients do not respond to Proton Pump Inhibitor (PPI) therapy, remaining symptomatic. Yadlapati et al. described the impact on the Health-Related Quality Of Life (HRQOL) doesn't depend on the GERD phenotype. The Northwestern Esophageal Quality of Life survey (NEQOL), assesses the HRQOL impact across different chronic esophageal diseases (CED). It has previously validated in an Ecuadorian Spanish-speaking population (NEQOL-S). The HRQOL impact among different GERD phenotypes has not been assessed by the NEQOL, especially in a Hispanic population.
Aims and Methods: We aimed to describe the HRQOL impact using NEQOL-S among GERD phenotypes in Ecuadorians PPI non-responders. Prospective cohort study performed at a single medical center from Ecuador (Sept-2016 to Sept-2017). PPI non-responder patients who underwent 24-hour pH-impedance monitoring test and completed the NEQOL-S and SF-12 (a very used survey to assess general-HRQOL in South America). Acid exposure time (AET) and symptomreflux association (SRA) were recorded. Participants were classified into cohorts based on test results: GERD (+AET), reflux hypersensitivity (RHS) (-AET/+SRA) and functional heartburn (FH) (-AET/-SRA). The sample size for each group was estimated using known mean PROMIS Global quality of life reported by Yadlapati et al., with an 80% statistical power. The pH-impedance test outcomes and HRQOL results were contrasted between groups through ANOVA or Kruskal-Wallis test. The relationship between HRQOL (NEQOL-S) vs. AET was estimated through Spearman's rank correlation coefficient (rho). A confirmatory analysis was done using SF-12. A p-value < 0.01 was considered to be statistically significant. Analyses were performed using R v3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).
Results: There were 85 cases with 24-hours pH-impedance monitoring test performed: 30 (35%) +AET, 14 (16%) -AET/+SRA, and 41 (48%) -AET/-SRA. Baseline characteristics and pH-impedance test outcomes are summarized on table 1. NEQOL median scores among groups were: 28.5, 25, 27; respectively ($p = 0.719$). SF-12 median scores among groups were: 40, 39, 39, respectively ($p = 0.977$). Relationship between acid exposure time and HRQOL, measured through NEQOL-S and SF-12 reached a rho = 9.0% ($p = 0.414$) and 7.3% ($p = 0.510$), respectively.
Conclusion: There is no statistical difference of HRQOL impact among GERD phenotypes, or relationship between HRQOL vs. AET. NEQOL-S results are

Abstract No: P0511: Table 1. Baseline characteristics, pH-metry outcomes and quality of life among GERD phenotypes.

	GERD [+AET] (n = 30)	Reflux Hypersensitivity [-AET/+SRA] (n = 14)	Functional heartburn [-AET/-SRA] (n = 41)	*p-value*
Age (years), mean (SD)	48.90 ± 14.5	39.64 ± 8.6	48.24 ± 13.0	0.069
Gender (female), n (%)	12 (40.0)	11 (78.6)	25 (61.0)	0.040
pH-impedance test outcomes, median (range)				
Total % Acid exposure time	9.4 (5.3–32.4)	1.2 (0.4–3.7)	1.3 (0.0–5.5)	< 0.001
Upright % acid exposure	12.5 (3.0–25.9)	1.9 (0.2–4.4)	2.5 (0.0–7.4)	< 0.001
Recumbent % acid exposure	5.8 (0.0–38.1)	0.5 (0.0–2.8)	0.0 (0.0–2.6)	< 0.001
Symptom association probability	0.0 (0.0–100.0)	99.9 (97.0–100.0)	0.0 (0.0–88.6)	< 0.001
DeMeester Score	30.9 (6.8–123.0)	5.5 (2.1–16.3)	5.4 (0.0–36.3)	< 0.001
Quality of life, median (range)				
NEQOL (worst 0 - best 56)	28.5 (1–52)	25 (6–41)	27 (1–52)	0.719
SF-12 (worst 12 - best 56)	40 (14–52)	39 (28–49)	39 (12–54)	0.977

concordant with Yadlapati et al. description, that RHS (-AET/+SRA) patients used to present a not significant lower HRQOL.
Disclosure: Nothing to disclose

P0512 FIRST SPANISH VALIDATED TRANSLATION OF A SINGLE HEALTH-RELATED QUALITY OF LIFE SURVEY FOR BROAD USE ACROSS DIFFERENT CHRONIC ESOPHAGEAL DISEASES: A PSYCOMETRIC EVALUATION OF THE NEQOL SURVEY IN AN ECUADORIAN POPULATION

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Introduction: Chronic Esophageal Diseases (CED) are related to significant disease burden, disability, and cost. Health-related quality of life (HRQOL) is a multidimensional construct that captures physical, mental, social and emotional aspects of patients' lives and how health status is impacted. In 2016, Northwestern Esophageal Quality of Life survey (NEQOL) was developed as the first hybrid questionnaire that allows for broad use across different CED, keeping sensitivity to specific conditions. It is a 14-items scale, measured through a Likert Scale (0–4); with fewer points meaning more HRQOL impact. There is no validated translation of the NEQOL into Spanish.
Aims and Methods: We aimed to better understand how HRQOL can be affected by different CED in Ecuadorians, through the development of a validated translation of NEQOL for its use in Spanish-speaking patients. Observational, prospective cohort study (Oct-2016 - Oct-2017). The translation was based on Sperber recommendations. NEQOL-Spanish version (NEQOL-S) and general HRQOL SF-12 survey were prospectively applied to a clinic-based population. NEQOL-S was reapplied 7 days later. The sample size was calculated using estimating proportion formula (5% margin error). Selection criteria: >18 years old, able to complete the survey, CED diagnosis was based on clinic, endoscopy, biopsy, pH-impedance or manometry findings, no history of esophageal cancer or corrosive esophagitis. NEQOL-S Psychometric analysis included: Internal consistency (Cronbach's alpha, CA), construct validity (Kaiser-Meyer-Olkin Index, KMO), criterion validity against SF-12 (Spearman's rank correlation coefficient (rho) & linear regression, R2), and test-retest reliability (Intraclass Correlation Coefficient, ICC). NEQOL-S utility describing HRQOL by each CED was defined through median (Kruskal-Wallis test). p-value < 0.01 was regarded as statistically significant. Analyses were performed using R v3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).
Results: After completing strict translation, any item was considered problematic. The sample size was calculated to be 385 patients, who were successful included: median age 48 (18–90) yo, 242 (63%) female, 24 months median length symptoms. Internal consistency was excellent (CA = 90%). Construct validity did not suggest to reduce survey number of items (KMO = 92%, $p < 0.01$). Criterion validity showed good coherence when correlated with the SF-12 survey (rho = 75%, $p < 0.01$) with an important impact of CED on general HRQOL (R2 = 57%, $p < 0.01$). Test-retest reliability showed very good correlation when repeating survey (ICC = 82%). Table 1 resumes how NEQOL-S results differed per CED ($p < 0.01$).

	NEQOL-S	SF-12
Achalasia	12 (0–49)	30 (12–52)
Barrett's esophagus	25 (0–50)	42 (19–55)
Gastroesophageal reflux disease (GERD)	27 (0–52)	40 (12–56)
Esophageal scleroderma	7 (1–17)	27.5 (27–35)
Reflux Esophagitis	23 (0–54)	40 (21–54)
Nonerosive Reflux Disease (NERD)	35 (9–50)	45 (9–50)

[Table 1. NEQOL-S and SF-12 survey results for each Chronic Esophageal Disease (CED) [median score (minimum - maximun range)]]
Conclusion: CED has a negative impact on HRQOL. NEQOL-S showed very good psychometric properties, which let us recommend it as a useful tool for measuring HRQOL in Spanish-speaking patients with CED.
Disclosure: Nothing to disclose

P0513 DIAGNOSTIC VALUE OF HIGH-RESOLUTION MANOMETRY IN HIATAL HERNIA DETECTION

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Introduction: Detection of hiatal hernia (HH) is usually done with contrast-enhanced X-ray examination of the esophagus, upper gastrointestinal endoscopy. The aim of this study was to assess the diagnostic value of high-resolution manometry (HRM) in HH detection.
Aims and Methods: 95 patients (37 women, age 23–84 years) with typical symptoms of gastroesophageal reflux disease (GERD) were evaluated using upper gastrointestinal endoscopy, HRM in supine position (HRM). Endoscopic size of HH was measured between the distal margin of the esophageal palisade vessels and the diaphragm hiatus. Manometrical length of HH detected between the lower margin of the lower esophageal sphincter (LES) and pressure inversion point (PIP).
Results: Upper endoscopy revealed HH in 87 (91.6%) GERD patients, which were subdivided in 3 groups (depending on endoscopic HH size). Group I (the maximum HH length is 4–6 cm) included 20 (21%) patients. Group II (the maximum HH length is 2–3.9 cm) - 44 (46.3%) patients. Group III (0.5–1.9 cm) - 23 (23.7%). HRM detected separation between the LES and CD only in 44 patients (45.4%). Moreover HH (≥2 cm separation between the LES and CD) [1] was confirmed just in 20 (21%) patients (all patients from group I). Among the 44 patients from group II HRM revealed separation between the LES and CD < 2 cm in 24 cases (EGJ type II)[1]. In group III HRM did not detect HH.
Conclusion: Endoscopic detection of HH correlates with esophageal manometric diagnosis only in case of big HH (HH > 4 cm long). Using upper endoscopy as the only diagnostic tool may lead to overdiagnosis in 70.5% cases. HRM is the more accurate and specific test for detecting HH than upper endoscopy.
Disclosure: Nothing to disclose

Reference

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P0514 ACCURACY OF HIGH-RESOLUTION MANOMETRY IN DIAGNOSIS OF HIATAL HERNIA IN MORBIDLY OBESE PATIENTS

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Introduction: Hiatal hernia (HH) is common in obese patients. Classically, HH is detectedby upper gastrointestinal endoscopy (UGIE) or fluoroscopic upper gastrointestinal (UGI) xray series, however intraoperative diagnosis of HH is considered the gold standard. High resolution manometry (HRM) showed a higher sensitivity and specificity than the classical techniques in non-obese patients. There are no data in morbidly obese population.
Aims and Methods: We aimed to evaluate in a population of obese patients candidated to bariatric surgery the agreement in the detection of HH between HRM and intraoperative diagnosis.
52 consecutive morbidly obese patients were prospectively recruited from an outpatient clinic devoted to the surgical therapy of obesity and related disorders. All underwent a preoperative assessment including standardized GERD questionnaire, UGI xray, an UGIE and HRM. All the surgical procedures were performed by a single surgeon who was blinded to HH presence/absence. For both HRM and UGIE or UGI xray, the ability to diagnose hiatal hernia was assessed by means of receiver operating characteristic (ROC) analysis with calculation of area under the curve (AUC). Sensitivity, specificity, and positive and negative predictive values were determined
Results: There was a significant correlation between the 3 morphological types of EGJ assessed by HRM and the presence of HH at UGIE (R = 0.28, p = 0.044). 34/52 enrolled patients underwent bariatric surgery; in 9/34 patients HH was intraoperatively diagnosed. The sensitivity of UGI xray or UGIE in detecting intraoperative diagnosis of HH was 77.8 % and the specificity was 44%; the positive predictive value was 33.3% and the negative predictive value 84.6%. The AUC for UGI xray or UGIE in detecting intraoperative diagnosis of HH was 0.609 (0.40/0.82) with a 95% CI. The sensitivity of the HRM in detecting intraoperative diagnosis of HH was 88.9% with a 60% specificity rate and a positive predictive value of 44.4% and a negative predictive value of 93.75%. The AUC for HRM in detecting intraoperative diagnosis of HH was 0.74 (0.55/0.91) with a 95% CI, p = 0.039.
Conclusion: HRM is a useful tool in the preoperative work-up of bariatric patients, since it shows a better sensitivity and specificity compared to traditional techniques and correlates with the diagnostic gold standard.
Disclosure: Nothing to disclose

P0515 HOW TO HANDLE TISSUE SPECIMENS AFTER ENDOSCOPIC MUCOSAL RESECTION FOR BARRETT'S ESOPHAGUS RELATED NEOPLASIA: A MULTICENTER RANDOMIZED TRIAL COMPARING THREE SPECIMEN HANDLING METHODS

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Introduction: Endoscopic resection is the cornerstone in treatment of Barrett's esophagus (BE) related neoplasia. The optimal method for handling of endoscopic mucosal resection (EMR) specimens directly after the endoscopy however, remains unknown. As a result, practice varies widely around the world.
Aims and Methods: The aim of this study is to compare 3 different specimen handling methods (pinning on paraffin, the cassette technique, and direct fixation in formalin) for 1) enabling optimal evaluation of all clinically relevant histologic parameters and 2) required time for specimen handling. In this multicenter, randomized trial, EMR specimens of visible lesions in BE with no suspicion of submucosal invasion during endoscopy were randomized to 3 different specimen handling methods: pinning on paraffin, direct fixation in formalin and the newly introduced cassette technique. The cassette is a small box in which an EMR specimen can be enclosed after stretching it out on paper. By closing the cassette, gentle pressure is applied on the specimen during the process of formalin fixation to prevent curling of the lateral margins of the EMR specimen. The pinning method comprises smooth stretching of the EMR specimen and pinning it out on cork or paraffin. Direct fixation of the EMR specimen in formalin requires no handling at all. Primary outcome parameter was an overall optimal evaluation score of 5, on a 5 point Likert scale, for assessment of all relevant histologic parameters. Secondary outcome parameters were evaluation scores for all histopathologic parameters separately and the time required for specimen handling. The histopathological evaluation scores were assessed by 2 BE expert pathologists blinded for the specimen handling method.
Results: In total, 127 specimens of 42 patients were randomized (83% male, mean age of 68.5, median BE segment of C1M4). A median of 2 specimens (IQR 1–4) were included per patient. Of the 127 randomized EMR specimens, 45 were assigned to pinning on paraffin, 40 to the cassette technique, and 42 to direct fixation in formalin. The percentages of specimens with overall optimal histopathological evaluation scores were similar for the pinning method (96%) and for direct fixation in formalin (93%), but significantly lower for the cassette technique (64%, $p < 0.001$). Additional analysis per histologic parameter shows that this difference is caused by 1) the ability to discern lateral from vertical margin ($p = 0.001$); 2) the ability to assess the deep vertical margin ($p = 0.005$); and 3) the ability to assess the lateral margin ($p = 0.003$). Time required for specimen handling was shortest when the EMR specimen was directly fixated in formalin ($p < 0.001$ vs. pinning and Cassette). Needle artifacts were present in 25 of the specimens handled with the pinning method (57%).
Conclusion: EMR specimens can be directly fixated in formalin, provided that there is no suspicion of submucosal invasion during endoscopy and that the specimens will be evaluated by experienced BE pathologists. Direct fixation in formalin is the preferred handling method, since it results in a significantly shorter handling time without derogating the histopathological evaluation.
Disclosure: This study was supported by the St. Antonius Research Fund. E.S. received speaker and consultancy fees from Boston Scientific. J.B. received financial support for clinical studies from Boston Scientific. C.S. received consultancy support for validation studies Philips. B.W. received financial support for IRB approved clinical studies from C2 Therapeutics, Inc. and speaker fee from Pentax. All other authors have nothing to disclose.

P0516 HPV EXPOSURE AND SEXUAL BEHAVIOUR ARE SIGNIFICANT RISK FACTORS FOR BARRETT'S DYSPLASIA/ ESOPHAGEAL ADENOCARCINOMA

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Introduction: There are comparable strains of high-risk HPV present in a subset of Barrett's dysplasia and esophageal adenocarcinoma as in head and neck squamous cell carcinomas and the anatomical proximity of both lesions.
Aims and Methods: We hypothesized that oral sex may increase the risk of Barrett's dysplasia/ esophageal adenocarcinoma. Therefore, we compared the sexual behaviour of patients with Barrett's dysplasia / esophageal adenocarcinoma and controls (hospital, reflux and Barrett's metaplasia to explore a plausible mechanism of viral transmission to the lower esophagus. A hospital-based case-control study involving 36 Barrett's dysplasia / esophageal adenocarcinoma subjects and 55 controls with known HPV DNA status and markers of transcriptional activity i.e p16INK4A and E6/E7 mRNA of the esophageal epithelium was conducted to evaluate differences in sexual history (if any).
Results: Barrett's dysplasia / esophageal adenocarcinoma patients were more likely than controls to be positive for HPV DNA (18 of 36, 50% versus 6/55, 11%, p for trend < 0.0001), be male ($p = 0.001$) and in a relationship ($p = 0.02$). Viral genotypes identified were HPV 16 ($n = 14$), 18 ($n = 2$), 11 ($n = 1$) and 6 ($n = 1$). HPV exposure conferred a significantly higher risk for Barrett's dysplasia / esophageal adenocarcinoma as compared with hospital/reflux/Barrett's metaplasia controls (OR = 6.8, 95% CI: 2.1–23.1, adjusted $p = 0.002$). On univariate analysis, ≥6 lifetime oral sex partners was significantly associated with dysplastic Barrett's esophagus and adenocarcinoma (OR, 4.0; 95% CI: 1.2–13.7, $p = 0.046$). After adjustment for confounders, HPV exposure and men with ≥2 lifetime sexual partners were at significant risk for Barrett's dysplasia / esophageal adenocarcinoma.
Conclusion: If these initial findings can be confirmed in larger studies, it could lead to effective prevention strategies in combating some of the exponential increase in the incidence of esophageal adenocarcinoma in the West.
Disclosure: Nothing to disclose

P0517 THE ARGOS PROJECT: COMPUTER AIDED DETECTION SYSTEM CAN DETECT BARRETT NEOPLASIA ON ENDOSCOPIC IMAGES WITH HIGH ACCURACY

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Introduction: Early neoplasia in Barrett's esophagus (BE) is difficult to detect during surveillance endoscopies. This is partly because of its subtle appearance and partly because most endoscopists rarely encounter early BE neoplasia and therefore are unfamiliar with its endoscopic appearance. Computer-aided detection (CAD) systems might assist endoscopists in the recognition of early BE neoplasia, thereby improving efficacy of BE surveillance. Ideally, a CAD system is incorporated in the endoscopy system and would run real-time on the background during surveillance endoscopies. In case a visible lesion is present, the CAD system would red-flag the lesion on the endoscopy screen, enabling the endoscopist to take a targeted biopsy. Clinically-inspired CAD systems are trained with labelled data and predefined image features. These systems have therefore shown to be suitable for small and unbalanced databases. The aim of this study was to develop a clinically inspired CAD system using high-quality endoscopic images of BE neoplasia.
Aims and Methods: Endoscopic overview images of 40 subtle early neoplastic BE lesions and 20 non-dysplastic (ND)BE patients were prospectively collected in White Light Endoscopy (WLE) in 3 tertiary referral centers. Between September and November 2017, 6 international BE experts annotated all neoplastic images using a proprietary online delineation module specifically designed for this project.
The overlap area of ≥4 expert delineations was considered to have the highest suspicion of visible neoplasia and was labeled as *the sweet spot*. The area with ≥1 expert delineations was labelled as *the soft spot*. The CAD system was trained on local color and texture features (using Gabor filters) of the images, where positive features were taken from the sweet spot of the neoplastic images and negative features from the area outside the soft spot and from the NDBE images. No preprocessing of the expert delineations prior to input into the algorithm was performed at this stage. Performance was evaluated using a leave-one-out cross validation on a per image basis.
Outcome parameters: 1) Detection scores: diagnostic accuracy of the algorithm per image in terms of accuracy, sensitivity, specificity, NPV and PPV; 2) Localization scores: Percentage of recognized neoplastic images where the delineation of the algorithm detected the soft spot and sweet spot.
Results: Accuracy, sensitivity, specificity, NPV and PPV for detection were 88.3%, 92.5%, 80%, 84.2% and 90.2% respectively. The percentage of the soft- and sweet spot that was recognized was 94.6% and 89.2%, respectively.
Conclusion: This CAD system detected early neoplastic BE lesions on endoscopic WLE images with high accuracy, thereby showing feasibility of CAD systems as a red-flag detection technique and taking an important step towards real-time automated detection of early BE neoplasia. Future work will focus on further development of the algorithm towards video analyses and the development of a deep learning algorithm.
Disclosure: Nothing to disclose

P0518 ARTIFICIAL INTELLIGENCE IDENTIFIES EARLY BARRETT'S NEOPLASIA IN *IN-VIVO* BIOPSY-CORRELATED VOLUMETRIC LASER ENDOMICROSCOPY IMAGES

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Introduction: Volumetric laser endomicroscopy (VLE) provides a circumferential near-microscopic scan of the superficial esophageal wall layers, and has potential

to improve the detection of early Barrett's esophagus (BE) neoplasia. However, the interpretation of numerous grey-shaded VLE images is complex and time-consuming. Artificial intelligence using novel machine and deep learning techniques may aid in this process. Recent studies have focused on neoplasia detection algorithms based on *ex-vivo* VLE images. Our study is the first to investigate the feasibility of *in-vivo* BE neoplasia detection using computer-aided detection of VLE images.

Aims and Methods: A prospective single-center study was conducted including 23 Barrett's patients with and without early neoplasia. High quality *in-vivo* VLE-histology correlation was provided by laser marking. Laser marked regions of interest consisted of non-dysplastic BE (88 NDBE), and high-grade dysplasia and/or esophageal adenocarcinoma (34 HGD/EAC). Conventional machine learning and recent deep learning techniques were evaluated for the analysis of these regions of interest and differentiate between non-dysplastic and neoplastic tissue. Tissue was first segmented with a pre-trained convolutional neural network (U-net) and clinically inspired features were used for classification between non-dysplastic tissue and neoplasia. Based on earlier findings, analysis was performed on the superficial esophageal wall layers (0.2–1.2 mm), as experiments have demonstrated this generated an optimal classification performance. The reproducibility of the results were independently validated by leave-one-out cross-validation.

Results: In total, 8 different machine learning methods were used for BE neoplasia detection resulting in area under the curves ranging from 0.82–0.90. The clinically derived feature layer histogram in combination with Naive Bayes Classifier demonstrated the most optimal performance. This *in-vivo* method resulted in an accuracy of 84.4% and an area under the curve of 0.90. Corresponding sensitivity was 73.5% and specificity was 88.6% for the differentiation between 88 NDBE and 34 HGD/EAC VLE images. Negative predictive value and positive predictive value were 89.7% and 71.4%, respectively. Average time for the computer algorithm to analyze a VLE image was 15 milliseconds.

Conclusion: Artificial intelligence, using both machine- and deep learning techniques, correctly identify *in-vivo* biopsy-correlated VLE images of early BE neoplasia. The clinically derived feature layer histogram shows high detection accuracy. This study shows feasibility of fast and objective computer aided detection, bringing real-time, red-flag identification 1 step closer.

Disclosure: Nothing to disclose

P0519 BLUE LIGHT IMAGING HAS AN ADDITIONAL VALUE TO WHITE LIGHT ENDOSCOPY IN VISUALIZATION OF EARLY BARRETT'S NEOPLASIA. AN INTERNATIONAL MULTICENTER COHORT STUDY

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Introduction: Detection and delineation of early neoplasia in Barrett's esophagus (BE) may be difficult. Blue Light Imaging (BLI; Fujifilm, Tokyo, Japan) is a new optical chromoscopy technique that may improve visualization of these lesions with White Light Endoscopy (WLE).

The aim of this study was to evaluate if BLI has additional value in the visualization of early Barrett's neoplasia.

Aims and Methods: In this multicenter prospective cohort study corresponding endoscopic WLE- and BLI images of 40 early neoplastic BE lesions in overview and magnification were obtained in three tertiary referral centers. A proprietary online scoring and delineation module, specifically for this project, was used by 6 international BE experts to assess images in three assessment rounds, each separated by a wash-out period of 2 weeks. Each assessment consisted of overview- and magnification images. Assessment 1: WLE images only; Assessment 2: BLI images only; Assessment 3: corresponding WLE- and BLI images in a side-to-side display. The order of images in each assessment round was randomized. During each assessment, the experts scored their appreciation of the macroscopic appearance and surface relief using visual analogue scales (VAS) and subsequently delineated each lesion using the proprietary software tool. Their delineation agreement was quantified by calculating the mean AND/OR ratio for each image in which the AND area was defined as the area delineated by $\geq$4 experts and the OR area as the area delineated by $\geq$1 experts.

Outcome parameters: 1) Experts' appreciation of macroscopic appearance and surface relief (VAS-scores); 2) Experts' ability to delineate the lesion (VAS-scores); 3) Experts' preferred technique for delineation (ordinal scores); 4) Experts' quantitative agreement on lesion delineations (AND/OR scores).

Results: Experts appreciated BLI images significantly better than WLE for visualization of macroscopic appearance (median 8.0 vs. 7.0, $p < 0.001$) and surface relief (8.0 vs. 6.0, $p < 0.001$). For both overview and magnification images, experts appreciated BLI significantly better than WLE for ability to delineate lesions (8.0 vs. 6.0, $p < 0.001$ and 8.0 vs 5.0, $p < 0.001$). There was no overall significant difference in AND/OR scores of WLE+BLI when compared to WLE, yet agreement increased significantly with WLE+BLI for cases with a low baseline AND/OR score on WLE, both in overview (mean difference 0.15, $p = 0.015$) and magnification (mean difference 0.10, $p = 0.01$).

Conclusion: This study demonstrates the additional value of BLI for the visualization of BE neoplasia. International BE experts appreciated BLI better than WLE for the different aspects of visualization of BE neoplasia and preferred BLI for delineation with the proprietary delineation tool. Their quantitative agreement for delineation increased significantly when BLI was offered next to WLE for lesions that were hard to delineate with WLE alone.

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P0520 SELF-SIZING RADIOFREQUENCY ABLATION BALLOON FOR ERADICATION OF BARRETT'S ESOPHAGUS: RESULTS OF AN INTERNATIONAL MULTICENTER RANDOMIZED TRIAL COMPARING THREE DIFFERENT TREATMENT REGIMENS

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Introduction: The 360 Express RFA balloon catheter (''360 Express'') for radiofrequency ablation (RFA) of Barrett's esophagus (BE) has the ability to self-adjust to the esophageal lumen ensuring optimal tissue contact during ablation.

Aims and Methods: Aim of this randomized clinical trial was to compare three different ablation regimens for treatment of BE using the 360 Express.

Patients with a 2–15 cm BE with low-grade dysplasia (LGD), high-grade dysplasia (HGD) or early cancer (EC) were included. Visible lesions were removed by endoscopic resection (ER) prior to RFA. Patients were randomly assigned on a 1:1:1 ratio to the standard (1×10J/cm2-clean-1×10J/cm2), simple-double (2×10J/cm2-no clean), or simple-single ablation regimen (1×10J/cm2-no clean). Sample size calculation showed that 36 patients would be necessary in

Abstract No: P0520: Table 1. Outcomes

Ablation regimen	Standard	Simple-single	Simple-double (arm early closed)
Number of patients	31	31	28
Median BE regression, % (IQR)	85 (75–94) 95% CI: 78%–92%	73 (48–90) 95% CI: 59%–85%	88 (81–93) 95% CI: 83%–92%
Patients with a poor regression response ($\leq$50% BE regression), n (%)	3 (10)	9 (29)	0 (0)
Median procedure duration, min (IQR)	31 (26–36)	17 (13–20)	17 (14–20)
Overall adverse event rate	5 (14)	5 (13)	7 (25)
Stricture requiring an intervention, n (%)	0 (0)	0 (0)	6 (21) Mild n = 1; Moderate n = 1, Severe n = 4
Minor laceration, n (%)	4 (11)	3 (8)	0 (0)
Other adverse events, n (%)	Unrelated death: 1 (3)	Minor bleeding: 1 (3) Pain and fever: 1 (3)	Near collapse: 1 (4)

each arm. Primary outcome: percentage of endoscopically visual surface regression of BE at 3 months as scored by 2 independent blinded endoscopists. Secondary outcomes: adverse events and procedure time.
Results: Inclusion started September 2015 and was completed by October 2017. A total of 103 patients (81 male, median 66 yrs, median C4M7 BE) were included. 43 patients underwent ER prior to RFA (EC, n = 22; HGD, n = 13; LGD, n = 6, non-dysplastic IM, n = 2). Worst histology prior to RFA: HGD, n = 42; LGD, n = 51; non-dysplastic IM, n = 10. In February 2017, after 28 patients were included in the simple-double arm, further inclusion in this arm was stopped because of an unexpected high risk of severe stenosis. 6 patients developed a stenosis (21%, 95% CI:10–39%) requiring a median of 6 dilations after simple-double ablation. The study was continued with the standard and simple-single arm. To date, a total of 90/103 patients have completed the study (standard, n = 31/37; simple-single, n = 31/38, simple-double, n = 28/28). Median BE regression was higher in the standard arm compared to the simple-single regimen: 85% (IQR 75–94), 95% CI:78–92% versus 73% (IQR 48–90), 95% CI:59–85% (p = 0.009). A poor response (defined as ≤50% regression) was found in 3/31 and in 9/31 patients in respectively the standard and simple-single arm (p0.05). The standard ablation procedure was significantly longer: median 31mins (IQR 26–36) versus 17mins (IQR 13–20), $p < 0.001$. Adverse events occurred in 5/37 patients in the standard arm (minor laceration n = 4, unrelated death n = 1) and in 5/38 patients in the simple-single arm (minor laceration n = 3, minor bleeding n = 1, pain and fever n = 1).
Conclusion: Results of this randomized controlled trial suggest that c-RFA with the 360 Express using the standard regimen results in significant better regression after one treatment session compared with the simple-single regimen. However, the procedure is longer when using the standard regimen. The simple-double ablation regimen is not advised given the unacceptable risk of severe stenosis.
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P0521 CD147 EXPRESSION CORRELATED WITH TREATMENT RESPONSE AND SURVIVAL IN PATIENTS WITH ESOPHAGEAL CANCER RECEIVED CHEMORADIOTHERAPY

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Introduction: Chemo-radiotherapy (CRT) play crucial roles in the management of esophageal squamous cell carcinoma (ESCC), but such an aggressive treatment may increase toxicity or even delay surgery in patients with poor CRT response. Therefore, we need a good biomarker to identify patients who may/may not benefit from CRT, and to choose the best therapy for patients. Previous studies had demonstrated CD147 plays important roles in inducing matrix metalloproteinases production, anti-apoptosis and induction of various multidrug transporters, we thus hypothesize the CD147 may participate in the CRT resistance and tumor progression.
Aims and Methods: We consecutively enrolled 100 patients with locally-advanced ESCC, who received CRT (51 pre-operative; 49 definitive) as initial treatment. All of the pre-treatment tumor tissues were tested for CD147 expression, defined into either low or high expression by immunohistochemistry. The CD147 levels were validated for the correlation to overall survival and response rate to CRT. In ESCC cell lines, CD147 expressions were determined by western blot. The migration ability of tumor cells was investigated by wound closure assay and transwell migration assay. Clonogenic assay and MTT cell viability assay evaluated the radiation and chemotherapy sensitivity.
Results: The overall clinical complete response rate after CRT was 55% and the pathological complete response rate in pre-operative CRT group was 39%. 42 subjects (42%) were defined to have high-CD147 tumors. The multivariate logistic regression model showed high-CD147 expression is an independent predictor for poor clinical CRT response (OR: **0.39**, 95% CI: 0.17–0.92) and poor pathological response (OR: **0.12**, 95% CI: 0.02–0.62). Patients with high-CD147 expression ESCC have poor survival than those with low-CD147 tumors (2-year survival: 35% vs. 60%; log-rank p = 0.007), both in definitive and pre-operative CRT groups. *In vitro*, we found high-CD147 expression cell lines (KYSE-150 and KYSE-510) constitute higher migration properties, and higher resistance to radiation and chemotherapy, compared to the low-CD147 cell lines (KYSE-50 and KYSE-70).
Conclusion: CD147 may participate in the tumor progression and the resistance to CRT in ESCCs. High-CD147 expression ESCCs are associated with a poor CRT response, and thus additional therapy, more aggressive surveillance shall be applied. CD147 inhibitor may be promising to enhance CRT response and inhibit tumor progression in the future.
Disclosure: Nothing to disclose

P0522 EFFICACY OF ARGON PLASMA COAGULATION WITH PRIOR SUBMUCOSAL INJECTION FOR THE ESOPHAGEAL LESIONS - IN VIVO PORCINE MODEL STUDY

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Introduction: Endoscopic resection is regarded as the best treatment for patients with early-stage gastrointestinal cancer. However, argon plasma coagulation (APC) is often selected as a treatment for such patients because of the patient's general condition or status of the lesions. Recently, we reported good long-term outcomes for patients with esophageal squamous cell carcinoma who underwent APC (local recurrence rate of 3.6% and the 5-year cause-specific survival rate of 100%) in ESGE days 2018. We considered that submucosal injection prior to APC would result in uniform and sufficient coagulation and would contribute to a good outcome. Previously, Manner et al. reported the efficacy of APC with prior submucosal injection (hybrid APC) by using a resected porcine esophagus; however, there has been no study using an *in vivo* model. In this study, we evaluated the efficacy of hybrid APC for the esophagus by using an *in vivo* porcine model.
Aims and Methods: We performed hybrid APC and direct APC without submucosal injection (standard APC) in various settings. In study 1, we sacrificed the pigs immediately after APC. In study 2, we sacrificed the pigs 1 week after APC. Pathological evaluation of the depth of coagulation from the basal layer (study 1) and non-atrophic muscle zone (study 2) in the resected specimens was carried out. According to a report by Georg et al., superficial tissue damage of the tunica mucosa was classified as type A damage and an injury pattern limited to the tunica muscularis was classified as type B damage in study 1. The tissue sections were stained with anti-α-SMA antibody, anti-CD107a antibody, anti-CD31 antibody and anti-MPO antibody in study 2. 9 random submucosal fields from each pig were photographed (high-powered field [HPF], × 400) and the stained cells were counted in a blinded manner.
Results: We performed all APC methods using the forced APC mode.
Argon gas flow of 2.0 L/min, 3 seconds, at 60 watts (W): hybrid APC (types A and B damage) vs standard APC (types A and B damage); 3200 μm (longitudinal muscle layer [ML]) and 3090 μm (ML) vs 2750 μm (circular muscle layer) and 3340 μm (ML).
Gas flow of 1.0 L/min, 6 seconds, at 40 W: hybrid APC vs standard APC; 70 μm (lamina propria mucosa [LPM]) and 1440 μm (submucosa [SM]) vs 1300 μm (SM) and 2710 μm (ML).
Gas flow of 1.0 L/min, 4 seconds, at 40 W: hybrid APC vs standard APC; 80 μm (LPM) and 1370 μm (SM) vs 630 μm (muscularis mucosa [MM]) and 3010 μm (ML).
Gas flow of 1.0 L/min, 3 seconds, at 40 W: hybrid APC vs standard APC; 80 μm (LPM) and 870 μm (SM) vs 510 μm (MM) and 2360 μm (ML).
Results (study 2):
Gas flow of 2.0 L/min, 3 seconds, at 60 W: hybrid APC (2 lesions) vs standard APC (2 lesions), 23.8 and 2.9 mm^2 vs 4.5 and 0 mm^2.
Gas flow of 1.0 L/min, 3 seconds, at 40 W: hybrid APC (2 lesions) vs standard APC (2 lesions), 9.6 and 11.0 mm^2 vs 4.2 and 3.0 mm^2.
Gas flow of 1.0 L/min, 1 second, at 40 W: hybrid APC (2 lesions) vs standard APC (2 lesions), 13.9 and 15.6 mm^2 vs 6.4 and 7.6 mm^2.
Immunohistochemical analysis demonstrated that the numbers of activated myofibroblasts and infiltrating neutrophils and macrophages were decreased in the hybrid APC group.
Conclusion: Submucosal injection prior to APC contributes to safe and sufficient coagulation for esophageal lesions.
Disclosure: Nothing to disclose

P0523 PREVENTION OF ESOPHAGEAL STRICTURE AFTER COMPLETE CIRCULAR ENDOSCOPIC SUBMUCOSAL DISSECTION IN PIGS USING STENT WITH ACELLULAR PORCINE DERMAL MATRIX

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Introduction: Circumferential endoscopic submucosal dissection (CESD) permits radical en-block removal of superficial esophageal neoplasms. However, CESD is regularly complicated by the development of esophageal stricture, often refractory to endoscopic treatment. Currently, an effective method for stricture

prevention is still missing. We hypothesized that a stent covered with acellular matrix of porcine dermis might lead to an earlier re-epithelisation and thus prevent the post-CESD stricture formation.
Aims and Methods: To assess the local effect of a metallic (SEMS) or biodegradable (BD) stent (with or without a acellular matrix) in preventing post-CESD esophageal stricture in pigs. The main outcome was the development of endoscopically non-passable stricture. Secondary outcomes were stricture severity and histopathological parameters. Methods: Pigs were randomized into 6 groups: A. control - CESD only (n = 6); B. CESD + systemic corticosteroids (SC, n = 6); C. SEMS (Wallflex) + SC (n = 8); D. SEMS + matrix + SC (n = 8); E. BD stent (ELLA-CS) + SC (n = 3); F. BD stent + matrix + SC (n = 2). CESD was performed by using a dual knife. The acellular matrix was attached to the outer surface of a stent prior to its deployment. SEMS were removed 21 days after CESD. Pigs were euthanatized if a significant stricture developed.
Results: A total of 33 pigs underwent CESD in the middle esophagus; the average length of the defect was 5.5 ± 0.3 cm. All pigs with BD stent experienced macroscopic inflammation, massive hypergranulation and food stagnation within the stent while stent biodegradation did not occur. Thus, we decided to stop using the BD stent prematurely and BD groups were excluded from the final analysis.
Significant strictures were developed in all pigs except 1 (group B - SC) after a mean of 12.9 ± 0.1 days from CESD (groups A and B) and in 13.9 ± 1.4 days after SEMS extraction (groups C and D). The longest stricture was observed in the group A (2.7 ± 1.3 cm) and the shortest in SEMS groups (C, D) (1.5 cm ± 0.8 cm and 1.6 ± 1.1 cm). The narrowest stricture occurred in groups A and C (8.5 ± 3.1 mm and 8.8 ± 3.7 mm) vs. groups B and D (14 ± 4.1 mm and 13.6 ± 7.7 mm), ($p < 0.05$).
Re-epithelization was present in 80% of animals in the group A, in all animals in the group B, in 42% of animals in the group C and in 71% of animals in group D. The widest re-epithelization layer (0.14 mm) was present in the group D.
Conclusion: None of the tested methods resulted in the effective prevention of post-CESD esophageal stricture. Coverage of SEMS using acellular matrix of porcine dermis resulted in a decrease in the severity of stenosis and improved healing quality. The BD stent is inappropriate in this indication.
Disclosure: Nothing to disclose

Reference

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P0524 ELIMINATION OF NFKB SIGNALLING IN VIMENTIN+ STROMAL CELLS ATTENUATES ESOPHAGEAL CARCINOGENESIS IN A MOUSE MODEL OF BARRETT'S ESOPHAGUS

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Introduction: The link between inflammation and cancer is well established. Esophageal carcinogenesis is an ideal model to study the underlying mechanisms of inflammation induced tumor initiation: Chronic inflammation induces Barrett's Esophagus (BE) which later advances to esophageal adenocarcinoma (EAC). In particular, elevated levels of IL-6, a downstream target of NF-kB, have been identified as an important mediator of tumorigenesis in the IL-1b mouse models of EAC.[1] In the IL-1b mouse model of BE and EAC, IL-1b induces chronic inflammation and spontaneous carcinogenesis in an IL-6 dependent manner. This inflammatory milieu often contains apart from cancer cells and infiltrating immune cells, myofibroblasts (MF) that express αSMA and Vimentin. In the L2-IL-Ib mouse model increased inflammation correlates with increased MFs and an accelerated phenotype.
Aims and Methods: As it is still uncertain, however, if and how activated MFs are important in tumour initiation, answerable only in the context of carcinogenesis studies, we here analyze the effect of MFs in our mouse model of esophageal carcinogenesis (L2-IL-1b). To analyze the effect of Nfkb signaling in MFs, we crossed IL-1b mice to tamoxifen inducible Vim-Cre (Vim-Cre^{Tm}) mice and floxed p65 (p65$^{fl/fl}$) mice to eliminate NfKb signaling in fibroblast during carcinogenesis (IL-1b. Vim-Cre^{Tm}.p65$^{fl/fl}$). Furthermore, we analyzed the interaction of epithelial cells and stromal cells in 3D organotypic cultures of mouse and human BE organoids.
Results: Histological scoring of IL-1b. Vim-Cre^{Tm}.p65$^{fl/fl}$ mice showed a significantly attenuated phenotype compared to IL-1b mice, with mild inflammation, decreased levels of metaplasia and no dysplasia. This correlated with decreased proliferation and crypt fission and increased differentiation in the junctional region at the gastric cardia where metaplasia and dysplasia would arise in IL-1b. Vim-Cre^{Tm}.p65$^{fl/fl}$ compared to IL-1b mice. Finally we observed decreasing numbers of recruited immune cells and mesenchymal cells in the microenvironment of IL-1b. Vim-Cre^{Tm}.p65$^{fl/fl}$ compared to IL-1b mice by immunohistochemistry. The changes of cytokines in local microenvironment in IL-1b. Vim-Cre^{Tm}.p65$^{fl/fl}$ mice was investigated by cytokine array and qPCR analysis. To confirm the impact of MF on epithelial cell growth we co-cultured activated fibroblasts from mouse stomach with IL-1b mouse BE 3D organoids with and without NfKb inhibitors and observed a significant impact of Nfkb inhibition on the growth of BE organoids.
Conclusion: In summary, we here analysed the role of fibroblasts in an inflammatory environment and conclude that NFkB in the stromal cells is an important driver of esophageal carcinogenesis. This also suggests that inhibition of inflammation in general or NfkB specifically could be an important treatment strategy to prevent tumor progression during surveillance of BE patients.
Disclosure: Nothing to disclose

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P0525 CLINICAL SIGNIFICANCES AND PREDICTORS OF ESOPHAGEAL GLANDULAR DUCTAL INVOLVEMENT IN EARLY ESOPHAGEAL SQUAMOUS CELL NEOPLASIA

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Introduction: The esophageal gland duct may serve as a pathway for the spread of early esophageal squamous cell neoplasia (ESCN) to a deeper layer. However, the significance of ductal involvement (DI) in patients receiving complete endoscopic submucosal dissection (ESD) has yet to be investigated.
Aims and Methods: We consecutively enrolled patients with early ESCN who were treated with ESD. The resected specimens were retrospectively reviewed for the number, morphology, resected margin, distribution and extension level of DI, which were then correlated to clinical factors and survival.
Results: A total of 160 lesions were analyzed, with en bloc and R0 resection rates of 97.5% and 95.6%, respectively. A total of 317 DIs (median: 3, range 1–40 per-lesion) in 61 lesions (38.1%) were identified. Of these lesions, 14 have DIs maximally extended to the level of lamina propria mucosa, 17 to muscularis mucosae, and 30 to the submucosal layer. Multivariate logistic regression analysis showed that tumors located in the upper esophagus (OR = 2.93, 95% CI, 1.02–8.42), large tumor circumferential extension (OR = 5.39, 95% CI, 1.06–27.47), deep tumor invasion depth (OR = 4.12, 95% CI, 1.81–9.33) and numerous Lugol-voiding lesions in background esophageal mucosa (OR = 2.65, 95% CI, 1.10–6.37) were risk factors for esophageal DI. The maximally extended level and total number of ducts involved were significantly correlated with the depth of cancer invasion ($p < 0.05$). The patients with DI had worse overall survival (log-rank p = 0.015) and recurrence-free survival (log-rank p = 0.028) than those without DI after successful ESD.
Conclusion: DI is not uncommon in early ESCN. Our findings may guide clinical decision making with regards to endoscopic treatment and surveillance.
Disclosure: Nothing to disclose

P0526 PREDICTION OF INDIVIDUALS AT HIGH ABSOLUTE RISK OF OESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Oesophageal squamous cell carcinoma (OSCC) is the dominant histological subtype of oesophageal cancer in Eastern countries and globally, and despite an increasing incidence of oesophageal adenocarcinoma in Western countries, OSCC remains a major type of oesophageal cancer also in these countries. In 2012, approximately 38,000 new cases of OSCC occurred in Europe, North America, and Oceania, accounting for around 60% of all cases of oesophageal cancer in these regions. OSCC is characterized by poor prognosis with a population-based overall 5-year survival rate of less than 20%, which has not improved much in recent years. Upper endoscopy for OSCC may be indicated to detect disease at curable stage, but universal endoscopic screening is not justified given the low absolute risk of OSCC in the population. A more feasible way may be to identify a limited group of individuals with high absolute risk of OSCC, who might benefit from tailored endoscopic screening and surveillance.
Aims and Methods: By combining readily identifiable risk factors, risk prediction modelling is a promising tool for selecting individuals with high absolute cancer risk. This study aimed to develop an OSCC risk prediction model for individuals. This was a nationwide Swedish population-based case-control study, including 167 new cases of OSCC and 820 randomly selected control participants. Associations between candidate predictors and risk of OSCC were assessed using multivariable unconditional logistic regression, producing odds ratios with 95% confidence intervals (CI). The discriminative accuracy of the model was assessed by the area under the receiver operating characteristic curve (AUC) with leave-one-out cross-validation. Models for projecting individuals' absolute 5-year risk of OSCC were developed by incorporating the age- and sex-specific incidence rates of OSCC and competing risk of death from other causes.
Results: A model including age, sex, tobacco smoking, alcohol overconsumption, education, duration of living with a partner, and place of residence during childhood generated an AUC of 0.81 (95% CI 0.77–0.84). A model based only on age, sex, tobacco smoking, and alcohol overconsumption reached a similar AUC (0.79, 95% CI 0.75–0.82). The estimated individuals' absolute 5-year risk of OSCC varied according to combinations of risk factors. Individuals' absolute risk assessment was available in an excel calculator.
Conclusion: To the best of our knowledge, this is the first study that developed a prediction model for the absolute risk of OSCC in a Western population. This

'easy-to-use' risk prediction model showed good discriminative accuracy and could identify individuals at high absolute risk of OSCC within the next 5 years. With further validation in independent populations, the model is potential for clinical use in identifying individuals at high absolute risk of OSCC who may benefit from tailored endoscopic surveillance for early tumour detection at a curable stage.
Disclosure: Nothing to disclose

P0527 DURABILITY OF RADIOFREQUENCY ABLATION FOR TREATMENT OF ESOPHAGEAL SQUAMOUS CELL NEOPLASIA: 5 YEAR FOLLOW-UP OF A PROSPECTIVE STUDY IN CHINA

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Introduction: Radiofrequency ablation (RFA) is an accepted treatment modality for early Barrett's neoplasia. Less is known about RFA for esophageal squamous cell neoplasia (ESCN). Our group has reported several prospective studies of RFA for ESCN in high-risk areas in China. Complete remission (CR) of ESCN was achieved in up to 87% of patients, but follow-up (FU) was restricted to 12 months[1,2].
Aims and Methods: We aimed to evaluate long-term 5 year outcomes after RFA for ESCN. Patients with flat type (Paris 0-IIb) unstained lesions (USLs) on Lugol's endoscopy, 3–12cm in length and with moderate or high grade intraepithelial neoplasia (MGIN/HGIN) or mucosal squamous cell cancer (ESCC-m) were treated with RFA every 3 months in the first year, until CR (defined as absence of MGIN or worse in biopsies) was established. All patients with CR at 12 months (CR12) were included in the current study extension, and underwent annual FU endoscopy with Lugol's and biopsies. Flat type USLs were treated with RFA; other lesions were treated per investigator's discretion. We also describe the clinical course of patients with persistent ESCN at 12 months (treatment failures), with treatment and FU per investigator's discretion.
Results: The 78 patients with CR12 were included in this extension. During a median FU of 48 months (IQR 48–48) with 5 endoscopies (IQR 4–6) after the first year, 67/78 patients (86%) sustained CR. Recurrence occurred in 7 pts (9%; MGIN:6, HGIN:1) and all were managed with RFA. CR was re-established in 4, and the other 3 were treated at the last FU endoscopy. 4 other pts (5%) had progression (non-flat HGIN:1; ESCC-sm:3) and were managed endoscopically with ESD. During FU, protocol violations (prolonged intervals, USLs left untreated or no adequate FU after retreatment) occurred in 46/78 patients (59%). Of the 12 treatment failures at 12 months, progression of ESCN occurred in 6 (50%), managed by endoscopic (1) or non-endoscopic (5) treatment. Overall, 2 patients developed subepithelial disease that was not clearly visible with Lugol's endoscopy. Post-hoc analysis on the 'pink-color sign' at baseline, showed that this reddish to pink color change after Lugol's staining significantly predicted recurrence or progression during FU as well as initial failure at 12 months (HR 4.0, 95% CI 1.8–9.2).
Conclusion: RFA is relatively easy to apply and can efficiently treat large areas with ESCN. Despite protocol violations that may have interfered with the efficacy of RFA treatment in 59% of patients, the great majority with CR12 had sustained CR during FU. However, some patients progressed to advanced disease and 2 patients developed subepithelial disease that was not visible with Lugol's. Based on currently available data, we advise to restrict the use of RFA for flat type MGIN and HGIN without pink-color sign on Lugol's chromoscopy.
Disclosure: This was a Medtronic, Inc. sponsor initiated study

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P0528 CHEMORADIOTHERAPY FOR LYMPH NODES RECURRENCE AFTER ESOPHAGECTOMY FOR ESOPHAGEAL CANCER

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Introduction: Recurrent esophageal cancer after esophagectomy has a poor prognosis, while we sometimes encounter patients with long-term survival. Lymph nodes recurrence is one of the common recurrence patterns after esophagectomy. Here we discuss the usefulness of chemoradiotherapy for lymph nodes recurrence after esophagectomy.
Aims and Methods: The aim of this study is to evaluate outcomes of chemoradiotherapy and prognostic factors for patients with only lymph nodes recurrence. Four hundred six patients underwent R0 esophagectomy for thoracic esophageal squamous cell carcinoma at our institution, between 1995 and 2014. Recurrence occurred in 148 patients (36%). Among these, 58 patients (39%) developed recurrence only in the lymph nodes. The median follow-up duration after recurrence was 13 months (range from 1 to 155 months). Post-recurrence survival was defined as the time between the first recurrence and death or most recent follow-up examination.
Results: The 58 patients with lymph node recurrence were 54 males and 4 females, with a median age of 64 years (range from 44 to 80 years). Of those, 16 (28 %) had pT1 cancer, 8 (14%) had pT2 cancer, 31 (53%) had pT3 cancer, and 3 (5%) had pT4 cancer. The number of patients at pN status (UICC 7th) N0/N1/N2/N3 was 16 (28%)/ 14 (24%)/ 19 (33%)/ 9 (16%), respectively. 11 patients (19%) had pM1 LYM. 3-field lymphadenectomy had been performed in 33 (58%) patients, and 2 or less-field lymphadenectomy was performed in 25 (42%) patients. The median time to recurrence after esophagectomy was 12.5 months (range from 1.8 to 47.5 months). M1 LYM recurrence occurred in 28 patients (48%) including 15 patients with both M1 LYM and regional lymph node recurrence, and 30 patients (52%) had only-regional lymph node recurrence. 34 patients (59%) had a single site of lymph node recurrence, and 24 patients (41%) had two or more recurrence sites. 43 patients (74%) had 1-field recurrence, and 15 patients (26%) had 2-field recurrence. Chemoradiotherapy was employed in 36 patients including 8 patients with surgery. The remaining 22 patients received other treatment; chemotherapy, radiotherapy, surgery, or best supportive care. The overall 1- and 3-year-survival rates in all patients after recurrence were 55% and 22%, respectively. By univariate analysis, the depth of tumor invasion (pT), the interval until recurrence, and the method of treatment were each found to be a factor affecting the survival ($p < 0.05$). The location and number of lymph nodes recurrence did not significantly affect survival. In multivariate analysis, the depth of tumor invasion (pT1,T2 vs. pT3,T4: hazard ratio 0.407; 95% confidence interval 0.212–0.754; $p = 0.0040$) and treatment (chemoradiotherapy vs. other treatment: hazard ratio 0.427; 95% confidence interval 0.234–0.786; $p = 0.0067$) were each found to be an independent prognostic factor. The 3-year-survival rate in patients with pT1,T2 was 36%, compared to 12% in those with pT3,T4 ($p = 0.0014$). The 3-year-survival rate in patients who received chemoradiotherapy was 29%, compared to 9% in those who received other therapy ($p = 0.0030$).
Conclusion: Our findings suggested that chemoradiotherapy could improve survival in those esophageal squamous cell carcinoma patients with only lymph nodes recurrence. The location and number of lymph nodes recurrence did not affect survival.
Disclosure: Nothing to disclose

P0529 ENDOSCOPIC CRYOBALLOON ABLATION IS SAFE, WELL-TOLERATED AND HIGHLY EFFECTIVE IN THE ERADICATION OF ESOPHAGEAL SQUAMOUS CELL NEOPLASIA

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Introduction: Globally, 80% of all esophageal cancer cases are esophageal squamous cell cancer (ESCC), arising from esophageal squamous cell neoplasia (ESCN). Patients with ESCC have poor prognosis, but when diagnosed at the stage of ESCN, curative endoscopic treatment can be performed. ESCN mainly occurs in developing countries like Central and Eastern Asia and Eastern and

Southern Africa, often with limited endoscopic expertise and resources. Hence, an easy-to-use, low-cost treatment for ESCN would be of great value. Focal Cryoballoon Ablation therapy (FCBA) (*C2 Therapeutics Inc. Redwood City, CA, USA*) is a novel endoscopic ablation therapy that comprises a through-the-scope catheter with a conformable balloon that obviates the need for sizing, a handle, and a small disposable cryogen cartridge. The balloon is simultaneously inflated and cooled with nitrous oxide from the cartridge, resulting in ice patches of approximately 2cm.[2] FCBA is handheld, easy to use and requires no capital equipment. Although early studies for FCBA of Barrett's esophagus have shown promising results, limited data are available for its use in ESCN.

Aims and Methods: We aimed to assess the safety, tolerability and efficacy of FCBA in the eradication of ESCN. In this single-center prospective trial in China, patients with 1 flat type (Paris 0-IIb) unstained lesion (USL) on Lugol's chromoscopy, < 6cm in length and $< 50\%$ of the esophageal circumference, with a diagnosis of Moderate or High Grade Intraepithelial Neoplasia (MGIN/HGIN) were enrolled. At baseline, the entire USL was ablated with side-by-side ablations of 10 seconds and tattoos were placed to identify the treatment area (TA). Safety phone calls were performed at days 2, 7 and 30. A second treatment was repeated within 3 months in the case of persisting USLs. All patients underwent a 12-month endoscopy with biopsies from the TA. Outcomes included safety, tolerability (11-point visual analog scale (VAS) for pain); complete response (CR; absence of MGIN or worse in all TA biopsies) rates at 3 and 12 months; and adverse events.

Results: We enrolled 80 patients (59 MGIN, 21 HGIN) with a median USL length of 3 (IQR 3–4) cm. Median 5 (IQR 4–7) side-by-side ablations were performed per patient over a median ablation time of 8 (IQR 5–10) minutes. After a single treatment, 70/78 patients (90%, per protocol) exhibited CR. The other 8 patients had residual USL and were retreated; all had CR 3 months later (4 LGIN, 4 esophagitis). 2 patients were lost to follow-up. At 12 months, 76/78 patients (97%, per protocol) or 76/80 (95%, intention to treat) patients exhibited CR. AT 12 months, 2 patients, both with MGIN at baseline, were found to have a USL with MGIN. No strictures or serious adverse event had been noted. 3 patients developed self-limiting mucosal lacerations upon balloon inflation. Post-procedure median VAS was 1 (IQR 0–2) at day 2, and 0 (0–0) at days 7 and 30. Median dysphagia score was 0 (0–0) on all days.

Conclusion: Results of our prospective cohort study in China suggest that focal cryoballoon ablation of esophageal squamous cell neoplasia is safe, well-tolerated, and highly effective in inducing endoscopic and histological remission. FCBA is a promising, easy to use and low-cost modality for the treatment of ESCN.

Disclosure: This study was financially supported by C2 Therapeutics, Inc.

P0530 LONG-TERM OUTCOMES OF ENDOSCOPIC RESECTION VERSUS SURGICAL RESECTION FOR MM-SM1 OESOPHAGUS SQUAMOUS CELL CARCINOMA USING PROPENSITY SCORE ANALYSIS

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Introduction: Because oesophageal squamous cell carcinoma (ESCC), confined to the muscularis mucosae (MM) or up to 200 μm of the submucosa (SM1), confers the risk for lymph node metastasis, it is defined as relative indication for endoscopic submucosal dissection (ESD) by the Japan Esophageal Society guidelines. Although additional surgical treatment after ESD is recommended, long-term outcomes of ESD compared with those of surgery have not been clarified.

Aims and Methods: This study aimed to evaluate the long-term outcomes of ESD and surgery for cN0M0 relative indication lesions of ESCC. Between 2006 and 2016, patients with relative indication lesions of ESCC who underwent ESD or surgery at eight participating hospitals were retrospectively examined. Using propensity-score matching, we evaluated the survival curves and hazard ratios for ESD compared with those for surgery.

Results: In total, 135 lesions in the ESD group and 87 lesions in the surgery group met the pathological criteria of relative indication for endoscopic resection. After matching, 51 matched pairs of patients who underwent ESD or surgery were selected. In the ESD group, 8 patients underwent additional chemoradiation and four underwent additional radiation. In the surgery group, four patients underwent additional chemotherapy. The 5-year overall survival rates were 88.5% [95% confidence interval (CI) 74.4–95.1] in the ESD group and 85.1% [95% CI 66.8–93.7] in the surgery group. The numbers of all-cause deaths were 9/51 in the ESD group and 6/51 in the surgery group. The Cox proportional hazard ratio of mortality for ESD compared with that for surgery was 1.16 (95% CI 0.41–3.27, $p = 0.78$). The 5-year recurrence-free survival rates were 89% [95% CI 73–95.8] in the ESD group and 89.3% [95% CI 73.9–95.9] in the surgery group. There were two cases of disease-specific deaths in each group. The 5-year disease-specific survival rates were 97.7% [95% CI 84.6–99.7] in the ESD group and 93.6% [95% CI 75.5–98.4] in the surgery group.

Conclusion: Compared with surgery, ESD does not compromise long-term outcomes. Further large-scale randomized controlled trials are necessary to confirm these results.

Disclosure: Nothing to disclose

Reference

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P0531 CLINICOPATHOLOGICAL EXAMINATION OF DUCTAL INVOLVEMENT IN T1A ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Intraductal spread is one of the forms of tumor spread in esophageal squamous cell carcinoma (ESCC). The treatment of superficial ESCC is mainly EMR or ESD, and ductal involvement (DI) could be resected by EMR and ESD. However, DI may not be treated by radio frequency ablation (RFA), and it may cause local recurrence after RFA. However, the details of DI aren't well known.

The aim of this present study is to clarify the incidence and characteristics of DI using specimens obtained by ESD.

Aims and Methods: 40 patients who had T1a esophageal squamous cell carcinoma (ESCC), and consecutively undergone esophageal ESD at the Saku Central Hospital Advanced Care Center, Nagano, Japan between Jan 2017 and Feb 2018 were enrolled to this study. Local recurrent cases after chemo-radio therapy or endoscopic resection were excluded.

In this study, diagnostic criteria for DI were defined by the presence of ductal cancerization accompanied by non-neoplastic ductal epithelium lined by a single layer of cuboidal cells or mucinous cells in the center of and/or external to the cancerous nest.

The patients included 32 men and 7 women, aged 56–86 years (mean, 70.3 years). The location of ESCC was sub-classified to upper (Up), middle (Md) and lower (Lo). And the number of Up, Md and Lo was 6, 22 and 6, respectively. Invasion depth, EP, LPM and MM were 6, 30 and 4, respectively. Mean tumor size was 24.7 (4–71) mm.

The resected specimen was spread out, pinned on a flat rubber, and fixed in 10% formalin solution. Fixed materials were sectioned serially at 2mm intervals and stained with hematoxylin and eosin. Diagnostic criteria for DI were defined by the presence of ductal cancerization accompanied by non-neoplastic ductal epithelium lined by a single layer of cuboidal cells or mucinous cells in the center of and/or external to the cancerous nest.

The histological findings such as invasion depth, ductal involvement was diagnosed by hematoxylin eosin staining. Esophageal duct was sub-classified into mucosal(MD) and submucosal duct (SMD), and the distribution of MD, SMD and proper esophageal gland (EG) with or without SCC involvement was investigated by expert pathologist. And the number of MD, SMD and EG with DI was counted.

Results: 1. The total number of MD, SMD and EG in 40 lesions were 569, 1008 and 1087, respectively. The reason why the number of SMD and EG were higher than that of MD was thought that esophageal duct makes branch in deep mucosal layer.

2. The total number of MD, SMD and EG within SCC were 120, 463 and 419, respectively.

3. The total number of MD, SMD and EG within non- neoplastic epithelium were 322, 545 and 664, respectively. There was no significant difference between SCC and non-neoplastic area.

4. The ratio of DI positive in MD, SMD and EG were 74% (89/120), 11% (52/463) and 2% (10/419), respectively.

5. The ratio of DI positive in MD, SMD and EG per person were 55%(22/40), 15% (6/40) and 10% (4/40).

6. There was no significant difference between DI and Age, Gender, macroscopic findings and location.

Conclusion: Ductal involvement in MD, SMD and EG per person were 55%, 15% and 10%, respectively.

RFA has the possibility to complete DI in MD. However, DI in SMD and EG may remain after RFA, and will cause local recurrence. Our study suggests the local recurrence rate after RFA may be more than 10%.

Disclosure: Nothing to disclose

P0532 CLINICOPATHOLOGIC CHARACTERISTICS OF SYNCHRONOUS MULTIPLE EARLY ESOPHAGEAL NEOPLASTIC LESIONS

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Introduction: Some studies had clarified that multiple esophageal lesions develop more frequently in patients who have undergone endoscopic treatment. Related study reported 30% patients found recurrent neoplasia after endoscopic

resection. However, there is rarely published study investigating the clinicopathologic features of synchronous multiple early esophageal neoplastic lesions. Therefore, this study aimed to investigate the clinicopathologic characteristics of synchronous multiple early esophageal neoplastic lesions so that clinicians can make better decisions for the preserved esophagus after endoscopic treatment.
Aims and Methods: The clinical data of 37 patients with synchronous multiple early esophageal neoplastic lesions who meet the inclusion criteria between May 2013 to May 2017 were analyzed. According to postoperative pathological results, patients were divided into 2 groups: Group A: all the lesions had confirmed high-grade intraepithelial neoplasia (HGIN) or esophageal cancer; Group B: only 1 lesion had confirmed HGIN or esophageal cancer, while other lesions were high-grade intraepithelial neoplasia (HGIN). The clinicopathologic features were compared between the 2 groups by univariate analysis.
Results: There were 20 patients, 44 lesions in group A and 17 patients, 34 lesions in group B. No significant differences were observed between the 2 groups in terms of age, gender, body mass index (BMI), family esophageal cancer history, heavy drinking, heavy smoking, flush after drinking, while significant differences were observed between the 2 groups in Lugol-voiding lesions (LVLs) grade ($p = 0.001$), submucosal involvement on EUS ($p = 0.005$), circumferential extent ($p = 0.000$), R0 resection rate ($p = 0.007$), lesion size ($p = 0.000$) and pathological upgrade rate ($p = 0.043$).
Conclusion: The higher LVLs grade, larger lesion size, circumferential extent $\geq 1/2$, non-R0 resection, postoperative pathologic estimation upgrade, and an EUS finding of submucosa involvement are considered high-risk factors in patients with synchronous multiple esophageal neoplastic lesions. Therefore, clinicians must remain vigilant and perform careful observations and surveillance on patients with such characteristics during endoscopic examination.
Disclosure: Nothing to disclose

P0533 GASTROPROTECTIVE EFFECT OF PANTOPRAZOLE ON MORPHOLOGICAL CHANGES OF GASTRIC MUCOSA IN RATS DURING ANTIPLATELET THERAPY

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Introduction: Acetylsalicylic acid (ASA) and clopidogrel in antiplatelet doses are effective in prevention of vessel crash connected to coronary heart disease. But development of erosive and ulcerative gastric lesions puts limitations to their administration.
Aims and Methods: To study morphologic characteristics of gastric mucosa lesions in rats under applying antiplatelets and pantoprasol equivalent to human doses.
White male rats with average body mass 150–180g were divided into 7 groups according to the treatment they received: ASA in dose 6.8 mg/kg of body weight (on conversion to 75 mg for an adult person); Clopidogrel 6.8 mg/kg of body weight (on conversion to 75 mg for an adult person); ASA 6.8 mg/kg of body weight + 6.8 mg/kg body weight of clopidogrel; ASA 6.8 mg/kg of body weight + pantoprasol 3.6 mg/kg (on conversion to 40mg for an adult person); Clopidogrel 6.8 mg/kg body weight + pantoprasol 3.6 mg/kg; ASA 6.8 mg/kg of body weight + Clopidogrel 6.8 mg/kg body weight + pantoprasol 3.6 mg/kg.
The drugs were introduced a 1-time per day during 14 days intragastrically. The following characteristics were analyzed: general histological parameters, apoptotic index (AI) and caspase-3 expression (CPP32).
Results: During a short time in ASA and clopidogrel groups the connective tissue of gastric mucosa became uncovered and microerosions appeared mostly in the antral region (in 94% of rats). Fundus was manifested by swollen connective tissue, subepithelial lamina propria with minute diapedetic extravasations and infiltration with the presence of single lymphocytes and plasmatic cells were revealed around the swollen area. Other groups didn't show erosions.
In ASA + clopidogrel group lesions of the basement membrane were found in 42% of rats vs 25% in ASA group and 10% in clopidogrel group and were not seen in other groups.
The expression of CPP32 in ASA group and ASA + clopidogrel group showed that the amount of positively stained cells was > 70%, and in control group - up to 10% ($p < 0.05$), which testifies to immaturity of epitheliocytes owing to their rapid death and renewal. In ASA + pantoprasol, clopidogrel + pantoprasol, ASA + clopidogrel + pantoprasol groups positively stained cells were 18%, 12% and 15% respectively ($p < 0.05$).
AI in control group was 2.9±0.32%, in clopidogrel group - 4.6±0.61%, in ASA group - 7.18±0.48%, in ASA + clopidogrel group −7.18±0.48%. The amount of apoptotic bodies in the form of unstructured roundish eosinophilic homogenous masses were increasing.
Comparing AI of control group with clopidogrel group - $p < 0.05$, ASA group - $p < 0.001$ and ASA + clopidogrel group - $p < 0.001$. In clopidogrel group AI was reliably lower ($p < 0.05$) comparing both ASA group and ASA + clopidogrel group, which can attest to less negative influence of clopidogrel on gastric mucosa comparing to ASA and ASA + clopidogrel combination.
In clopidogrel + pantoprasol, ASA + pantoprasol and ASA + clopidogrel + pantoprasol groups AI was 3.5±0.42%, 4.1±0.56% and 3.4±0.31% respectively. Differences in AI in clopidogrel + pantoprasol, ASA + pantoprasol and ASA + clopidogrel + pantoprasol groups were absent ($p > 0.05$).
Conclusion: Microerosion formation was the main morphologic feature of gastropathy which is not always revealed by macroscopic examination of gastric mucosa during application of ASA and clopidogrel. Pantoprasol use on the background of ASA and clopidogrel promotes to prevention of gastric mucosa necrosis due to stabilization of apoptotic activity of gastric epitheliocytes.
Disclosure: Nothing to disclose

P0534 DOES PPI PLAY A PROTECTIVE ROLE IN GASTRIC MUCOSA IN PATIENTS TAKING DOACS?

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Introduction: Over 5 years have already passed since direct oral anticoagulants (DOACs) was released in Japan. It was not just known that DOACs have similar efficacy as vitamin K antagonists (VKA), but might be a more mucosal-friendly agent than VKA[(1)]. However, for reducing the incidence of mucosal injuries, we don't know what kind of agents is helpful to use concomitantly for patients taking DOACs as well as VKA.
Aims and Methods: The aim of this study is to explore whether proton pump inhibitors (PPI) play a protective roll for gastric mucosa in patients taking DOACs or VKA. To reveal the roll of PPI, we compared the severity of gastric mucosal injury between PPI users and nonusers in the subjects taking DOACs or VKA, individually. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2015 and December 2017. Of the 3,900 subjects analyzed, we focused on 203 subjects who took DOACs (Dabigatran, Edoxaban, Rivaroxaban, Apixaban) or VKA (Warfarin). After excluding subjects who took other type of antacid (histamine 2 receptor blockers or potassium competitive acid blockers) in each group, we divided subjects into 2 subgroups: those who were taking PPI, and those who were taking no antacids. Severity of gastric mucosal injury was evaluated endoscopically according to the modified LANZA score (MLS) [(2)]. Statistical analyses were performed by Fisher's exact test.
Results: This study included 88 subjects in DOACs users (62 men, 26 women; mean age 72.9 years; 58 PPI user, 30 nonuser) and 72 subjects in VKA users (45 men, 27 women; mean age 74.9 years; 49 PPI user, 23 nonuser). In patients taking DOACs, average MLS of PPI users and nonusers was, respectively, 0.24±0.76 and 0.63±1.45 ($p = 0.263$). In patients taking VKA, average MLS of PPI users and nonusers was, respectively, 0.59±1.38 and 1.91±2.25 ($p = 0.045$). In the subjects taking VKA, gastric mucosal injury was statistically significantly mild in PPI users, but not in the subjects taking DOACs.
Conclusion: PPI play a protective role in gastric mucosa in patients taking VKA but not in patients taking DOACs.
Disclosure: Nothing to disclose

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P0535 FACTORS OF PROTON PUMP INHIBITOR RESISTANCE MODELED BY COMPARATIVE DISSOLUTION TESTING

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Introduction: Among the reasons for proton pump inhibitor (PPI) resistance is different quality of enteric coatings, as a result of which PPIs acid degradation in the stomach leads to its release there. The influence of factors such as pathologic duodenogastric reflux (PDGR) with pH ≥ 7 followed by its decrease and the pH increasing ≥4 within multiple PPIs dosing in patients with gastro-esophageal reflux disease (GERD) on coatings and premature active compounds degradation has not been studied specifically. PDGR and pharmacological acid suppression can be reliably modeled with comparative dissolution testing (CDT). In PDGR, pH ≥ 7 exposure time for omeprazole and rabeprazole is 4 and 12 minutes, respectively. Omeprazole or rabeprazole detection in the pH 7 buffer after 4 or 12-minute exposure should be estimated as PPIs degradation in the stomach due to PDGR. The stability of PPIs in case of an inhibited gastric acid secretion can be confirmed by drug compounds absence in the pH 4 buffer.
Aims and Methods: CDT (pH 1.2±0.05; pH 4.0±0.05, pH 7.0±0.05) has been used to estimate influence of PDGR and pharmacological acid suppression on omeprazole and rabeprazole gastric release and degradation. The additional aliquots were taken from the pH 7.0±0.05 solution after 4 minutes for original omeprazole (OO) and generics (GO1, GO2, GO3) and 12 minutes for rabeprazole (OR, GR1, GR2). PDGR resistance for PPIs capsules and tablets was determined by active substances presence or absence.

Results: The drug release was not detected in the pH 1.2 buffer. Drugs were moved from solution with pH 1.2 ± 0.05 to pH 7.0 ± 0.05. The drug release in the pH 7.0±0.05 after 4-minute exposure was 4.7±0.7%, 0, 80.8±3.6%, 82.5±1.7% for OO, GO1, GO2, GO3, respectively. OR and generics were subjected to the same conditions during 12 minutes with only GR1 detected final release (5.4±0.4%). Therefore, PDGR model demonstrated poor reflux influence on OO and GR1, strong influence on GO2 and GO3 with the almost complete omeprazole release and its potential degradation after following pH decrease.
Any omeprazole was not detected in the pH 4.0±0.05. Pellet destructions were not registered for OO, GO1 and GO3 while GO2 pellets were totally degraded. Non-degraded pellets were moved to pH 7.0±0,05 where their release was determined. In the same dissolution conditions, rabeprazole amount from GR2 after 10; 15; 20; 30; 45; 60 minutes was 0; 0; 5.5±0.4%; 38.8±0.4%; 58.0±0.3%; 82.4±0.5%; 68.9±0.5%. No OR and GR1 release or visible tablets destruction were registered. Pharmacological acid suppression model had demonstrated OO, OR, GO1, GO3 and GR1 resistance while total GO2 and partial GR2 degradations were determined.
Conclusion: Omeprazole and rabeprazole generics with high-risk degradation under PDGR and multiple PPIs dosing were determined by CDT. Omeprazole was totally degraded in pH 4.0±0.05 but not rabeprazole.
Disclosure: Nothing to disclose

P0536 COMPARISON OF SAFETY AND OUTCOMES BETWEEN ENDOSCOPIC AND SURGICAL RESECTIONS OF SMALL (≤ 5 CM) PRIMARY GASTRIC GASTROINTESTINAL STROMAL TUMORS

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Introduction: Endoscopic resection is increasingly performed for gastric gastrointestinal stromal tumors (GIST). However, the safety and outcomes remain elusive.
Aims and Methods: We aimed in this retrospective study to compareoperative complications and prognosis between endoscopically and surgically resected small (≤ 5 cm) GIST tumor groups. In this single-center retrospective study, we compared demographics and clinical outcomes including operative complications, postoperative courses, and the R0 resection rate between the endoscopy (n = 268) and surgery (n = 141)groups. Only GIST tumors in size of ≤ 5.0 cm were recruited for this comparison study.
Results: Overall, the mean age of patients was 59.0 years (range: 31.0–83.0). The male-female ratio was 0.68. The most common site of GIST was, in a descending order, the gastric fundus (55%), corpus (27.6%), cardia (10.8%), antrum (6.6%). Compared with the surgery group, GIST tumors in the endoscopy group was significantly smaller (1.69±0.9 cm, compared to 3.20±1.2 cm in the surgery group; $p < 0.001$) in size; postoperative hospital stay was significantly shorter (4.66±1.5 days, compared to 8.11±5.0; $p < 0.001$); post-resection time to first fluids diet was significantly shorter (1.94±1.1 days, compared to 4.63±2.6; $p < 0.001$); incidence of operative and post-operative complications was significantly fewer ($p < 0.05$), and hospital costswere significantly lower (20115.4±5113.5¥ compared to 43378.4±16795.7¥; P < 0 .001). The R0 resection rate was significantly lower in the endoscopy (93.3%) than in the surgery (99.3%) groups ($p < 0.01$). In the endoscopy group, 176 (65.7%), 69 (25.7%), 14 (5.2%) and 9 (3.4%) patients were found to be very low, low, intermediate, and high risk, respectively. In contrast, 27 (19.1%), 87 (61.7%), 14 (10.0%), 13 (9.2%) patients were found to be very low, low, intermediate, and high risk in the surgery group, respectively. The risk stratification was significantly different between the endoscopy and surgery groups ($p < 0.001$). Among 409 cases, 50 (12.2%) patients were found to be intermediate or high risk. Among 50 patients, only 20 patients received adjuvant therapy with imatinib after resection. 7 of the 20 patients took imatinib 1 to 3 months because of its side effects and high costs. However, during 33.5 months of follow-up, no local or distant tumor recurrence was observed and 2 patients were died of other disease in surgery group.
Conclusion: Endoscopic resection of selected gastric GISTs (≤5cm) is feasible and safe, and is associated with a better intraoperative outcome and an equal postoperative course compared with surgery group.
Disclosure: Nothing to disclose

P0537 LONG-TERM OUTCOMES AND PROGNOSTIC FACTORS OF NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC CANCER IN ELDERLY PATIENTS

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Introduction: Gastric cancer is still one of the leading causes of cancer-related death in Japan. Due to wide-spread use of endoscopic submucosal dissection (ESD), physicians are facing dilemma as to the indication for additional gastrectomy in elderlies treated by non-curative ESD. This is due to little information with regards to the long-term outcomes and prognostic factors of non-curative ESD for gastric cancer in elderly patients.
Aims and Methods: We aimed to clarify the long-term outcomes and prognostic factors of non-curative ESD for gastric cancer in elderly patients. Among 1,358 patients with early gastric cancer (EGC) treated by ESD at our institution during 2002–2012, we enrolled 87 patients with ages ≥75 yrs, who were treated by non-curative ESD. First, clinicopathological findings and long-term outcomes up to the end of 2017 were evaluated. Next, the prognostic factors were analyzed using the Kaplan-Meier methods and a Cox proportional hazards model.
Results: 27 of 87 patients died of any cause. However, only 1 patient died of gastric cancer. 3-year overall survival (OS) and 5-year OS were 89.7% and 79.3%, respectively. The univariate analyses revealed that patients who were in Eastern Cooperative Oncology performance status of 2 or 3, high Charlson comorbidity index (CCI) (≥3), high neutrophil to lymphocyte ratio (≥3.3), low prognostic nutritional index (< 44.8), antral location of EGC and depressed or completely flat configuration of EGC were factors associated with death. The high CCI (≥3) was found to be an independent prognostic factor associated with OS (hazard ratio: 2.79, 95%CI: 1.16–6.69, $p = 0.021$).
Conclusion: After non-curative ESD for gastric cancer in elderlies, CCI may be a clue for decision making of additional gastrectomy. Careful follow up without additional gastrectomy may be an acceptable strategy for elderly patients.
Disclosure: Nothing to disclose

P0538 CORRELATION OF ENDOSCOPIC FINDINGS OF GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA WITH RECURRENCE AFTER COMPLETE REMISSION

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Introduction: In gastric mucosa-associated lymphoid tissue (MALT) lymphoma, the clinical significance of various endoscopic findings has not yet been determined. This study aimed to compare the time to complete remission (CR) and relapse-free survival (RFS) in gastric MALT lymphoma based on endoscopic findings.
Aims and Methods: In this single-center retrospective cohort study, the medical records of 122 consecutive adult patients with gastric MALT lymphoma were collected over a period of 12 years. CR was defined by the absence of macroscopic or microscopic features of lymphoma on 2 subsequent follow-ups. Relapse was clinically defined by a positive endoscopic biopsy after CR.
Results: The median time to CR did not differ significantly between treatment methods. However, it was significantly longer in the group with polypoid endoscopic appearance than in the groups with diffuse infiltration or ulceration (7.83, 3.43, and 3.10 months, respectively; $p = 0.003$). 6 patients relapsed after CR. Kaplan-Meier analysis showed that RFS differed significantly between groups based on Ann Arbor staging, treatment methods, and initial endoscopic findings.
Conclusion: In gastric MALT lymphoma, the endoscopically defined polypoid type was characterized by a longer duration to CR, with a higher likelihood of recurrence, compared to the endoscopically defined diffuse infiltration or ulceration types.
Disclosure: Nothing to disclose

P0539 FLAP FORMATION TIME AS A NEW ENDPOINT OF TECHNICAL SUCCESS OF ESD FOR SUPERFICIAL DUODENAL EPITHELIAL TUMORS; A TIMELINE ANALYSIS

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Introduction: Though ESD has been a standard treatment for superficial epithelial neoplasia of various gastrointestinal tracts, duodenal ESD has been still technically challenging due to anatomical features of duodenum. Procedure time has been recognized as a scale for technical difficulties of ESD; however, there have been few studies analyzing in what part of the procedure the time was consumed. At the beginning of ESD procedure, making a mucosal flap may be important step because we can obtain stable visual field by exposure of

submucosa using distal hood of the endoscope. We hypothesized time to flap formation would be a surrogate endpoint for technical success for duodenal ESD.
Aims and Methods: The aim of this study was to assess the feasibility of time to flap formation as endpoint for duodenal ESD. This was a retrospective observational study from a university hospital. A total of 102 cases that underwent ESD for duodenal superficial neoplasia from July 2013 to June 2017 were included in this study. ESD was performed using DualKnife J (Olympus medical systems, Tokyo, Japan) and short tip type transparent hood (ST hood, FUJIFILM Medical Co., Ltd. Tokyo, Japan). An endoscopist reviewed all movies of the procedures and measured time to flap formation and total procedure time. In this study, flap formation was defined as the timing when complete exposure of submucosa using upper rim of the hood was obtained. The distribution of total procedure time and time to flap formation was analyzed in addition to other short-term outcomes. Those were compared according to the skill level of endoscopists (expert: >100 duodenal ESD, and the others). Moreover, we analyzed the linear regression between total procedure time and time to flap formation and other clinical features of the lesion using least square methods.
Results: As for location of the lesion, 13.7% located in bulbs, 73.5% in descending part, 3.0% in horizontal part, and 9.8% located in superior duodenal angle (SDA) or inferior duodenal angle (IDA). The mean lesion diameter was 32.5 ± 16.5 mm. Resection in a single piece and R0 resection was 98.0% and 86.3%, respectively. Bleeding and perforation was found in 3.0% and 5.9% of patients, respectively. Mean procedure time was 55.8 ± 3.9 min and mean time to flap formation was 13.5 ± 1.1 min. It was significantly shorter by expert's hand (12.1 ± 1.1 min vs 24.0 ± 2.9 min, $p < 0.0001$). Multiple linear regression analysis revealed time to flap formation as well as lesion size, location, and endoscopists' skill were independently correlated with total procedure time (Table 1).
Conclusion: Time to flap formation reflected the skill level of the endoscopists and predicted total procedure time independently of the size and the location of the lesion. It could be a surrogate endpoint for technical success of duodenal ESD.

	β coefficient	t value	P value
Flap formation time	1.32	5.41	<0.0001
Lesion size	90.59	10.01	<0.0001
Location (SDA or IDA)	454.09	2.66	0.0092
Endoscopistś skill	788.18	3.27	0.0015

[The results for multiple linear regression analysis about total procedure time]
Disclosure: Nothing to disclose

P0540 EFFECT OF THE DURATION TIME OF UPPER GASTROINTESTINAL ENDOSCOPY ON THE DETECTION RATE OF GASTRIC NEOPLASTIC LESIONS

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Introduction: Early detection and prompt treatment using upper gastrointestinal endoscopy are important to reduce the mortality rates of gastric cancer. Previous reports on esophagogastroduodenoscopies (EGD) have stated that compared to observation cohorts of less than 7 minutes, the detection rates of high-risk gastric lesions are significantly higher in observation cohorts of 7 minutes or longer. Nevertheless, there are few reports assessing the relationship between EGD examination time and the detection rates of high-risk gastric lesions, and it remains unclear if longer observation times can increase the detection rate of lesions.
Aims and Methods: In this study, we examined whether a longer examination time increased the detection rate of gastric neoplastic lesions. From June 2017 to December 2017, we investigated 1019 patients (501 men and 518 women, mean age: 62.8±16 years) who underwent a first screening EGD at our hospital. Endoscopists were classified as fast or slow based on the mean amount of time it took them to perform a normal screening endoscopy. We used the histopathological tissue results of biopsies to retrospectively examine the detection rate of neoplastic lesions such as early-stage gastric cancers, gastric adenomas, lymphomas, by both fast and slow endoscopists. Furthermore, we also used multivariate analysis to examine the factors that contribute to the detection of gastric neoplastic lesions.
Results: Of normal 782 endoscopies, the median duration time was 6.85 minutes (range, 2–24). Based on the results, we used 7 minutes as the cut off time. The fast group was defined as 12 endoscopists with a mean duration time of 5.97 ± 2.03 min, and the slow group was defined as 12 endoscopists with a mean duration time of 9.59 ± 2.80 min. Screening endoscopies were performed for 596 cases (305 men and 291 women, mean age: 62.8 ± 16 years) in the fast group and for 423 cases (196 men and 227 women, mean age: 62.7 ± 16 years) in the slow group. Overall, biopsy was performed by 237 cases (23.2%) of screening endoscopy, 36 neoplastic lesions were diagnosed, of which 16 lesions (1.6%) were early gastric cancers, 9 lesions (0.9%) were adenomas, 8 lesions (0.8%) atypical lesion and 3 lesions (0.3%) were lymphoma. Compared to the slow group, the fast group had significantly higher rates of staff performing exams 327 (62.8%)/ 211 (49.8%) ($p < 0.001$), significantly lower rates of sedation 380 (63.8%)/ 332 (78.5%) ($p < 0.001$), significantly lower rates of biopsy implementation 124 (20.8%)/ 113 (26.7%) ($p = 0.027$). The detection rates of neoplastic lesions in the fast and slow groups were 23 (3.9%)/13 (3.1%), so no significant difference was observed.
In the multivariate analysis, men ($p = 0.012$; odds ratio 2.60, 95% CI 1.23–5.49), age≥60 ($p = 0.004$; odds ratio 4.03, 95% CI 1.55–10.52), and staff performing the examinations ($p = 0.035$; odds ratio 2.60, 95% CI 1.07–6.31) were independent factors that contributed to the detection of gastric neoplastic lesions.
Conclusion: In this study, a longer examination time did not increase the detection rate of gastric neoplastic lesions. In the multivariate analysis, the staff implementing the exams was an independent factor that contributed to the detection of gastric neoplastic lesions. In the EGD, it is thought that the detection of gastric neoplastic lesions is made possible using a short examination time and efficient biopsies due to the accumulation of experience.
Disclosure: Nothing to disclose

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P0541 VALIDITY OF SUBMUCOSAL PATTERN ANALYSIS OF EUS FOR PREDICTING DEPTH OF INVASION IN ULCERATIVE EARLY GASTRIC CANCER

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Introduction: Accuracy of endoscopic ultrasonography (EUS) for predicting depth of invasion in early gastric cancer (EGC) accompanied with endoscopic ulcer or ulcer scar was lower than that without ulcer.
Aims and Methods: We tried to evaluate the validity of submucosal pattern analysis of EUS for predicting depth of invasion in ulcerative EGC. Demographic, endoscopic and EUS features of 176 consecutive endoscopically suspected EGC patients who underwent the EUS examination and the endoscopic treatment or surgery were retrospectively reviewed. The EUS findings were classified as the (1) no deformity type, (2) fan-shaped deformity type, and (3) arch-shaped or punch-shaped deformity type, according to submucosal layer change. The EUS findings also classified into 2 groups; submucosal fibrosis and no fibrosis groups.
Results: 73 among total 176 cases (41.5%) were accompanied with the active or healing staged endoscopic ulcer, whereas S1-staged ulcer was found in 62 cases (35.2%) and no ulcer group was 41 cases. The EUS fibrosis was combined in 71 cases (41%). Fan-shaped deformity and arch-shaped deformity in submucosal layer was noted in 88 cases and 48 cases, respectively. The histologic submucosal fibrosis was found more frequently in the EUS fibrosis group than no fibrosis group (51.6% vs 10.4%, p≤0.001). The Arch-shaped submucosal deformity was a significant independent predictive factor for presence of submucosal cancer invasion than Fan type or no SM deformity group.(80.9% vs 18.2% vs 19.5% odds ratio 11.83) ($p < 0.001$). With regard to the results of endoscopic resection, curative, and complete resection rate were significantly lower in EGCs with the arch-type submucosal deformity than those with no SM change or fan-type SM change groups ($p < 0.001$).
Conclusion: Pattern analysis of the submucosal deformity on EUS examinations can be an useful tool for predicting the presence of the histologic ulcers and cancer invasion in ulcerative EGC.
Disclosure: Nothing to disclose

P0542 FEASIBILITY AND OUTCOMES OF SECONDARY (REDO) ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LOCALLY RECURRENT OR INCOMPLETELY RESECTED GASTRIC NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is an accepted curative treatment option for gastric tumors with very low local recurrence. However, residual or locally recurrent tumors occur rarely after ESD. Although secondary (Redo) ESD is technically demanding, it can be applied to residual or recurrent tumors with scar and dense fibrotic submucosa. Here, we investigated the feasibility and safety of secondary ESD for gastric tumors.
Aims and Methods: Between 2010 and 2017, 1623 consecutive patients underwent ESD for gastric neoplasms at a single tertiary referral center. Among these, 28 patients underwent secondary ESD for a residual or locally recurrent tumor. Our analysis compared clinicopathologic factors between primary ESD and secondary ESD groups.
Results: The en-bloc resection and curative rate of resection of secondary ESD were 92.9% and 89.3%, respectively. The average procedure time of secondary ESD was significantly longer than primary ESD (78.2 vs. 55.1 minutes, $p = 0.004$) and the adverse events rate was slightly higher in secondary ESD group than primary ESD group without statistical significance (10.7 vs. 3.8%, $p = 0.095$).

Patients who received secondary ESD had favorable outcomes without severe adverse events. During a mean follow-up period, no local recurrence occurred in patients who received secondary ESD.
Conclusion: Although it requires greater technical efficiency and a longer procedure time, secondary ESD of residual or locally recurrent gastric tumors appears to be a feasible and curative treatment.
Disclosure: Nothing to disclose

P0543 A NEW HISTOPATHOLOGICAL CLASSIFICATION OF GASTRIC ADENOCARCINOMA OF FUNDIC GLAND TYPE AND CLINICOPATHOLOGICAL FEATURES OF GASTRIC ADENOCARCINOMA OF FUNDIC GLAND MUCOSAL TYPE (A MULTICENTER STUDY OF 80 CASES)

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Introduction: Gastric adenocarcinoma of fundic gland type (GAFG) is newly added as a special type cancer in Japanese classification of gastric carcinoma, the 15th Edition 1). GAFG is an uncommon variant of gastric adenocarcinoma which has a distinct clinicopathological, immunohistochemical, and endoscopic features 2–4). GAFG is defined by positive immunohistochemical staining for pepsinogen-I (a marker of chief cells) and/or H+K+-ATPase (a marker of parietal cells) and is not associated with *H. pylori* infection. We suggested that a progression of GAFG might be associated with *GNAS* mutations 5). Histopathologically, GAFG is classified into pure GAFG and gastric adenocarcinoma of fundic gland mucosal type (GAFGM) which exhibited differentiation toward gastric foveolar epithelium in addition to fundic gland differentiation. However, the histopathological classification of GAFG including GAFGM have not been established, and clinicopathological features of GAFGM have not been well investigated.
Aims and Methods: The aim of this study was to establish a new histopathological classification of GAFG and clarify the clinicopathological features of GAFGM by comparisons with pure GAFG. A total of 80 GAFG cases from April 2004 to December 2017 were retrospectively collected from 27 institutions. We performed an immunohistochemical analysis using pepsinogen-I, H+K+-ATPase, MUC5AC (a marker of foveolar epithelial cells) and MUC6 (a marker of mucous neck cells) to classify these GAFG cases as pure GAFG (MUC5AC+, $< 10\% <$ MUC6+ < pepsinogen-I and/or H+K+-ATPase +, n = 57) or GAFGM (MUC5AC+, $\geq 10\% <$ MUC6+ < pepsinogen-I and/or H+K+-ATPase +, n = 23). In addition, GAFGM was classified to 3 subtypes, as follows; Type 1. Tissue construct of foveolar epithelium and fundic gland is maintained, and tumor is exposed on the surface (n = 9), Type 2. Tissue construct of foveolar epithelium and fundic gland is collapsed, and tumor is exposed on the surface (n = 10), Type 3. Tissue construct of foveolar epithelium and fundic gland is collapsed, and tumor is not exposed on the surface (n = 4). We then compared the pure GAFG and GAFGM cases, and 3 subtypes of GAFGM via a clinicopathological evaluation and the frequency of *GNAS* mutation.
Results: There were no significant differences between the 2 groups (pure GAFGs vs. GAFGMs) in the following findings: location of lesion, macroscopic type, method of treatment, depth of invasion, lymph node metastasis, proliferative activity, p53 protein overexpression, *H. pylori* infection, and activating mutations in *GNAS*. The average of tumor size (8.6mm vs. 21.3mm, $p < 0.01$) and depth of submucosal invasion (310μm vs. 1242μm, $p < 0.05$) were significantly greater in GAFGMs than in pure GAFGs. Furthermore, the rates of lymphatic and venous invasion were significantly higher in GAFGMs than in pure GAFGs (1.8% vs. 34.8%, $p < 0.01$). The average of tumor size (11mm vs. 31.8mm vs. 18.5mm, $p < 0.05$) was significantly greater and the rates of lymphatic invasion (0% vs. 60% vs. 0%, $p < 0.05$) was significantly higher in Type 2 than in Type 1 and 3.
Conclusion: This histopathological classification of GAFG is useful to estimate its malignant potential. GAFGM should be categorized as a new aggressive variant of GAFG that has high malignant potential and differ in malignancy by tissue construct of foveolar epithelium and fundic gland.
Disclosure: Nothing to disclose

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P0544 RISK FACTORS FOR EARLY AND DELAYED POST-OPERATIVE BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) has become widely accepted as a standard treatment for gastric neoplasm. The safety of gastric ESD has been mostly established, Although, complication such post-operative bleeding and perforation remain problematic.
Since 2012, an endoscopic approach involving continued administration of low-dose aspirin (LDA) for patients at high risk of thromboembolism has been recommended in Japan. This approach is similar to the one stated in the guidelines of the European Society of Gastrointestinal Endoscopy; however, there is insufficient date to support this guideline in Japan.
Aims and Methods: The aim of this study was to identify risk factors for early and delayed post-operative bleeding after gastric ESD and to evaluate the relationship between the use of antithrombotic agents and post-operative bleeding. From January 2004 to December 2017, we analyzed 922 patients (673 men and 249 women, mean age: 72.7±14years) 961 gastric neoplasms who treated by ESD at our hospital. Traditionally, we have interrupted therapy 5–7 days before gastric ESD for patients using LDA. However, since January 2012, we have followed the above mentioned guidelines, thus performing ESD with continued LDA for patients at high risk of thromboembolism.
In this study, post-operative bleeding was defined as a decrease in the blood hemoglobin level of > 2g/dL accompanied by an occurrence of hematemesis or melena.
Bleeding within 6 days after ESD was defined as early post-operative bleeding, whereas bleeding on the sixth day or later post-operatively was defined as delayed post-operative bleeding.
Risk factors for early and delayed post-operative bleeding were retrospectively examined using univariate and multivariate analysis.
Results: The overall post-operative bleeding rate was 4.4%. The mean duration until post-operative bleeding was 6.2±4.6days. The post-operative bleeding rates for patients who continued LDA, discontinued antithrombotic agents, or received heparin replacement (HR) were 11.1%, 5.5%, and 13.1%, respectively. In the multivariate analysis, chronic kidney disease (CKD) requiring hemodialysis ($p < 0.005$; odds ratio 6.71, 95% CI 1.79–25.1), HR ($p < 0.001$; odds ratio 4.15, 95% CI 1.73–9.93) and a specimen size of ≥ 50mm ($p = 0.024$; odds ratio 2.27, 95% CI 1.11–4.62) were independent risk factors for post-operative bleeding.
Early post-operative bleeding rate was 1.9%. In the multivariate analysis, CKD requiring hemodialysis ($p < 0.002$; odds ratio 14.2, 95% CI 2.62–77.0), and a specimen size of ≥ 50 mm ($p = 0.023$; odds ratio 3.35, 95% CI 1.18–9.51) were independent risk factors for early post-operative bleeding.
Delayed post-operative bleeding rate was 2.5%. In the multivariate analysis, HR ($p < 0.002$; odds ratio 5.69, 95% CI 1.92–116.8) was independent risk factor for delayed post-operative bleeding.
Conclusion: Continued LDA was not risk factor for post-ESD bleeding. CKD requiring hemodialysis, and specimen sizes ≥50 mm are independent risk factors for early post-operative bleeding, whereas HR is an independent risk factor for delayed post-operative bleeding. The timing of post-operative bleeding differs with the factors. Careful observation is required for patients at high risk of post-operative bleeding.
Disclosure: Nothing to disclose

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P0545 IS C-REACTIVE PROTEIN A PROGNOSTIC FACTOR FOR THE WHOLE GEP-NET GROUP?

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Introduction: Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) constitute a heterogeneous group of tumors with variable clinical presentations, different growth rates and unpredictable prognoses. In our study, we aimed to identify the independent prognostic markers for the patients in the whole GEP-NET group.
Aims and Methods: 93 patients who were diagnosed with GEP-NET within the specified period were included in this study. The data were retrospectively analysed. The relationship between all independent variables with 5-year survival status and calculated follow-up period (months) was assessed. In addition, the relationship between the independent variables was investigated.
Results: When we compared the 5 year survival rate, there was a statistically significant relationship between age at diagnosis, male gender, tumor size, tumor stage, liver and / or distant metastasis, tumor grade determined by Ki-67 level and mitotic count and the level of CRP that 1 of the biochemical data. The mean survival (OS) of the study group was 102.5 ± 6.3 (SD) months. The percentages of 1, 3 and 5-year survival were 90%, 72% and 61%, respectively. Of the 93 patients in the study, 63 had a Ki-67 and the mitotic count determined same grade. Ki-67 levels in 29 patients and mitotic count in only 1 patient were higher grade. Risk of death rising %4 by the every 1 increase in the age at

diagnosis, for male sex 2.0-fold, G3 according to mitosis count 3.0-fold, G3 according to Ki-67 level 3.7-fold, tumor stage 3 or 4 cases 12.7-fold, 1 cm increase in tumor size 9%, liver metastasis 6.1-fold, by every 1 mg/dl increase in CRP level 1.5%. There was a significant difference between the pancreas and stomach NETs in favor of stomach tumors in terms of survival.
Conclusion: As a result, it was observed that 1 of the biochemical parameters, CRP affected the course of the progression in the worst way (particularly if it is > 20 mg / dl). With the need for larger scale and prospective studies, it was suggested that CRP level might be a poor prognostic factor for the entire GEP-NET group.
Disclosure: Nothing to disclose

P0546 ACCURACY OF ENDOSCOPIC SIZE MEASUREMENTS OF EARLY GASTRIC SIGNET RING CELL CARCINOMA

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Introduction: Indications for endoscopic submucosal dissection (ESD) of early gastric cancer (EGC) are expanding, but signet ring cell (SRC) carcinoma is still unclear because of its unclear lateral margin.
Aims and Methods: The purpose of this study was to compare pathologic size and endoscopic size in early gastric SRC and to find risk factors associated with tumor size underestimation. A retrospectively medical records reviewed of total 137 patients with diagnosed early gastric SRC between January 2009 and December 2016 at our tertiary hospital. According to pathologic and endoscopic tumor sizes, classified into correct estimation, underestimation and overestimation groups, and risk factors related to underestimation were analyzed.
Results: Among 137 patients with early gastric SRC, 77 patients (56.2%) had undergone correct estimation, 43 patients (31.4%) had underestimation and 17 patients (12.4%) had overestimation. Mean pathologic size (SD) was 20.1 (13.8) mm and mean endoscopic size (SD) was 17.9 (10.1) mm, the correlation coefficients were 0.919 ($p = 0.000$) and there was no significant difference between the two groups. Multivariate analysis showed that more than 20mm endoscopic tumor size (OR, 3.419; 95% CI, 1.271–9.194, $p = 0.015$) and atrophy (OR, 6.011; 95% CI, 2.311–15.633, $p = 0.001$) was a risk factor for tumor size underestimation.
Conclusion: There was no significant difference in pathologic and endoscopic size in early gastric SRC. Therefore ESD may be considered as a therapeutic option if the size of the tumor is less than 20 mm and atrophy is not present in the surrounding mucosa.
Disclosure: Nothing to disclose

P0547 INCREASED INCIDENCE OF RECURRENT NEOPLASM AFTER ENDOSCOPIC RESECTION IN PATIENTS WITH SYNCHRONOUS GASTRIC NEOPLASM

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Introduction: Metachronous gastric neoplasm is the major concern after endoscopic resection (ER) for early gastric cancer (EGC). Several studies showed that patients with EGC with synchronous neoplasm had increased recurrence rate after ER than those with single EGC. However, the incidence and prognosis are not well-known in patients with synchronous neoplasm including adenoma.
Aims and Methods: In this study, we compared the outcome between patients with single neoplasm and synchronous neoplasm including adenoma after ER. We also compared the outcomes of synchronous neoplasm subgroup which were divided according to the diagnostic histology.
A total of 1569 patients who underwent ER for gastric neoplasm were divided into 2 groups: those with single neoplasm and with synchronous neoplasm which was detected at the initial evaluation or within 1 year follow-up period. The patients with synchronous neoplasm were further divided into 3 subgroups according to the diagnostic histology: subgroup 1 compromised the patients with cancers, subgroup 2 with cancer and adenoma, and subgroup 3 with adenomas. We compared the clinicopathologic characteristics and the incidence of metachronous neoplasm between the patients with and without synchronous gastric neoplasm. Furthermore, we also compared the outcomes of three synchronous neoplasm subgroups.
Results: Synchronous gastric neoplasms were found in 182 patients in a total of 1,569 patients (11.6%). There were no significant differences in gender, proportion of initial tumor pathology, location, and depth of invasion, the incidence of *Helicobacter pylori* infection, and duration of follow-up between the patients with single and synchronous neoplasm. The median follow-up period was 30 months (range, 1–161) in single neoplasm group and 25 months (range, 1–112) in synchronous group. In synchronous groups, multiple adenomas were most commonly found (n = 84, 46.1%), followed by a combination of adenoma and cancer (n = 68, 37.3%), and multiple cancers (n = 30, 16.4%). The risk of metachronous neoplasms was significantly higher in patients with synchronous neoplasm than those with single neoplasm [OR, 2.3 (95% CI, 1.53–3.36); $p < 0.001$]. There was no difference in the risk of metachronous neoplasm in 3 synchronous subgroups. However, cancer was more frequently found in subgroups including cancer than the group including only adenoma during the follow-up period ($p = 0.0026$). When the subgroups including cancer were combined into 1 group, the cancer risk was significantly higher in these patients than those with only adenomas [OR, 4.89 (95% CI, 1.32–31.51); $p < 0.001$].
Conclusion: Patients with synchronous gastric neoplasm including adenoma had increased risk of metachronous neoplasm than those with single lesion. There was no difference in the risk of metachronous neoplasm in three synchronous subgroups. However, the incidence of metachronous cancer was significantly higher in subgroups with cancer than subgroup with only adenomas. Therefore, we have to consider the strict follow-up strategy in the presence of synchronous neoplasm not only EGC but also adenoma.
Disclosure: Nothing to disclose

P0548 MATRIX METALLOPROTEINASE MULTIPLEX SCREENING IDENTIFIES INCREASED TIMP-4 SERUM CONCENTRATIONS IN GASTRIC CANCER PATIENTS

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Introduction: The phenomenon of active inflammatory crosstalk between tumor cells and the surrounding stroma has attracted more and more attention [1]. Some investigations have indicated that inflammation-related proteins, such as matrix metalloproteinases (MMPs), may facilitate the growth, proliferation, and migration of tumor cells, including GC [2–4]. This study was carried out to reveal and testify their significance as candidates for tumor markers of GC.
Aims and Methods: Plasma samples from 12 GC patients (3 cases for each clinical stage from I to IV) and 10 non-neoplastic gastric disease (NGD) patients (3 cases with chronic superficial gastritis, 4 cases with chronic atrophic gastritis and/or intestinal metaplasia and 3 cases with dysplasia) were collected from November 2016 to March 2017 as training set. Human MMP arrays (RayBiotech, Norcross, GA, USA) were used to quantitative measurement of 7 major MMPs (MMP-1, MMP-2, MMP-3 MMP-8, MMP-9, MMP-10, and MMP-13) and 3 their endogenous tissue inhibitors (TIMP-1, TIMP-2, and TIMP-4) simultaneously. Then the levels of them were compared between the GC and NGD groups and their diagnostic value was assessed by ROC curve. The candidate differential subtypes were validated by corresponding serum microchips in another group of patients, which included 40 GC patients and 38 NGD patients. Additionally, the levels of alpha fetoprotein (AFP), carcinoembryonic antigen (CEA), carcinoma antigen 125 (CA125), and carbohydrate antigen 19-9 (CA19-9) in plasma of the 52 GC patients were determined by electrochemiluminescence assay (Roche cobas e 601, Switzerland).
Results: Compared to the NGD group, except MMP-2, MMP-3 and MMP-13, other MMPs showed an increased trend in the GC group, but no significant difference in the training set. Only TIMP-4 increased significantly in the GC group than NGD group, $p < 0.05$. The area under the curve (AUC) of the MMPs were from 0.500 to 0.858, and combined AUC of them was 0.858 (95% CI, 0.699-1.000) for the diagnosis of GC. Particularly, TIMP-4, whose AUC was the highest, 0.858 (95% CI: 0.692–1.000). At the optimal cut-off value of 2438.3 pg/mL, its sensitivity, specificity and accuracy for the diagnosis of GC were 83.3%, 80.0% and 81.8%, respectively. In the validation set, the concentration of TIMP-4 in GC and NGD group were 1101.2 + 703.3 pg/mL and 890.1 + 454.7 pg/mL, respectively. Compared with the NGD group, the concentration of TIMP-4 increased in the GC group, but no statistical difference was found. Its AUC value for the diagnosis of GC was 0.574 (95% CI: 0.444–0.704). Furthermore, the positive rates of AFP, CEA, CA125 and CA19-9 in both sets for the diagnosis of GC and early gastric cancer (EGC), as shown in Table 1.
Conclusion: The diagnostic value of the conventional tumor markers is limited. However, MMP profiles may have potential value for the diagnosis and screening of GC. TIMP-4 is a promising biomarker for the auxiliary diagnosis of GC.

Variable	Training	set	Validation	set
	GC (n = 12)	EGC (n = 3)	GC (n = 40)	EGC (n = 10)
AFP	0	0	0	0
CEA	25.0	0	18.9	11.1
CA125	20.0	0	8.3	0
CA19-9	8.3	0	10.8	0
Combined	33.3	0	32.4	11.1

[Positive rates of traditional serological tumor markers for the diagnosis of GC and EGC (%).]
Disclosure: Nothing to disclose

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P0549 CLINICAL COURSE AFTER NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER WITHOUT ADDITIONAL SURGERY

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Introduction: Even when early gastric cancer (EGC) is not curatively treated by endoscopic submucosal dissection (ESD), additional surgical gastrectomy is not performed for various reasons.

Aims and Methods: The aim of this study was to assess clinical courses for patients who did not undergo additional surgery for non-curative EGC after ESD. From January 2004 to July 2017, 2,156 patients underwent ESD for EGC at Sendai City Medical Center. Among patients defined as being not curative based on clinicopathological evaluation according to the Japanese Gastric Cancer Treatment Guidelines 2018, 109 patients who did not undergo additional intervention, such as surgery, were included in this study. After elimination of 18 patients who were alive during an insufficient follow-up period of < 3 years, risk factors for short survival (< 3 years) were evaluated by using univariate and multivariate analyses.

Results: Of the 109 patients, the median age was 75.8 years (range, 48–93 years) and 78% were male. The median Charlson Comorbidity Index (CCI) was 2.0 (range, 0–7). The ratio of the patients with low level activity of daily living (ADL), with which the patient could not go out by him/herself, was 13%. As to pathological outcomes, the depth of cancer invasion was M in 28% of the patients, SM1 in 28%, SM2 in 41%, and unclear in 3%. The median tumor size was 35 mm (range, 9–98 mm). The histological type was diagnosed as the differentiated type in 81%, undifferentiated type in 3%, mixed type in 14%, and others in 2%. Lymphatic and venous invasion were observed in 23% and 7%, respectively. The rates of lateral and vertical margin involvement were 3% and 8%. Ulcerative findings were observed in 31%. The risk of lymph node metastasis was defined as being high in 9%, intermediate in 49%, and low in 42% in the eCura system (Hatta et al. *Am J Gastroenterol* 2017). Procedure-related adverse events occurred in 10% (perforation, 3%; postoperative bleeding, 4%; and pneumonia, 3%). The 3- and 5-year overall survival rates (OS) were 87.7 and 81.7%, respectively. Both of the 3- and 5-year disease-specific survival rates (DSS) were 98.7% (median follow-up period, 68.5 months; range, 2.0–165.7 months). Among the 26 patients (23.9%) who died during clinical follow-up, the cause of death was gastric cancer in only 1 patient (37.6 months after ESD) and other causes in 25 patients (median survival period, 45.4 months [range, 4.3–94.8 months]). From univariate analyses, advanced age ($\geq$ 85 years) ($p = 0.043$), high CCI ≥ 3 ($p = 0.007$), low ADL level ($p < 0.001$), and low serum albumin level < 3.5 g/dl ($p = 0.043$) were significantly associated with short survival period. Multivariate analysis revealed that the high CCI (odds ratio [OR], 4.8; 95% confidence interval [CI], 1.1–21; $p = 0.036$] and low ADL level (OR, 6.2; 95% CI, 1.2–31; $p = 0.028$) were independent risk factors for the short survival period.

Conclusion: Given the relatively high OS and DSS, ESD without additional surgery for non-curative EGC was found to be an acceptable option for patients with poor surgical tolerance. Although the survival period was shorter in patients with some comorbidities and those with low ADL level, it is unclear whether additional surgical resection is appropriate or not because the cause of death was not gastric cancer for most of the patients.

Disclosure: Nothing to disclose

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P0550 RISK ASSESSMENT OF LYMPH NODE METASTASES IN EARLY GASTRIC ADENOCARCINOMA FULFILLING EXPANDED ENDOSCOPIC RESECTION CRITERIA

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Introduction: Early gastric cancer (EGC) is known to present low rate of lymph nodal metastasis (LNM). Gastrectomy with D2 lymphadenectomy is usually curative for EGC. Endoscopic submucosal dissection (ESD) is a well-accepted treatment modality for lesions that meet the classic criteria, a mucosal differentiated adenocarcinoma measuring 20 mm or less, without ulceration. Expanded criteria for ESD have been proposed based on null LNM metastasis rate from large gastrectomies series coming from Japan. The expanded criteria for ESD are as follows: intramucosal non-ulcerative well-differentiated tumor > 2 cm, intramucosal ulcerative differentiated tumor ≤ 3 cm, or intramucosal non-ulcerative undifferentiated tumor ≤ 2 cm or superficially submucosal (sm1) differentiated tumor ≤ 3 cm. Patients with positive LNM have been reported in western centers, creating a need for validation of expanded criteria.

Aims and Methods: Our aim was to assess the risk LNM in gastrectomy specimens of patients with EGC who met the expanded endoscopic treatment criteria for ESD.

Evaluation of gastrectomy specimens including LNM staging of patients submitted to gastrectomy for EGC in a 39-year retrospective cohort.

Results: A total of 389 surgical specimens were included. We identified 53 patients with lymph node metastases in our casuistic (13.6%). Patients with indication of surgical treatment (S) had higher incidence of lymph node metastases ($p < 0.001$). From the 135 patients which fulfilled criteria for endoscopic resection, none of the 31 patients with classic criteria had LNM. Of the 104 patients with expanded criteria, 3 had LNM ($n = 104$, 2.9% 95% CI 0.7–8.6%), all of them with undifferentiated tumors without ulceration and less than 20 mm.

Conclusion: There is a small risk of LNM in EGC when expanded criteria for ESD are met. Refinement of the expanded criteria for the risk of LNM metastasis may be desirable in West. Meanwhile the decision to complement the endoscopic treatment with gastrectomy will have to take into consideration the individual risk of perioperative morbidity and mortality.

Disclosure: Nothing to disclose

P0551 COMPARATIVE EFFICACY OF VARIOUS ANTI-ULCER MEDICATIONS AFTER GASTRIC ENDOSCOPIC RESECTION: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: The comprehensive efficacy of various anti-ulcer medications after gastric endoscopic resection has not been fully evaluated. Recently, vonoprazan, a novel potassium-competitive acid blocker, has also been used in ulcer treatment after endoscopic resection.

Aims and Methods: We searched for all relevant randomized controlled trials examining the efficacy of anti-ulcer medications after gastric endoscopic resection, published through October 2017. Healing of iatrogenic ulcers was investigated at 4–8 weeks after the procedure. A network meta-analysis was performed to calculate the network estimates.

Results: 23 studies with 2137 patients were included in the meta-analysis. Concerning the comparative efficacy for ulcer healing at 4 weeks after the procedure, no network inconsistency was identified (Cochran's Q-test, $df = 12$, $p = 0.22$; $I^2 = 22\%$). A combination therapy of proton pump inhibitor (PPI) and mucoprotective agent was superior to all other regimens (risk ratio [RR] [95% confidence interval, CI]: vs. PPI, 1.69 [1.23–2.31]; vs. vonoprazan, 1.97 [1.09–3.56]; vs. H_2 receptor antagonist, 1.73 [1.02–2.93]; vs. mucoprotective agent, 1.68 [1.06–2.65]). Concerning the ulcer healing rate at 8 weeks after the procedure, however, vonoprazan was superior to PPI (RR [95% CI] = 1.27 [1.03–1.56]). Additionally, vonoprazan tended to be superior to the combination therapy of PPI and mucoprotective agent (RR [95% CI] = 1.20 [0.96–1.51]).

Conclusion: A combination therapy of PPI and mucoprotective agent was superior to other anti-ulcer drug regimens for ulcer healing at 4 weeks after endoscopic resection. However, vonoprazan tended to be superior to the combination therapy of PPI and mucoprotective agent for ulcer healing at 8 weeks after the procedure.

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P0552 SERUM PEPSINOGEN II AS A POTENTIAL BIOMARKER FOR DETECTION OF DIFFUSE TYPE GASTRIC CANCER AMONG YOUNG ADULTS IN KOREA

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Introduction: The usefulness of pepsinogen (PG) I and I/II ratio as biomarker for screening gastric cancer (GC) has been well established in Japan. PG II is known to be a non-invasive marker of gastric inflammation, but clinical interest in diagnosis of GC was relatively low and its role has not been clearly established either. The purpose of this study is to investigate the role of PG II in the screening of GC.

Aims and Methods: Total of 2,956 subjects, including patients with GC (n = 1,136), gastric dysplasia (n = 346) and controls (n = 1,474) who underwent gastroscopy with well-defined biopsy sampling protocol, were enrolled in this study during 2006–2017. Serum tests of PG and Helicobacter pylori (HP) infection tests (Giemsa stain, CLOtest and culture) were performed. Each PG level were divided into 3 categories. The usefulness of PG levels to detect GC compared to controls was validated by using multivariate logistic regression. Odds ratios and 95% CIs were calculated.

Results: In the cross-sectional analysis, PG I, PG II and PG I/II ratio (especially PG I/II ratio) were associated with the presence of GC. When classified by histology, the prevalence of diffuse type GC was higher in high PG II levels group (OR = 2.20, $p < 0.001$). Furthermore, high PG II levels were strongly related with subgroup of below age 40 (OR = 4.77, $p < 0.001$) and female diffuse GC patients (OR = 6.77, $p < 0.001$). By combining PG II with PG I/II ratio, higher ORs were obtained when the young age group with PG II ≥22.1 ng/mL and PG I/II ratio < 3 was defined as high-risk group (OR = 18.77, p = 0.005).

Conclusion: High PG II levels are associated with the risk of diffuse type GC. Serum PG II ≥22.1 ng/mL and PG I/II ratio < 3 could be used to identify high risk individuals for diffuse type GC, particularly in young adults in Korea.

	Control n =	Gastric cancer		Intestinal type GC		Diffuse type GC	
		n =	OR (p-value)	n =	OR (p-value)	n =	OR (p-value)
PG I							
<30	197	292	Reference (NA)	199	Reference (NA)	88	Reference (NA)
30–70	811	490	0.41 (.000)	297	0.36 (.000)	181	0.50 (.000)
≥70	466	354	0.51 (.000)	158	0.34 (.000)	182	0.87 (.387)
PG II							
<11.3	520	327	Reference (NA)	215	Reference (NA)	105	Reference (NA)
11.3–22.1	484	375	1.23 (.034)	230	1.15 (.222)	137	1.40 (.019)
≥22.1	470	434	1.47 (.000)	209	1.08 (.531)	209	2.20 (.000)
PG I/II ratio							
<3	492	602	Reference (NA)	362	Reference (NA)	224	Reference (NA)
3–7	844	498	0.48 (.000)	271	0.44 (.000)	213	0.55 (.000)
≥7	138	36	0.21 (.000)	21	0.21 (.000)	14	0.22 (.000)

[Correlation between pepsinogen and gastric cancer]

Disclosure: Nothing to disclose

P0553 ABOUT CLASSIFICATION OF CHRONIC GASTRITIS

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Introduction: The problem of adequate diagnostics and interpretation of chronic gastritis, as well as identical understanding of an essence of process, remains a stumbling block between pathologists, endoscopists and gastroenterologists. Attempts to compare an endoscopic picture with histologic have shown the prevailing importance of microscopy as in definition of a form and stage of gastritis, and risk of malignization on his background.

Aims and Methods: Justification of the uniform scheme of the endoscopic conclusion at chronic gastritis. Results of 59710 endoscopic conclusions and 38421 microscopic investigations of 3593 patients with chronic gastritis were studied in long dynamic observation from 2000 to 2016.

Results: The analysis of endoscopic signs in the descriptive picture of chronic gastritis, regardless of the prescription of the disease, revealed three main common indicators: diversity, roughness, focuses of atrophy of the gastric mucosa. The analysis of a microscopic picture has revealed similar atrophic - hyperplastic processes of different degree of varying severity with different forms of chronic gastritis (according to Current International Statistical Classification of Diseases and Related Health Problems (ICD-10) of classification of gastritis (K29 code)).

The correlation between frequencies of endoscopic signs is not found (Spearman R = −0.213057, p = 0.484630), but the frequency of endoscopic signs varied significantly depending on the severity of atrophy (Chi-Square = 15330.83 df = 12 $p < 0.000000$). A high degree of correlation between endoscopic and microscopic signs was found (Spearman Rank Order Correlations = 0.985610760609162; t (N-2) = 11.6619037896906; p = 0.000309). The scheme of a current and visual interpretation of chronic gastritis is offered.

The fact and quality of endoscopic diagnosis of chronic gastritis depends on the doctor's understanding of the phases of chronic gastritis. Accumulation of visual atrophic changes and community microscopic changes at the different area of atrophy of the gastric mucosa make the endoscopic conclusion 'chronic subatrophic gastritis' from an uneven mucous membrane without visible foci of atrophy right up to the appearance of a picture of atrophic gastritis.

Conclusion: The establishment of the fact of chronic subatrophic gastritis requires morphological verification of the degree of atrophy and the risk of carcinogenesis using the OLGA or OLGA-IM protocol.

Disclosure: Nothing to disclose

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P0554 CLINICOPATHOLOGIC IMPACTS OF TP53 AND SMAD4 INACTIVATION IN GASTRIC ADENOCARCINOMA WITH ENTEROBLASTIC DIFFERENTIATION

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Introduction: Gastric adenocarcinoma with enteroblastic differentiation (GAED) is a rare variant of gastric adenocarcinoma characterized by fetal gut-like structures with glycogen-rich clear cytoplasm and frequent expression of AFP, Glypican-3 (GPC3) and SALL4 [1–5]. Clinicopathologically, GAED shows aggressive behavior characterized by frequent vascular invasion, lymphatic invasion and, liver metastasis even in early cancer [6–7]. Last year, our group reported by comprehensively analysis using next generation sequence (NGS) that GAED had high frequency of *TP53* mutation associated with p53 overexpression. Furthermore, we also showed that *ERBB2* amplification and HER2 overexpression were observed as is seen in conventional gastric adenocarcinoma (CGA) and that Trastuzumab could be used as a therapeutic target therapy in this tumor.

Aims and Methods: This study aimed to further clarify the inactivation mechanism of *TP53* in GAED. In addition, the frequency and prognostic impact of *SMAD4* expression and loss of heterozygosity (LOH) of this gene were also assessed, because *SMAD4* was identified as one of the frequently deleted genes by copy number variation (CNV) analysis of NGS. We enrolled 51 cases (early:17, advanced:34) of GAED for this study. We performed sanger sequence for *ATM* mutation that were shown to be related to the inactivation of p53, and also evaluated the DNA promoter methylation status of *TP53* by methylation-specific PCR (MS-PCR) and LOH analysis of *TP53* locus. Furthermore, we evaluated LOH of *SMAD4* locus and *SMAD4* mutations. In addition, we performed immunohistochemistry for *SMAD4* and ten-eleven translation (TET)1 related to the methylation of the promoter and examined their clinicopathological correlations. Regarding the frequencies of the genetic alterations, obtained data were compared to those of CGA from TCGA [8].

Results: We found only 1 case of *ATM* mutation. The frequency of LOH at *TP53* locus was 39.2%, and the promoter methylation of *TP53* was detected in 20%. Among cases with promoter methylation of *TP53*, 40% (4/10) did not show p53 overexpression by immunohistochemistry. These findings suggest that p53 dysfunction in GAED is in part caused promoter methylation, in addition to *TP53* mutation/LOH. 14 cases harbored both LOH at *TP53* locus and either missense or nonsense mutation of *TP53*, however, p53 inactivation did not affect patients' prognosis in GAED. Reduced TET1 expression was found in 16 cases (32%), however, the reduced expression of TET1 was not associated with promoter methylation of *TP53*. LOH at *SMAD4* locus was found in 23 cases (45%) and was significantly higher in GAED compared to CGA. *SMAD4* mutation was not found in any case. Reduced *SMAD4* expression was found in 18 cases (36%) and was significantly associated with advanced stage of GAED. LOH at *SMAD4* locus was not associated with reduced *SMAD4* expression. LOH status of *SMAD4* locus did not affect patients' overall survival in GAED.

Conclusion: Inactivation mechanism of *TP53* other than gene mutations or LOH seemed to be rare in GAED. Frequent *TP53* mutation is one of the characteristics of GAED, however, does not contribute to the aggressive biological behavior in this tumor. In contrast, The LOH rate (45%) of *SMAD4* locus in GAED

was significantly higher than that of CGA, suggesting that this locus is one of the susceptibility genes in this tumor, although *SMAD4* mutation was not detected. Furthermore, dysfunction of *SMAD4* seemed to contribute to the acquisition of the aggressive behavior of GAED.
Disclosure: Nothing to disclose

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P0555 COMPREHENSIVE BIOINFORMATIC ANALYSIS OF ABERRANTLY EXPRESSED PROFILES OF MIRNAS AND LNCRNAS WITH THE ASSOCIATED CERNA NETWORK IN GASTRIC CANCER

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Introduction: Increasing evidence has highlighted the critical roles of miRNAs as biomarkers and therapeutic targets for cancer. MiRNAs are also regarded as a major part of competing endogenous RNA (ceRNA) network due to its regulation on protein-coding gene expression by acting as sponges. However, functional roles of miRNA-mediated ceRNAs in gastric cancer (GC) remain unclear.
Aims and Methods: To clarify relevant potential mechanisms, we comprehensively compared the expression profiles of mRNAs, lncRNAs and miRNAs between 55 GC tissues and 55 non-tumor tissues, based on GEO databases. Then, we selected most relevant genes through GO and pathway analysis, together with target gene prediction. We also set up a ceRNA network through the certain algorithm.
Results: The flow chart of our study was shown in Figure 1. A total of 11 miRNAs, 299 lncRNAs and 1118 mRNAs were identified as aberrantly expressed in all of the four databases (GSE67354, GSE78775, GSE79973 and GSE19826). After screening by GO and pathway analysis, 364 significant mRNAs were selected ($p < 0.05$) and they had correlations with tumorigenesis and/or progression of GC. Further screening was performed using targeting gene prediction and 179 mRNAs were chosen. Then, a dysregulated miRNA-associated ceRNA network was successfully constructed, which inculdes 70 lncRNAs, 11 miRNAs and 112 mRNAs (Figure 2A). Finally, 2 out of the 11 dysregulated miRNAs functioned as prognostic biomarkers for GC patients according to the overall survival analysis, which is a higher expression of hsa-miR-125-5p and hsa-miR-130-3p represented a lower prognosis rate (P value = 0.0259 and 0.0236, respectively) (Figure 2B). We then examined the miRNAs' expression in our 30 GC tissues and 30 control tissues. MiR-125 and miR-130 were both decreased in GC tissues.
Conclusion: In summary, our study identified novel miRNAs as candidate prognostic biomarkers and potential therapeutic targets for GC, based on large-scale sample size. More importantly, the newly identified ceRNA network will be beneficial for improving the understanding of miRNA-mediated ceRNA regulatory mechanisms in the pathogenesis of GC.
Disclosure: Nothing to disclose

P0556 ADIPOCYTES CAN INCREASE THE INVASIVE POTENTIAL OF PERITONEAL METASTASIS FORMATION IN GASTRIC CANCER

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Introduction: According to the progression of gastric cancer (GC), released cancer cells from stomach surface attach to peritoneal mesothelial cells. As the result, peritoneal metastatic nodules occur in omentum and mesentery which contain rich adipocytes. However, the interaction between gastric cancer cells and adipocytes in the process of peritoneal metastasis has not sufficiently elucidated. In this study, we clarified adipocytes enhanced gastric cancer progression by transforming to juvenile phenotype.
Aims and Methods: Adiponectin which is one of adipokine in the omental fat tissue from resected specimen was measured using ELISA and western blot analysis. Matured adipocyte derived from progenitor adipocyte 3T3-L1 was co-cultured with gastric cancer cell MKN45 and OCUM-2MD3. After that, differential markers and cytokines from adipocyte were analyzed using quantitative RT-PCR and fluorescence immunostaining.
Results: Adiponectin in the fat tissue adjacent primary tumor revealed lower expression in the patients with high T stage than with low T stage. Adipocytes co-cultured with gastric cancer cell showed decreased expression of adiponectin. PPARg and C/EBPa as differential marker of adipocytes also decreased. On the other hand, expression of IL-6 and PAI-1 as SASP (Senescence-associated Secretory Phenotype) factors were increased in the co-cultured adipocytes. These cells also showed high expression of aSMA as EMT marker and FAP (fibroblast-activated protein) as CAFs (cancer-associated fibroblasts) marker.
Conclusion: These results suggest that transformed adipocytes in cancer microenvironment are induced expression of SASP factors, facilitating tumor growth and invasion. A part of adipocytes might differentiate to fibroblasts and involve formation of peritoneal metastasis in GC.
Disclosure: Nothing to disclose

P0557 THE EXPRESSION OF WNT-SIGNALING PATHWAY COMPONENTS IN DIFFUSE GASTRIC CANCER

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Introduction: The Wnt genes encode a large family of secreted molecules that play important roles in controlling tissue patterning, cell fate and cell proliferation within a broad range of embryonic contexts, including the gastrointestinal tract. Dishevelled (DVL) proteins are the central mediators in this pathway which enable its fine regulation. The interactions of Wnt ligands and Frisbee receptors are modulated by the secreted Wnt antagonists, which can be divided into 2 functional classes: the soluble frizzled related protein (SFRP) and the dickkopf (Dkk) class. Wnt antagonists interact directly and indirectly to affect Wnt signalling and influence a wide variety of biological processes, including developmental cell fate, differentiation and tumorigenesis.
Aims and Methods: The aim of the study was to investigate the expression of components of the Wnt - signaling pathway SFRP1, SFRP3, DVL-2 and DVL-3 in diffuse gastric cancer and healthy gastric tissue samples. Samples of 60 diffuse gastric carcinoma and adjacent nontumoral tissues were collected from the Department of Pathology, University Hospital Center Zagreb, Croatia. The tumor tissues were formaline fixed, parrafin embedded**.** All tumors were studied by pathologists and classified as diffuse gastric carcinoma according to the WHO criteria. Immunohistochemistry was performed in order to establish the levels of expression (absent, poor, moderate, intense) and cellular localization (membrane, nucleus, cytoplasm) of SFRP1, SFRP3, DVL-2 and DVL-3. Statistical analyses were performed using GraphPad Prism 5.01 (GraphPad Software, Inc., San Diego, CA, USA) and Principal component analysis (PCA) was done using Matlab Software PLS Toolbox. The stereological data were evaluated by descriptive statistics.
Results: SFRP1 expression was observed in the cytoplasm. In gastric tissue SFRP1 expression was found in glandular cells. We found statistically significant difference in the number of SFRP1 positive cells between normal and tumor tissues ($p < 0.05$). The amount of SFRP1 protein expression in normal tissues was higher compared to the one observed in tumor tissue. Subcellular localization of SFRP3 protein in gastric tissue was observed in cytoplasmic and membranous glandular. We found statistically significant difference in the number of SFRP3 positive cells between normal and tumor tissues ($p < 0.05$). The amount of SFRP3 protein expression in normal tissues was higher compared to the one observed in tumor tissue. DVL-2 and DVL-3 expression was observed in the cytoplasm of glandular cells. We found statistically significant difference in number of DVL-2 positive cells between normal and tumor tissues ($p < 0.05$). The amount of DVL-2 protein expression in tumor tissues was higher compared to the one observed in normal tissue. There was no statistically significant difference in the number of DVL-3 positive cells between normal and tumor tissues, although the amount of DVL-3 expression was higher in tumor tissue.
Conclusion: Despite some recent advances, gastric cancer remains the third leading cause of cancer-associated death worldwide. This indicates the absence of therapeutic options, stemming from the limited understanding of the molecular mechanisms involved in carcinogenesis. According to our data there is a statistically significant difference in the expression of SFRP 1, SFRP3 and DVL-2 between normal gastric tissues and tumor tissues, thus indicating that the loss of Wnt inhibitors and overexpression of Wnt cell fate regulators in tumor tissues may play an important role in gastric carcinogenesis.
Disclosure: Nothing to disclose

P0558 SAFETY AND EFFICACY OF THE NEW THULIUM / ERBIUM LASER SYSTEM IN PATIENTS WITH GASTROINTESTINAL BLEEDING FROM VASCULAR LESIONS

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Introduction: Recent pilot studies ascertained the safety and feasibility of the Thulium/Erbium laser system (TELS) as a new therapeutic tool for endoscopic haemostasis, ablation and resection.

Aims and Methods: We investigated for the first time ever, the safety and efficacy of endoscopic treatment with TELS in patients with gastrointestinal bleeding due to vascular lesions. This single-centre, open-label study prospectively enrolled consecutive patients referring for chronic gastrointestinal bleeding plus moderate/severe anaemia due to vascular lesions at IRCCS Policlinico San Donato Hospital between March 2016 and April 2018. Data were collected retrospectively.

The primary endpoints were the safety and the technical success of TELS treatments. As secondary outcomes, we investigated the biological success comparing the lowest haemoglobin values ± 1month prior to and after treatment, along with the need of packed red blood cells (PRB) transfusions ± 6month prior to and after treatment. Patients requiring blood transfusions for major comorbidities or surgery not related to gastrointestinal bleeding were ruled out from the assessment of biological parameters. The symptoms and the endoscopic score proposed by Dray X et al.[1] were used to evaluate the clinical and endoscopic success in patients with radiation proctitis (RP). A new scoring system was developed to assess the severity and the endoscopic success of TELS in gastric antral vascular ectasia (GAVE; 1–3 points according to a relative mucosal involvement $< 30\%$, 30–50% or $> 50\%$, respectively plus 3 or 5 points for traces of blood or active bleeding). For each procedure, image/video documentations and TELS technical parameters (i.e., lasing time, power output and total energy employed) were recorded. The Wilcoxon signed rank test was employed to challenge the quantitative results obtained.

Results: 11 patients underwent 16 endoscopic treatments with the TELS according to the diagnosis of GAVE (4 pts and 8 procedures), angioectasias (4 pts and 4 procedures) and RP (3 pts and 4 procedures). All procedures resulted in a complication-free technical success, thereby succeeding the primary study endpoints. According to preliminary data available in April 2018, haemoglobin values showed a significant rise (Δ_{lowest}Hb±1month = +1.6 g/dl, 95%CI = 0.45–3.20, p-value = 0.008) along with a decreased need of PRB transfusions (Δ_{PRB} ± 6months = −5 units, 95CI% = 1–9; p-value = 0.046). Consistently, the median values of GAVE endoscopic severity and of RP-related symptoms improved (from 5 to 2 and from 3 to 1 respectively), while preliminary data on RP endoscopic severity showed no remarkable changes in terms of severity of residual lesions.

The median Thulium/Erbium power output adopted during treatments were 6/2W, 5/1W and 5/2W with a median lasing time equal to 5'33'', 1'50'' and 3'45'' accounting for a median total energy of 1676/414J, 675/193J and 1024/417J for GAVE, angioectasias and RP, respectively.

Conclusion: This pilot study conducted in real-life setting suggests the TELS as a safe and effective tool for the endoscopic luminal treatment of patients with gastrointestinal bleeding caused by various types of superficial vascular lesions. Our data further confirmed the manoeuvrability of this new therapeutic tool, which mostly enables a complete eradication of large vascular lesions within few endoscopic procedures. Randomized-controlled studies involving established endoscopic techniques for haemostasis and ablation of gastrointestinal vascular lesions in larger cluster of patients are now warranted.

Disclosure: Nothing to disclose

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P0559 IS GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION FEASIBLE UNDER THE DIRECT ORAL ANTICOAGULANTS ADMINISTRATION?

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Introduction: Several studies have reported that anticoagulant therapy on gastric endoscopic submucosal dissection (ESD) increases the risk of postoperative bleeding [1, 2]. Previously, we have reported that the continuous warfarin administration does not increase the bleeding risk after gastric ESD compared to intravenous heparin bridge therapy (HBT) [3]. Currently, direct oral anticoagulants (DOAC) have been frequently used for the prevention and treatment of cardiovascular diseases instead of warfarin. Therefore, we investigated the effect of DOAC for postoperative bleeding after gastric ESD in comparison with those of warfarin and HBT.

Aims and Methods: A total of 89 gastric neoplasms in patients with anticoagulant therapy were treated with ESD at New Tokyo Hospital between September 2008 and December 2017. 37 out of 89 patients underwent gastric ESD with continuous warfarin, 27 done with intravenous HBT, and 20 done with DOAC. In patients with continuous warfarin, the dose of warfarin was controlled to maintain the PT-INR under 3.0. Patients with DOAC were treated with interrupted DOAC on the day of ESD. We assessed the clinical findings and outcomes of gastric ESD with anticoagulant therapy.

Results: The rates of complete en bloc resection were 100% in the continuous warfarin group and the HBT group, and 95% in the DOAC group ($p = 0.238$). The rates of postoperative bleeding were 10.8% in the continuous warfarin group, 18.5% in the HBT group, and 15.0% in the DOAC group ($p = 0.672$). All bleeding events were successfully managed with endoscopic hemostasis. One patient in the HBT group developed a delayed perforation resultantly required for an emergency surgery. The period of hospitalization was higher in the HBT group than in the other 2 groups (median [IQR], 13 [11–16] days in HBT, 6 [5–7] days in continuous warfarin, 6 [5–8] days in DOAC; $p < 0.001$).

Conclusion: The bleeding rate was not statistically different in the 3 groups. Gastric ESD under the DOAC administration was considered to be feasible and acceptable.

Disclosure: Nothing to disclose

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P0560 QUANTIFYING EXCESS CARDIO-RESPIRATORY EVENTS AND ADMISSIONS FOLLOWING DAY CASE DIAGNOSTIC GASTROSCOPY

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Introduction: Age-stratified estimates of adverse events after endoscopy will inform clinical decisions about appropriate investigation in those at high risk. We have quantified the absolute risks of cardiovascular and respiratory events in both primary and secondary care following day case diagnostic gastroscopy.

Aims and Methods: Patients undergoing day case diagnostic gastroscopy were identified in the English population from the linked hospital data in the Clinical Practice Research Datalink, and frequency matched with replacement on decade of birth to 4 times as many controls from this population, who were alive and registered at the time of the endoscopies. Follow up was censored on the earliest of; diagnosis of cancer, subsequent interventional procedure, emergency hospital admission, transfer out the study population, or death.

The first acute event of cardiac, cerebrovascular, or respiratory disease was identified in the 30 days after either the endoscopy or matched index date,

Abstract No: P0559: Baseline characteristics and therapeutic outcomes in patients with anticoagulant therDOAC, direct oral anticoagulants; HBT, heparin bridge therapyapy

	Continued warfarin (n = 37)	HBT (n = 27)	DOAC (n = 20)	P value
Age, mean ± SD, y	78.0 ± 5.5	73.0 ± 7.8	77.0 ± 7.5	0.015
Sex (male), n (%)	31 (83.8)	24 (88.9)	18 (90.0)	0.722
CHADS2 score	3 (2–3)	1 (1–2.5)	3 (2–3)	< 0.001
Specimen size, median (IQR), mm	31 (25–36)	33 (27–42)	34 (27–39)	0.318
Complete resection, n (%)	37 (100.0)	27 (100.0)	19 (95.0)	0.238
Postoperative bleeding, n (%)	4 (10.8)	5 (18.5)	3 (15.0)	0.672
Hospitalization, median (IQR), days	6 (5–7)	13 (11–16)	6 (5–8)	< 0.001

Abstract No: P0560

Age group	Primary Care Consultations		Emergency Hospital Admissions		Total	
	Absolute total risk (%) adjusted for censoring, competing risks, age, gender and co-morbidity	Absolute excess risk (%) compared to controls adjusted for censoring, competing risks, age, gender and co-morbidity	Absolute total risk (%) adjusted for censoring, competing risks, age, gender and co-morbidity	Absolute excess risk (%) compared to controls adjusted for censoring, competing risks, age, gender and co-morbidity	Absolute total risk (%) adjusted for censoring, competing risks, age, gender and co-morbidity	Absolute excess risk (%) compared to controls adjusted for censoring, competing risks, age, gender and co-morbidity
20–29 years	1.7	0.7	0.4	0.3	2.2	1.0
30–39 years	2.0	0.7	0.3	0.2	2.2	0.9
40–49 years	2.3	0.7	0.5	0.3	2.7	1.0
50–59 years	2.7	0.8	0.9	0.5	3.6	1.3
60–69 years	3.5	0.7	1.5	0.7	5.0	1.4
70–79 years	4.1	0.5	2.5	1.0	6.6	1.6
>79 years	4.1	0.6	4.4	1.9	8.5	2.5

from linked primary care consultations, underlying cause on death certificates, or the main diagnosis from emergency hospital admissions.
The age-stratified risks following day case diagnostic gastroscopies were estimated from a Cox regression model adjusted for age, gender and pre-existing co-morbidity.[1] Then excess risks were calculated, adjusted for censored and competing events, by using cumulative incidence functions derived from this Cox model.
Results: 307,925 day-case diagnostic gastroscopies were identified (among 248,217 people) with 13,411 cardiovascular or respiratory events within 30 days, of which 1,644 were emergency admissions and 351 were deaths. 1,584,660 matched index dates were identified (among 1,074,214 unique controls) with 51,681 cardiovascular or respiratory events within 30 days, of which 4,769 were emergency admissions and 1,105 were deaths.
After adjusting for age, gender, co-morbidity, and competing events, the absolute predicted risk for a cardiovascular or respiratory event within 30 days of a gastroscopy procedure was 2.2% for those under 30 years and 8.5% for those 80 years and older (table 1). This translated to an absolute excess risk over the control population of 1.0% (< 30 years) to 2.5% (≥80 years) respectively. Having a day-case diagnostic gastroscopy was correspondingly associated with an overall 2.1-fold relative increase in risk of cardiovascular or respiratory admissions (95% confidence interval 2.0–2.2, adjusted for age and gender), which was reduced to 1.9-fold (1.8–2.0) after adjusting for pre-existing co-morbidity.
Conclusion: This study showed an important excess risk of acute cardiovascular and respiratory events in primary and secondary care following day-case diagnostic gastroscopy compared to the general population. The excess risk of such an event was 1 in 100 procedures for those under 30 years of age and 1 in 40 procedures for those aged 80 or over. Almost 1 in 50 of those over 80 experienced an additional event which required hospital admission. We believe this information will be of value to clinicians deciding on whether to request routine tests, and patients in the consent process.
[Cardio-respiratory events in primary care consultations or emergency hospital admissions, and excess compared to age matched population controls]

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P0561 THE ITALIAN SOCIETY FOR DIGESTIVE ENDOSCOPY (SIED) ACCREDITATION PROGRAM 2014-2018: AN UPDATE

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Introduction: Accreditation is one method of assuring quality and requires the setting of standards and the creation of a reliable process for assessing them. Accreditation is a well-established form of external peer review that can help in reducing medical errors, and in one study the improvement was found to be around a 50% reduction in medical administration errors (1). In 2014 the Italian Society For Digestive Endoscopy (SIED) launched a national program for accreditation of all endoscopy centres.
Aims and Methods: An 8-member group, endorsed by SIED, prepared standards for accreditation, developed from national and international guidelines and approved by SIED Central Committee. These standards were published on the SIED internet site, open to all SIED members. An independent third party certification body (Kiwacermet-Bologna-Italy) was chosen to provide assessment and certification. The working group prepared 295 quality indicators centered on patient experience, efficiency and operations, precedure-related endoscopy unit issues, safety and infection control, reprocessing. Reprocessing quality indicators were prepared in collaboration with the Italian Endoscopist Nurses Society (ANOTE). A group composed of 2 endoscopists, 1 nurse and a Kiwacermet representative tested the quality indicators during a one-day site-visit to endoscopy centres requiring accreditation. Expenses were covered by SIED and enrollment of endoscopy centres is free of charge.
Results: So far we have evaluated 23 centres scattered all over Italy. During the site-visits we have pointed out 162 critical issues, not in accordance with the SIED accreditation program. In all centres visited we found critical issues about targets and periodic evaluation of results. In the procedure-related domain, we have found 68 critical issues for gastroscopy, 75 for colonoscopy, 20 for percutaneous gastrostomy and 13 for retrograde colangio-pancreatography. In the reprocessing domain 46 critical issues have been discovered. In the post-polypectomy surveillance domain we have noticed 8 negative remarks. All these critical issues have been corrected by the 18 accreditated centres. To date 3 centres have not been granted by the SIED accreditation award and 2 centres are complying with the SIED requests. Eleven centres are waiting for a 2018 site-visit.
Conclusion: The SIED free accreditation program has the potential to identify and correct flaws responsible for suboptimal performance. Reprocessing and polyps surveillance are 2 of the greatest weaknesses of the Italian endoscopy services.
Disclosure: The Italian Accreditation program is entirely funded by an unrestricted grant of SIED-Italian Society for Digestive Endoscopy-Rome. M Capelli is part of the medical advisory board for Kiwacermet-Bologna-Italy. All other authors disclosed no financial relationships relevant to this work.

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P0562 THE ROLE OF THE CLINIC AND OF THE ORGANIZATIONAL COMPLEXITY ON THE MORTALITY FROM ACUTE UPPER GASTROINTESTINAL BLEEDING

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Introduction: The role of the Gastroenterologist and of the Department of Gastroenterology and Gastrointestinal Endoscopy is crucial for the management of patients with upper gastrointestinal bleeding, variceal, non-variceal and non-ulcer. With the Ministry of Health decree n.70 of April 2nd 2015, the Italian health system features hierarchical levels of healthcare complexity of hospitals. The emergency network is made up with hospitals with different healthcare complexity according to the model hub and spoke. D.E.A. hospitals of second level work as Hub and are institutionally referable to Hospital Agencies, University Hospitals and certain Healthcare Centers of Scientific Research (IRCCS).
Aims and Methods: Evaluate the impact of 1) patients' clinical conditions and 2) organizational and health care courses on mortality from upper gastrointestinal bleeding in hospitalized patients.
The analysis of the healthcare setting of upper gastrointestinal bleeding in Campania has been carried out processing the data from the hospital discharge reports of 2015. The level of healthcare complexity of hospital facilities has been evaluated taking into account two profiles: Regional Hospital Agencies (AO) and Local Healthcare Companies (ASL). The University Hospitals of Naples, the Institute of Cancer Research and the Pediatric Hospital have been excluded as not involved in the management of acute gastrointestinal bleeding. The mortality rate of 30 has been considered as the measure of clinical efficiency, the length of hospital stay has been considered as the measure of efficiency.
Results: 8707 hospital discharge reports were initially selected, which met the recruitment criteria; at the end of the exclusion process the data of 3368 patients were included in the analysis; considering that the average resident population in 2015 was 5,856,189, the rough rate of upper gastrointestinal bleeding in 2015 was 575 per 1,000,000 inhabitants. The patients discharged from local healthcare agencies were 2,192 (65.1%) with 1,980 males (58.8%), the average age was 65.4±DS 18.7. The non-variceal bleedings were 2,980 (88.5%).

The average age was slightly older in the ASL (65.9 ± DS vs AO 64.4 ± DS 19.6). The number of patients with variceal bleeding discharged from AO was higher: 199/1176 (16.9%) vs 198/2192 (8.6%) p < 0.000. The overall mortality rate in the two healthcare settings was similar: 8.0% in AO vs 6.7% in ASL Pr = 0.184. The overall mortality rate for patients discharged from Gastroenterology Units (regardless AO or ASL) was 4.7% vs 7.9% in other departments p < Pr = 0.002. Considering together the healthcare setting ASL or AO and the patients discharged from Gastroenterology Units (Table) we can see that those discharged from gastroenterology units show a lower mortality rate. This datum is less relevant in non-variceal bleedings but much more relevant in variceal ones. In the multi-varied analysis the mortality risk factors were: age over 79 OR 2.80 (95% CI 2.12 to 3.69) variceal bleeding OR 2.84 (95% CI 1.98 to 4.06), while protection factors were discharge from a Gastroenterology Unit OR 4.77 (95% CI 3.2 to 7.0) and hospitalization in AO and in Gastroenterology Unit OR 9.6 (95% CI 9.3 to 9.9).
Conclusion: AO hospital facilities present the same mortality rate as ASL ones. The hospital stay in Gastroenterology Units reduce all mortality cases and was similar in both AO and ASL. Mortality in non-gastroenterology unit both in AO and ASL is similar.

	AO No Gastro	AO Yes Gastro	ASL No Gastro	ASL Yes Gastro	p-value
Mortality Overall	11.2%	4.5%	6.9%	5.3%	<0.001
Mortality Non Variceal	9.4%	3.8%	6.5%	4.2%	<0.002

[Mortality rate by AO or ASL with patients discharged Yes or No from Gastroenterology Unit]
Disclosure: Nothing to disclose

P0563 SIMPLE "PURE" ENDOSCOPIC TECHNIQUE OF PEG-J-PLACEMENT IN ADVANCED PARKINSON'S DISEASE- A RETROSPECTIVE SINGLE-CENTER STUDY

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Introduction: Levodopa is absorbed mainly in the upper intestine and is metabolized rapidly, consequently requiring frequent applications. Continuous levodopa/carbidopa infusion straight into the proximal jejunum via percutaneous endoscopic gastrostomy with jejunal extension tube (PEG-J) connected to a portable infusion pump has emerged as a promising tool in the treatment of Parkinson's disease (PD). [1–2]
Aims and Methods: We aim to assess effectiveness and safety of PEG-J placement under direct endoscopic control and with no additional imaging tools in patients with Parkinson's disease.
Study group includes 76 patients with advanced PD who underwent PEG-J placement in the period June 2014 - February 2018.
In all patients, a nasojejunal tube was inserted initially to assess levodopa-carbidopa efficacy and dosage. After a short period of time (4–7 days) a PEG-J (Freka® PEG CH15, and Freka® CH9 Intestinal Tube for CH15 PEG) was placed under i.v. propofol infusion. Peri interventional drug prophylaxis included antibiotic, proton pump inhibitor and analgetics.
All patients underwent placement of both PEG tube (via the pull method) and J-tube in a single procedure. J-tube placement technique used was grasping the tube tip with forceps and advancing it along with the endoscope into the distal duodenum. The scope was then slowly withdrawn into the stomach while the forceps is advanced blindly to hold the tip of the J-tube in place. Finally J-tube was advanced approximately 80–90 cm in the jejunum. No fluoroscopy, nor any other imaging tool was used to determine accurate J-tube position. Patient's clinical response to levodopa/carbidopa infusion indicated procedure effectiveness, instead.
Results: PEG-J was successfully placed in all patients, confirming high technical effectiveness of the PEG-J endoscopic guidance placement method.[3]
No single serious adverse event has been reported in 48-hours postrocedural clinical observation period. Additionally, there was no need of J-tube reposition in any of the patients. We registered 1.52% late complications (within one month after procedure): a case of mesenterial thrombosis and another one of *C. difficile* colitis, both requiring hospital admission. Both patients were successfully managed.
Conclusion: Endoscopic guided PEG-J placement with 'blind' jeunal extension insertion is a highly effective, fast and simple procedure with limited adverse events. Clinical response to levodopa/carbidopa is suitable and sufficient indicator for accurate jejunal position of the J-extension. Further, PEG-J placement followed by continuous levodopa/carbidopa infusion was associated with improvement in quality of life and clinical symptoms in PD patients with advanced disease.
Disclosure: Nothing to disclose

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P0564 GASTROINTESTINAL SYMPTOMS IMPACTING ON QUALITY OF LIFE: A COMPARATIVE COHORT STUDY IN PATIENTS WITH ORGANIC AND FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS) IN THE TERTIARY HOSPITAL OUTPATIENT SETTING

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Introduction: For many gastrointestinal (GI) diseases the severity of the impairment of Quality of life (QoL) is a key driver for health care utilisation and health care costs. However, very little is known about the of the impact of specific GI symptoms on QoL in different patient cohorts.
Aims and Methods: We aimed to determine and compare the proportion of patients with severe or very severe impairment of QoL due to specific GI symptoms in patients with selected highly prevalent GI diseases in the outpatient setting of a tertiary hospital. From a cohort of 10,000 consecutive occasions of service (OOS) of patients presenting during a 12 month period at a tertiary teaching hospital in Brisbane we identified patients with Functional gastrointestinal diseases (FGIDs), inflammatory bowel diseases (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) and celiac disease (CeD). In addition, we included patients with cured hepatitis C infection as 'controls'. The records of patients with one of the above primary diagnoses documented in the electronic medical record were reviewed and assessed. At each OOS the patients had completed the validated Structured Assessment of Gastrointestinal Symptoms (SAGIS) to capture the severity of symptoms. SAGIS assesses the severity of symptoms on a 5-point scale with the 2 most severe defined as 'severe:...influence daily activity...' and 'very severe symptoms: . . .markedly influence daily activities and/or require rest...'. Prevalence rates and the 95% confidence intervals for postprandial pain, epigastric pain, constipation, diarrhea and, pain and discomfort during defecation and bloating were determined.
Results: Out of the total of 10,000 OOS, we identified 1,157 patients with CD, 936 with UC, 999 with FGIDs, 173 with cured HCV, 150 with GI cancers, 136 with CeD and 173 with cured HCV. The proportion of OOS when patients reported severe or very severe symptoms was highest in FGID patients. Even for symptoms that were frequently observed in patients with IBD (e.g. diarrhea, pain or urgency during defecation), the proportion of patients with severe or very severe symptoms was substantially higher in FGID patients.
Conclusion: The disease burden as measured by the proportion of patients reporting severe or very severe impairment of QoL by specific GI symptoms is highest in patients with FGIDs. Overall the symptom 'bloating' was reported by 40% of FGID patients as severely impacting QoL. The burden by the symptom diarrhea

Abstract No: P0564: Baseline characteristics and therapeutic outcomes in patients with anticoagulant therDOAC, direct oral anticoagulants; HBT, heparin bridge therapyapy

	Cured HCV (n = 173) n (95% CI)	Cancer (n = 150) n (95% CI)	Celiac disease (n = 136) n (95% CI)	CD (n = 1157) n (95% CI)	UC (n = 936) n (95% CI)	FGIDs (n = 999) n (95% CI)
Post prandial pain	4.0 (1.6–8.2)	14.0 (5.5–15.2)	8.8 (4.6–14.9)	9.5 (3.6–19.5)	4.8 (3.5–6.4)	28.7 (25.9–31.6)
Epigastric pain	3.5 (1.3–7.4)	10 (5.7–16.0)	6.6 (3.1–12.2)	8.4 (6.9–10.1)	4.3 (3.1–5.8)	25.2 (22.6–28.0)
Diarrhea	4.0 (1.6–8.2)	8.7 (4.7–14.4)	5.1 (2.1–1.3)	16.2 (14.1–18.4)	11.1 (9.2–13.3)	22.4 (19.9–25.1)
Constipation	4.0 (1.6–8.2)	8.7 (4.7–14.4)	10.3 (5.7–16.7)	4.8 (3.7–6.2)	4.3 (3.1–5.8)	20.3 (17.9–23.3)
Pain/ discomfort at defaecation	4.0 (1.6–8.2)	10 (5.7–16.0)	11.8 (6.9–18.4)	12.2 (10.4–14.2)	11.5 (9.6–13.8)	28.2 (25.5–31.1)
Bloating	3.5 (1.3–7.4)	11.3 (6.7–17.5)	16.2 (10.4–23.5)	13.1 (11.2–15.1)	9.1 (7.3–11.1)	40.4 (37.4–43.6)

was significantly more severe in FGID patients as compared to patients with IBD. This high disease burden in patients with FGID likely reflects the lack of effective therapies in FGIDs.
[Prevalence of severe and very severe symptoms in various patient cohorts.]
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00-17:00
H. Pylori I - Hall X1____

P0565 INCREASE OF BMI AND DECREASE OF SERUM LEVEL OF LIPID WERE OBSERVED AFTER *H. PYLORI* ERADICATION WITHOUT CORRESPONDING CHANGE OF DAILY INTAKE OF NUTRIENT IN JAPANESE FEMALES

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Introduction: In western populations, increase of body mass index (BMI) has been shown after successful eradication of *H. pylori* infection. However, influence of *H. pylori* eradication on nutritional intake has not been well studied. Since Japanese health insurance system approved eradication therapy for all infected patients, there has been significant increase in the number of subjects who receive eradication of *H. pylori* without dyspeptic symptoms. The aim of this study was to investigate the influence of *H. pylori* eradication on nutritional metabolism considering daily nutritional intake in a Japanese population.
Aims and Methods: Healthy adults who received health survey both in 2012 and 2014 were entered into the study. We measured *H. pylori* stool antigen (Testmate EIS) and titer of serum antibody to *H. pylori* (E-plate). Subjects were considered as *H. pylori*-infected when positive stool antigen test and/or serum antibody titer >10 U/mL were observed. Non-infected subjects were defined as negative stool antigen test, serum antibody titer of <3 U/mL and without past history of eradication therapy. Patients who received successful eradication after the survey in 2012 and diagnosed as non-infected in 2014 were considered as eradicated group. Patients were extracted adjusting sex and age from subjects who were diagnosed as infected in both 2012 and 2014, as control (persistent infection) group. Subjects who were taking PPI and/or had previous history of gastric surgery were excluded. Daily intake of lipid and carbohydrate during one month prior to the survey was calculated using a brief-type comprehensive self-administered diet history questionnaire. Change of daily intake of nutrients, BMI, serum level of lipid and HbA1c were compared for between eradicated group and control group.
Results: Daily intake of lipid and carbohydrate was not different between 2012 and 2014 in both male and female in 33 eradicated patients and 66 control subjects. In female eradicated patients, BMI was significantly increased from 22.1±3.3 to 22.4±3.3 ($p=0.022$) while serum level of HDL-C and LDL-C decreased from 75.9±13.7 to 71.0±15.0 mg/dL and 125.8±26.2 to 119.3±27.9 mg/dL, respectively ($p=0.003$ and $p=0.021$). In eradicated male and control subjects, no significant change were observed in BMI and serum levels of lipid. HbA1c was not changed in both male and female in both groups.
Conclusion: In female subjects without dyspeptic symptoms, increase of BMI and decrease of serum level of HDL-C and LDL-C were observed after eradication of *H. pylori* without corresponding changes of daily intake of lipid and carbohydrate.
Disclosure: Nothing to disclose

P0566 RACK1 IS A NEW REGULATOR IN THE NF-κB SIGNALING PATHWAY INDUCED BY *HELICOBACTER PYLORI* INFECTION

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Introduction: The receptor of activated protein kinase C 1 (RACK1, GNB2L1) is a 36-kDa cytosolic protein involved in multiple physiology and pathology processes. Recent reports indicated RACK1 was an anti-oncogene in gastric cancer. Herein, we aimed to investigate investigated the relationship between *Helicobacter pylori* (*H. pylori*) infection, proinflammatory NF-κB activation and RACK1.
Aims and Methods: The study used *in vivo* and *in vitro* experiments. TCGA data base analysis, tissue microarrays, luciferase reporter, quantitative real-time PCR, Western Blot, immunofluorescence, chromatin immunoprecipitation sequence, *H. pylori* infection, and immunohistochemical assays were used.
Results: TCGA analysis of gastric cancer indicated RACK1 protein level was lower in the *H. pylori* positive gastric cancer group in comparison with *H. pylori* negative gastric cancer group**.** Our results indicated that *H. pylori* infection increased RACK1 mRNA expression and decreased RACK1 protein levels in gastric cancer cells, gastric mucosa of mice and gastric cancer tissues. *H. pylori* infection increased the activity of NF-κB reporter and p-NF-κB (Ser 536) protein level in vitro and in vivo. Moreover, the overexpression of RACK1 inhibited the activation of NF-κB signaling pathway induced by *H. pylori* infection, as determined by Western Blot, PCR, luciferase reporter assays. Immunohistochemistry analysis demonstrated a significant positive correlation between IκBα and RACK1 expression levels ($r^2=0.762$, $p<0.01$) and a significant negative correlation between NF-κB and RACK1 expression levels ($r^2=0.762$, $p<0.05$) in gastric mucosa of mice.
Conclusion: RACK1 is a new regulator in NF-κB signaling pathway induced by *H. pylori* infection. The decreased expression of RACK1 following *H. pylori* infection and activation of NF-κB provides a link between infection, inflammation and gastric tumourigenesis.
Disclosure: Nothing to disclose

P0567 ENTEROENDOCRIN CELL COMPARTMENT SIZE DECREASES DURING H. PYLORI INFECTION IN PATIENTS WITH INTESTINAL METAPLASIA BUT IS RESTORED AFTER ERADICATION

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Introduction: Gastric cancer, the fifth leading cause of cancer, develops following Correa's cascade: well defined steps involving several premalignant lesions, the most common of which is intestinal metaplasia (IM). The mechanism by which these premalignant lesions develop and progression is driven is still largely unknown. The largest risk factor for development of both IM and gastric cancer is infection with the pathogen Helicobacter Pylori (HP). One of the theories is that HP-associated inflammation causes a disbalance of gastric hormone levels by causing destruction of the somastatin-producing D-cell compartment. This in turn would cause a relative increase of gastrin which has several proliferative and pro-oncogenic effects. In this study we determine the effect of both HP and eradication on the enteroendocrine cell compartments of the antral stomach in patients with intestinal metaplasia.
Aims and Methods: Antral gastric biopsies were taken systematically in a surveillance cohort of patients with IM or gastric atrophy (PROREGAL Cohort). HP positivity was determined by serology and histology. Patients were scored as having active infection when histology was positive, and negative when both histology and serology were negative. Presence or absence of IM was scored by trained pathologist. We included 24 HP-naïve patients and 23 biopsies from patients infected with HP. Of the HP infected patients, also biopsies were obtained 1 year after successful eradication of HP. Immunohistochemical staining of G-cells and D- cells was performed using anti-gastrin and anti-somatostatin antibodies respectively. The number of positive cells per high power field were counted and intensity of staining was scored. Means of 4 biopsies were represented using the Allred score. Significance was determined using students T-test.
Results: As expected, antral biopsies from IM patients show patches of IM as well as normal crypts. In IM both the G-cell ($p<0.0001$) and D-cell ($p=0.0002$) compartments are reduced as compared to non-IM crypts. In patients infected with HP, total D-cell numbers were significantly reduced as compared to patients without HP ($p=0.0001$), in line with findings described in literature. Unexpectedly however, we also observed a significant reduction of G-cells in in patients with active HP infection ($p=0.0008$). Interestingly, 1 year after HP eradication, this reduction in enteroendocrine cell compartment size was no longer apparent and both D-cell and G-cell levels were normalized to the levels seen in patients that have never been infected. Enteroendocrine cell compartment size is not associated with either progression or regression of gastric premalignant lesions in this cohort.
Conclusion: These results confirm previous studies showing that HP infection causes a reduction in the antral D-cell compartment in IM crypts. However, we further demonstrate that this reduction is not restricted to D-cells, but also affects antral G-cells. After eradication of HP, enteroendocrine cell compartments return to sizes comparable to non-infected patients even though the gastric premalignant lesions persist. These results suggest that antral G-cell compartment size is likely of minor importance in early gastric carcinogenesis.
Disclosure: Nothing to disclose

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P0568 PEPSINOGEN I/II RATIO IS AN EXCELLENT BIOMARKER TO ESTIMATE THE GRADE OF GASTRIC ATROPHY IN BOTH HELICOBACTER PYLORI-INFECTED AND NONINFECTED SUBJECTS: OPTIMAL CUTOFF POINT TO IDENTIFY SEVERE ATROPHIC GASTRITIS

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Introduction: Atrophic gastritis is one of the most important clinical manifestations of *Helicobacter pylori* (HP) infection. To know grade of atrophic gastritis is valuable for estimating not only gastric cancer risk but also gastric acid-related diseases. Pepsinogen I is secreted by chief and mucous neck cells in the fundic glands, whereas pepsinogen II is also secreted by cells in the pyloric and Brunner's glands. When atrophic changes develop to the corpus, the level of pepsinogen I decreases, whereas the level of pepsinogen II remains high or stable. Therefore, pepsinogen I/II ratio decreases in a stepwise manner. We

aimed to evaluate the adequacy of measuring pepsinogen I/II ratio as a non-invasive maker of grade of atrophic gastritis.
Aims and Methods: A total of 959 consecutive subjects who underwent esophagogastroduodenoscopy and measurement of serum pepsinogen level at the same day were enrolled. To avoid the influence to pepsinogen levels, the following subjects were excluded; (1) those who had received successful HP eradication therapy in the past, (2) those who had undergone gastrectomy, (3) those who were taking proton pump inhibitors for various reasons, and (4) those having renal failure (Creatinine > 3.0 mg/dl). HP infection status was determined by the titer of serum HP IgG (E plate). Endoscopic grades of atrophic gastritis were classified into three groups: none to mild (C-0 and C-1), moderate (C-2 and C-3), and severe (O-1, O-2, and O-3) using the Kimura-Takemoto Classification. The correlation of pepsinogen I/II ratio with endoscopic grade of atrophic gastritis was analyzed by Kruskal-Wallis test. Receiver operating characteristic (ROC) curves were constructed to evaluate the ability of pepsinogen I/II ratio for discriminating endoscopic severe atrophic gastritis (≥ O-1 atrophy) and to extract the corresponding cutoff value for severe atrophic gastritis (≥ O-1 atrophy).
Results: The 959 enrolled subjects comprised 466 males, with a mean age of 52. Of the enrolled subjects, 236 had HP IgG positive test results, whereas the remaining 723 had HP IgG negative test results. Significant correlation between pepsinogen I/II ratio and endoscopic grade of atrophic gastritis was found in both HP infected- and non-infected-subjects ($p < 0.001$ in both comparisons). ROC curves were used to assess the diagnostic accuracy of pepsinogen I/II ratio for discriminating endoscopic severe atrophic gastritis. The areas under the curve (95% confidence intervals) were 0.93 (0.91–0.96) in the entire cohort, 0.81 (0.75–0.86) in the HP infected subjects, and 0.88 (0.80–0.95) in the HP noninfected subjects, respectively. In the HP infected subjects, a pepsinogen I/II ratio of 2.3 was indicated to be best cutoff value for predicting severe atrophic gastritis, with a corresponding sensitivity of 81.6% and specificity of 67.6%. Meanwhile, in the HP noninfected subjects, a pepsinogen I/II ratio of 4.9 was indicated to be best cutoff value for predicting severe atrophic gastritis, with a corresponding sensitivity of 73.1% and specificity of 87.5%.
Conclusion: We confirmed the presence of a significant correlation between pepsinogen I/II ratio and endoscopic grade of atrophic gastritis. In ROC analysis, pepsinogen I/II ratio is indicated to be an excellent biomarker to estimate the grade of atrophic gastritis. Clinical use of pepsinogen I/II ratio as a surrogate marker of gastric atrophy may be valuable for not only estimating the grade of atrophic gastritis but also assessing longitudinal changes in gastric atrophy of each patient.
Disclosure: Nothing to disclose

P0569 APPLICATION OF CONVOLUTIONAL NEURAL NETWORKS IN THE DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION STATUS BASED ON ENDOSCOPIC IMAGES

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Introduction: We recently reported the role of artificial intelligence in the diagnosis of *Helicobacter pylori (H. pylori)* gastritis based on endoscopic images, and showed that the ability of the convolutional neural network (CNN) was comparable to experienced endoscopists, and diagnostic time was considerably shorter (*EBioMedicine* 2017). However that study includes only *H. pylori*-positive and negative cases, and excluded eradicated cases.
Aims and Methods: In this study, we constructed CNN, and evaluated its ability to diagnose *H. pylori* infection status, that is *H. pylori* positive, negative, or eradicated. We performed standard esophagogastroduodenoscopy (EGD) and captured esophagogastroduodenal mucosal images. Clinical diagnosis of *H. pylori* as reference standard was performed by blood or urine anti-*H. pylori* IgG levels, fecal antigen test, rapid urease test, or urease breath test. Patients who tested positive on any of these assays were classified as *H. pylori*-positive. Among patients who tested negative for the assays, those who had never received eradication therapy in the past were classified as *H. pylori*-negative. Those who had succeeded in eradication therapy were classified as *H. pylori*-eradicated. A deep CNN was pre-trained and fine-tuned on a dataset of 98564 images from 5236 patients (17432 images of 742 *H. pylori*-positive patients, 64934 images of 3649 *H. pylori*-negative patients, and 16198 images of 845 *H. pylori*-eradicated patients) obtained from December 2015 to April 2017. The CNN was trained using these images classified according to 8 anatomical locations of the stomach (cardia, upper body, middle body, lesser curvature, angle, lower body, antrum, and pylorus). A separate test data set (23699 images from 847 patients (70 *H. pylori*-positive, 493 *H. pylori*-negative, and 284 *H. pylori*-eradicated) obtained from May to June 2017) was evaluated by the CNN.
Results: The trained CNN output a continuous number between 0 and 1 as the probability index for *H. pylori* infection status per image (Pp for *H. pylori*-positive, Pn for negative, and Pe for eradicated. (Pp + Pn + Pe = 1). Most probable (largest number of Pp, Pn, and Pe) of the 3 infectious status was selected as the 'diagnosis of the CNN'. Among 23699 images, the CNN diagnosed as positive for 418, negative for 23034, and eradicated for 247 images, respectively. Among the 655 cases the CNN diagnosed negative for all the images, 466 cases (71%) were negative for *H. pylori*. While among the remaining 192 cases the CNN diagnosed as positive or eradicated for at least 1 image, 165 cases (86%) were positive or eradicated for *H. pylori*. As for the 119 cases the CNN diagnosed as eradicated for at least 1 image, 83 (70%) were *H. pylori*-eradicated. Time needed to diagnose 23699 images was 261 seconds.
Conclusion: *H. pylori* infection could be diagnosed based on endoscopic images using CNN in a considerably short time. It was suggested that the CNN can be introduced to aid endoscopists in diagnosing *H. pylori* infectious status.
Disclosure: Nothing to disclose

P0570 THD FECAL TEST FOR NON-INVASIVE *HELICOBACTER PYLORI* DETECTION: A DIAGNOSTIC ACCURACY STUDY

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Introduction: We aimed to assess THD fecal test diagnostic accuracy for detecting *Helicobacter pylori*, using ^{13}C-urea breath test as the reference standard. We additionally explored bacterial antibiotic resistance.
Aims and Methods: We conducted a prospective two-center diagnostic test accuracy study. We enrolled consecutive people ≥18 years without previous diagnosis of infection, referred for dyspepsia between February and October 2017. At enrolment, all participants underwent ^{13}C-urea breath test. Participants aged over 50 years were scheduled to undergo upper endoscopy with histology. Participants collected stool samples 1–3 days after enrolment for THD fecal testing. The detection of bacterial 23S rRNA subunit gene indicated infection. We also used the index diagnostic test to examine mutations conferring resistance to clarithromycin and levofloxacin. Independent investigators analyzed index test and reference test standard results blinded to the other test findings. We estimated sensitivity, specificity, positive (PPV) and negative (NPV) predictive value, diagnostic accuracy, positive and negative likelihood ratio (LR), together with 95% confidence intervals (CI).
Results: We enrolled 294 consecutive participants (age: median 37.0 years, IQR 29.0–46.0 years; men: 39.8%). 95 (32.3%) participants had a positive^{13}C-urea breath test. 23 (7.8%) participants older than 50 years performed upper endoscopy with histology. There was full concordance between ^{13}C-urea breath test and histology in detecting *Helicobacter pylori* infection in these participants. THD fecal test sensitivity was 90.2% (CI:84.2%–96.3%), specificity 98.5% (CI:96.8%–100%), PPV 96.5% (CI:92.6%–100%), NPV 95.6% (CI:92.8%–98.4%), accuracy 95.9% (CI:93.6%–98.2%), positive LR 59.5 (CI:19.3–183.4), negative LR 0.10 (CI:0.05–0.18). Out of 83 infected participants identified with the THD fecal test, 34 (41.0%) had bacterial genotypic changes consistent with antibiotic-resistant *Helicobacter pylori* infection. Of these, 27 (32.5%) had bacterial strains resistant to clarithromycin, 3 (3.6%) to levofloxacin, and 4 (4.8%) to both antibiotics.
Conclusion: The THD fecal test has high performance fornon-invasive diagnosis of *Helicobacter pylori* infection while additionally enabling assessment of bacterial antibiotic resistances.
Disclosure: We thank THD Spa, Correggio (Italy), for providing free of charge THD fecal test for all participants included in the study.

P0571 ENDOSCOPIC DIAGNOSIS OF *HELICOBACTER PYLORI* BASED ON THE ARRANGEMENT OF COLLECTING VENULES IN A EUROPEAN POPULATION

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Introduction: *Helicobacter pylori* (Hp) is the major cause of gastritis and gastritis-associated diseases. The development of high definition endoscopy in recent years has allowed a better characterization of the gastric mucosa and the identification of endoscopic findings that correlate with the diagnosis of Hp. One of the features that has shown better results is the detection of a regular arrangement of collecting venules (RAC) of the mucosa in the lower part of the gastric body. The presence of RAC has a sensitivity and negative predictive value (NPV) higher than 90% in Hp uninfected patients, but most of the studies have been conducted in Asian population and we do not know their reproducibility in our population.

Aims and Methods: The aim of the study was to evaluate the value of the arrangement of collecting venules as a diagnostic method of Hp infection in our population.
Secondary objective was to assess whether age, sex, concomitant antiplatelet therapy, anticoagulants or non-steroidal anti-inflammatory drugs, or history of Hp eradication modify the prevalence of the infection. Retrospective analysis of a prospectively collected database of patients who underwent upper gastrointestinal endoscopy from February 2017 to March 2018. The inclusion criteria were: age over 18 years, absence of treatment by proton pump inhibitors in the last 10 days and absence of a history of gastrectomy, gastric lymphoma or portal hypertension. We excluded those patients with presence of blood or food in gastric lumen that precluded an adequate exploration of the mucosa.
Explorations were performed with high-definition endoscopes by three expert endoscopists and under sedation by anesthesiologist. The RAC pattern was defined as the presence of starfish-like minute points regularly distributed throughout the lesser curvature of the gastric body. We considered significative endoscopic findings the presence of erosive gastroduodenal lesions, atrophic gastritis, intestinal metaplasia and gastric polyps. Pictures were taken during the procedure. The gold standard tests for Hp infection were the anatomopathological study and/or rapid urease test.
Results: 111 patients were included with an Hp infection rate of 29.73%. 37 of 111 patients (33.3%) presented a RAC pattern. No differences were observed in RAC prevalence regarding to sex, concomitant treatment or previous history of Hp eradication. In contrast, the mean age of patients with RAC pattern was lower (45 vs 53 years, $p = 0.01$) and had less significative endoscopic findings (43% vs 65%, $p = 0.03$).
None of the patients with Hp presented RAC pattern. Contrarily, the RAC pattern was observed in all uninfected patients. Performance characteristics endoscopic diagnosis of Hp based on the arrangement of collecting venules pattern were: sensitivity 100% (CI 87%–99,7%), specificity 47.4% (CI 36.1%–59%), negative predictive value 100% (CI 88.3%–99.7%) and positive predictive value 44.6% (CI 33.2%–56.6%).
Conclusion: Careful observation of the gastric mucosal pattern in lower curvature with high-definition endoscopy can accurately predict Hp uninfected cases when RAC is present, avoiding the obtention of biopsies.
Disclosure: Nothing to disclose

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P0572 COMPARISON OF STOOL ANTIGEN TEST MONOLAB® AND UREA BREATH TEST FOR DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION

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Introduction: According to current clinical guidelines, the stool antigen test (SAT) may be an alternative method to the urea breath test (UBT) to diagnose *Helicobacter pylori (H. pylori)* infection, provided a monoclonal laboratory test (ELISA) is used. Since 2015 the Monolab Test, which is not an ELISA test but an immunochromatographic monoclonal test, has been incorporated to our regional health system.
Aims and Methods: The aim of the present study was to compare the diagnostic accuracy of SAT Monolab Test and UBT, considering UBT the gold standard. A prospective multicentre study (Hospital Reina Sofia in Tudela -HRS- and Complejo Hospitalario de Navarra in Pamplona -CHN-) was performed in consecutive patients since November 2016 (HRS) and June 2017 (CHN) until October 2017. All patients who were submitted to gastroenterology outpatient clinic to perform a UBT according to standard clinical practice were enrolled and SAT Monolab was simultaneously determine. Sensitivity, specificity and negative and positive predictive values (NPV and PPV respectively) adjusted to prevalence were determined, and SAT accuracy was compared with UBT.
Results: 450 patients, 183 CHN and 267 HRS were included, with the features detailed in table 1. Both tests were performed for initial diagnosis of infection in 230 cases and to check the efficacy of eradication treatment in 220. The prevalence of *H. pylori* infection was 35% before treatment and 12% after eradication therapy. Concordance between AST Monolog and UBT was 78% (sensitivity 82%, specificity 77%), with a kappa index of 0.51 (moderate concordance). Before treatment, NPV was 66% and PPV 89%, whereas after eradication therapy PPV was of 34% and NPV 97%.
Conclusion: Compared with the diagnostic reference test, UBT, the AgH Monolab test differs in the diagnosis of *H. pylori* infection in up to 22% of patients. There is a striking amount of false positives, which is increased especially in patients evaluated after eradication treatment.

	Hospital Reina Sofia	Complejo Hospitalario de Navarra	Total
Sex (women)	60%	58%	59%
Medium age	47.5 ± 16,7	52.5 ± 13,4	49.6 ± 15,6
Etiology: peptic ulcer/dyspepsia/other (%)	9/63/28	3/70/27	5/67/28
Tests Pre-treatment/Post- treatment	Pre 50%	Pre 53%	Pre 51%
Concordance	77%	80%	78%
H. pylori prevalence Pre-treatment/Post-treatment (%)	36/10	34/16	35/13

[Patients characteristics according to the center]
Disclosure: Nothing to disclose

P0573 PHOTOMETRY OF RAPID UREASE TEST FOR DIAGNOSTICS OF *HELICOBACTER PYLORI* IN PATIENTS WITH DYSPEPTIC SYMPTOMS

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Introduction: Eradication of *H. pylori* significantly reduces the risk of stomach cancer and prevents the development of rebleeding. Rapid urease test allows well-timed and adequate diagnosis of *H. pylori* in patients with dyspeptic symptoms to be performed achieving correct evaluation of the results of the eradication after treatment. There is now the digital rapid urease test with photometry available that excludes possible errors of the visual evaluation of the test results.
Aims and Methods: The diagnostics by the new rapid urease test photometer that allows to trace kinetics of the enzyme activity through multiple readings of the test-slides was compared with the validated visual-evaluation rapid urease test. The two-center study with the total of 585 patients (female 344 and male 241, age 55.1±13.3 years) having symptoms of dyspepsia was performed. All of the patients underwent endoscopy of the upper gastrointestinal tract and histological examination in accordance with the OLGA classification. In cases of discrepancy, the results of the histological examination, stool-PCR test and ^{13}C UBT were used as a reference. 2 biopsy samples of the same localization were taken to perform the 2 rapid urease tests: 1 for AMA RUT Expert with AMA RUT Reader, AMA Co Ltd. and 1 for *Helicobacter Pylori* Quick Test, Biohit Oyj.
Results: *H. pylori* was detected in 204 patients - 34.9%. In the group of patients ($n = 283$), who haven't had anti-helicobacter therapy (naive), 52% of patients ($n = 147$) showed positive results for *H. pylori*, as detected by AMA RUT Expert. In the group of patients ($n = 302$), previously subject to various forms of eradication therapy, *H. pylori* was detected in 21% of patients (63 patients). In all cases of discrepancy where the Quick Test showed positive and AMA RUT Expert showed negative, the results of the 3 reference methods confirmed absence of *H. pylori*. In 23 cases where AMA RUT Expert was positive and the Quick Test negative, the reference methods of histology and stool-PCR proved the presence of the infection in 21 patients. Histologically *H. pylori* was detected in 237 patients, of which AMA RUT Expert revealed the presence of *H. pylori* urease activity in 234 patients. The sensitivity of AMA RUT Expert was 98.7% and the specificity was 100%, the accuracy was 99.4%. Thus our study revealed higher sensitivity and specificity of AMA RUT Expert compared to the Quick Test (98.4% vs 93.6% and 100% vs 87.8%). Meta-analysis of studies evaluating the sensitivity and specificity of various visual-evaluated rapid urease tests has shown their sensitivity ranging from 56.3 to 97.4%, with an average of 89.9%. The specificity of different rapid urease tests ranged from 70 to 100%, with an average of 94.4%. Differences for sensitivity and specificity were statistically significant at $p < 0.001$.
Conclusion: The results obtained by the AMA RUT Expert test-slides with the AMA RUT Reader showed higher values of diagnostic sensitivity and specificity than those in the visual-evaluated rapid urease tests, both in our study and in the data of meta-analysis. To achieve the most accurate diagnostics of *H. pylori* in patients with dyspeptic symptoms it is recommended to routinely use the photometry of the enzymatic reaction. Nothing to disclose
Disclosure: Nothing to disclose

P0574 MEDICATION DIARY CARD ON THE ERADICATION RATE AND SYMPTOM REMISSION OF PATIENTS INFECTED BY *HELICOBACTER PYLORI*

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Introduction: *H.pylori* is closely related to the genesis of diseases such as chronic active gastritis, peptic ulcer and gastric cancer [1–2]. Typically, about $< 1\%$ of patients infected by *H.pylori* will finally develop into intestinal-type gastric cancer [3–4]. Guideline emphasizes that, the major objective of eradicating *H.pylori* is to reduce the incidence risk of gastric cancer [5]. Therefore, eradicating *H.pylori* is the important measure for preventing intestinal-type gastric cancer. Moreover, the rates of *H.pylori* resistance to drugs are increasing in recent years, the eradication rate of standard triple therapy is lower than 80% [6]. Additionally, relaxed mastering of clinical eradication indications, irregular therapeutic scheme and patient compliance difference have added to the difficulties in eradication. Consequently, informing the patients of *H.pylori* eradication guidance in the manners of the medication method, time and filling in the medication diary card can increase patient understanding to *H.pylori* therapeutic scheme, then improve compliance, raising the *H.pylori* eradication rate and relieving the clinical symptoms.

Aims and Methods: We aimed to explore the influence of eradication rate of *Helicobacter pylori* (*H.pylori*) and symptom remission by means of distributing medication diary cards and giving medication guidance.

The current study was a prospective randomized controlled clinical observational study, and treatment-naive patients diagnosed with chronic gastritis accompanying with *H.pylori* infection through gastroscopy and histopathology were selected as the objects of study. Specifically, the bismuth-based quadruple standard eradication regimen was adopted for patient treatment. Patients conforming to the inclusion criteria had signed the informed consent before they were randomly divided into the record group and the control group. In addition, all patients were informed of the dose, time, precautions and potential adverse reactions in details by designated physicians. The control group was given the above education only, while the record group was given a diary card covering the detailed medication method upon the completion of education, which asked the patients to record their time, dose and adverse reactions during medication. Moreover, the patients should return their medication diary cards upon the end of treatment. Besides, both groups were carried out ^{13}C or ^{14}C urea breath test (UBT) 28 days after withdrawal to evaluate the eradication of *H.pylori*.

Results: A total of 120 patients conforming to the inclusion criteria were enrolled in the current study, including 60 in the record group and 60 in the control group. The eradication rates of *H.pylori* in 2 groups were 91.67% (55/60) and 73.33% (44/60), respectively, analyzed using intention-to-treat (ITT), while those were 93.2% (55/59) and 80.0% (44/55), respectively, analyzed using perprotocol population (PP). Difference in eradication rate between record group and control group was statistically significant ($p = 0.008$, $p = 0.037$). Difference in symptom scores between 2 groups before treatment was not statistically significant ($p > 0.05$). Comparing the total response rate between 2 groups after treatment, symptoms in record group after treatment had remarkably improved relative to those in control group ($p = 13.348$, $p < 0.001$).

Conclusion: Distributing the medication diary cards to inform the patients to take medicine as required can improve the medication compliance of patients. Favorable medication compliance can markedly improve the eradication rate of *H.pylori* and evidently improve the clinical symptoms.

Disclosure: Nothing to disclose

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P0575 THE EFFECT OF PERIODONTAL THERAPY FOR GASTRIC *HELICOBACTER PYLORI* ERADICATION: A PROSPECTIVE RANDOMIZED CONTROLLED CLINICAL TRIAL IN THAILAND

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Introduction: Chronic gastritis associated *H. pylori* infection was found in 50% of the global population and was etiologically relative gastric cancers (63%) or approximately 5.5% of all cancers worldwide, and account for 25% of cancers related with etiology of infection; and is a main public health problem. The recurrence rate is relatively high and still a main public health problem. Oral cavity may be a potential reservoir for gastric infection and transmission.

Aims and Methods: This study aims to evaluate the association between *H. pylori* in the oral cavity and stomach and to investigate the possible way of their treatment in Thailand. Patients were enrolled for 1-week triple therapy (esomeprazole 20 mg bid, clarithromycin 500mg bid, or metronidazole 400mg tid if clarithromycin resistant and amoxicillin 1000 mg bid; group 1, $n = 347$) and triple therapy plus periodontal therapy (group 2, $n = 342$). After completion of therapeutic protocol, stool antigen tests, the rapid urease test and histopathological examination were performed and finally proved by PCR.

Results: A total 689 patients with *H. pylori* associated gastritis patients who underwent EGD at Suranaree University of Technology Hospital. The 16S rRNA and ureA genes were detected in all 689 (100 %) gastric biopsy samples while was detected in oral cavity samples 549 (79.7%) of the 689 patients. The association was observed between oral cavity *H. pylori* and gastric biopsy *H. pylori* ($p = 0.007$).*H. pylori* treatment plus periodontal therapy significantly decreased the recurrence rate of *H. pylori* infection compared with gastric *H. pylori* treatment alone (OR 2.48; 95% CI 1.52 to 5.68; $p = 0.001$) by PP analysis, whereas the eradication rate was not significant differences (OR 0.91; 95% CI 0.87 to 1.13; $p = 0.091$). ITT analysis showed that, the recurrence rate was significantly different between the 2 groups (OR 2.28; 95% CI 1.29 to 4 .75; $p = 0.001$) while the eradication rate was not significant differences (OR 0.96; 95% CI 0.67 to 1.25; $p = 0.083$).

Conclusion: The association between oral cavity *H. pylori* and gastric biopsies *H. pylori* was observed, suggests that oral cavity might be considered as a potential reservoir for gastric *H. pylori* infection and re-infection. Therefore, periodontal therapy should be given to patients. This could be a promising approach for diminishing *H. pylori* infection and reducing the risk of *H. pylori* recurrence in this re-infection associated gastritis.

Disclosure: Nothing to disclose

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P0576 EVALUATION OF BACKGROUND FACTORS AFFECTING THE SUCCESS RATE OF FIRST-LINE TRIPLE THERAPY WITH VONOPRAZAN FOR *HELICOBACTER PYLORI* INFECTION

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Introduction: Recent studies have reported the superior efficacy of vonoprazan (VPZ) compared to that of proton pump inhibitors (PPIs) in first-line triple therapy for *Helicobacter pylori* (HP) infection. However, it is considered that there remains room for improvement because the eradication rate of triple therapy with VPZ in usual post-marketing studies was reported to be lower than that in a phase III study.

Aims and Methods: In the current study, we determined background factors affecting the success rate of first-line triple therapy with PPIs or VPZ to identify those that contribute to the improvement of the eradication rate. The relation between success rate of first-line triple therapy with PPIs (PPI group) or VPZ (VPZ group) and background factors (age, sex, body mass index [BMI], clarithromycin [CAM] resistance of HP determined by a microbial sensitivity test, a history of endoscopic treatment for early gastric cancer, Brinkman index, weekly amount of alcohol intake, daily amount of coffee intake, and estimated glomerular filtration rate [eGFR]) was retrospectively evaluated in 704 patients with HP infection treated between August 2014 and December 2017.

Results: A total of 704 patients (383 men, 321 women; mean age, 62.5 years [range 27–89 years]; PPI group, 369; VPZ group, 335) were enrolled in the study. The first-line eradication rate was significantly higher in the VPZ group than in the PPI group (77.5% vs. 86.6%, $p = 0.002$) and significantly lower in patients infected with CAM-resistant HP than in those infected with CAM-sensitive HP (PPI group, 57% vs. 88.0%, $p < 0.01$; VPZ group, 79.5% vs. 89.8%, $p = 0.02$). A multiple logistic regression analysis showed that the odds ratios (ORs) for CAM-resistant HP infection to CAM-sensitive HP infection for successful eradication in the PPI and VPZ groups were 0.18 (95% CI, 0.10–0.34; $p < 0.001$) and 0.41 (95% CI, 0.19–0.86; $p = 0.019$). In the PPI group, the eradication rate was significantly lower among patients with a high eGFR ($\geq$100 ml/min/1.73 m^2; $n = 52$ [14.1%]) than in the others (59.6% vs. 80.6%, $p < 0.001$) and the OR for patients with a high eGFR compared to that in the others was 0.33 (95% CI, 0.15–0.69; $p = 0.004$), as shown by the multiple logistic regression analysis. In contrast, there was no significant difference in the eradication rate between patients with a high eGFR and the others in the VPZ group. On the other hand, the eradication rate in the VPZ group was significantly lower in the patients whose alcohol intake was more than 140 g/week than in the patients whose alcohol intake was 140 g/week or less (78.5% vs. 88.6%, $p = 0.004$) and the OR for the patients whose alcohol intake was more than 140 g/week compared to that in the others was 0.25 (95% CI, 0.11–0.57; $p = 0.001$), as shown by the multiple logistic regression analysis.

Conclusion: In contrast to the eradication rate of first-line triple therapy with PPIs, the eradication rate of first-line triple therapy with VPZ for HP infection was not affected by a high eGFR (≥100 ml/min/1.73 m^2). Alcohol restriction to or less than 140 g/week can contribute to the improvement in the eradication rate of first-line triple therapy with VPZ.
Disclosure: Nothing to disclose

P0577 THE IMPACT OF *HELICOBACTER PYLORI* ERADICATION ON THE NUTRITIONAL HEALTH IN HEMODIALYSIS PATIENTS

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Introduction: Previous study showed that nutritional condition was a strong predictor of overall mortality in patients with end-stage renal failure on maintenance hemodialysis (HD patients), which indicates that maintaining favorable nutritional condition is vitally important for HD patients in which malnutrition is common. It has been also reported that *Helicobacter pylori* (*H.pylori*) infection negatively affected the absorption of nutrients and the production of hormones related to the appetite and growth, which indicates that *H.pylori* infection has potential to be one of the causes of malnutrition. Therefore, *H.pylori* eradication can be a strategy for improving nutritional condition of HD patients infected with *H.pylori*. However, the relationship between *H.pylori* eradication and the nutritional health in HD patients is still unknown.
Aims and Methods: The aim of this study was to clarify the effect of *H.pylori* eradication on the nutritional health in HD patients. HD patients who were infected with *H.pylori* and achieved successful *H.pylori* eradication at Omihachiman Community Medical Center between January 2012 and December 2017 were investigated retrospectively. All patients included in this study were received triple therapy comprising amoxicillin or metronidazole, clarithromycin and proton pump inhibitor twice daily for 1 week. *H.pylori* negativity after eradication therapy was confirmed by urea breath test in 2 months or later since eradication. Nutritional condition was evaluated using the Geriatric Nutritional Risk Index (GNRI: 14.89 × serum albumin, g/dL + 41.7 × dry weight/ideal body weight). The change of GNRI in 6 months before *H.pylori* eradication (ΔGNRI-pre6: GNRI at eradication - GNRI at 6 months before eradication) was compared with that in 6 months and 12 months after eradication (ΔGNRI-post6: GNRI at 6 months after eradication - GNRI at eradication, ΔGNRI-post12: GNRI at 12 months after eradication - GNRI at eradication).
Results: A total of consecutive 14 patients were analyzed. Subjects comprised 10 men and 4 women with a mean age of 60.1±8.5 years. The mean values of GNRI/serum albumin around *H.pylori* eradication were 94.5±7.5/3.79±0.37 (6 months before eradication), 93.9±7.4/3.74±0.38 (at eradication), 96.7±6.2/3.94±0.37 (6 months after eradication), and 95.6±6.0/3.85±0.28 (12 months after eradication). The mean values of ΔGNRI-pre6/ΔGNRI-post6/ΔGNRI-post12 were −0.64±3.0/2.87±6.0/1.70±5.0, which showed that GNRI tended to increase after successful *H.pylori* eradication (ΔGNRI-pre6 vs ΔGNRI-post6, $p = 0.11$: ΔGNRI-pre6 vs ΔGNRI-post12, $p = 0.24$). The mean values of ΔGNRI-pre6/ΔGNRI-post6/ΔGNRI-post12 in 11 patients whose GNRI at eradication was < 98 (having nutritional risk) were 0.95±2.6/4.74±4.7/3.25±3.6, which showed that GNRI in patients having nutritional risk significantly increased after successful *H.pylori* eradication (ΔGNRI-pre6 vs ΔGNRI-post6, $p = 0.006$: ΔGNRI-pre6 vs ΔGNRI-post12, $p = 0.02$).
Conclusion: The present study showed that eradication therapy of *H.pylori* improved the nutritional health in HD patients, especially having nutritional risk, which may contributes to extend a life prognosis of HD patients.
Disclosure: Nothing to disclose

P0578 COMPARISON OF STANDARD, SEQUENTIAL, AND CONCOMITANT FIRST-LINE ERADICATION THERAPY FOR *HELICOBACTER PYLORI*

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Introduction: Approximately 50% of world's population is infected with *Helicobacter pylori*. In developing countries, the prevalence has been reported to be as high as 70%. As *H. pylori* can be a major cause of gastric diseases such as chronic gastritis, gastroduodenal ulcers, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer, eradication of *H. pylori* infection is important. However, the eradication rates after fist-line standard triple therapy have continuously decreased, mainly because of the widespread development of antibiotic resistance, particularly towards clarithromycin. In fact, many guidelines recommend alternative regimens such as sequential and concomitant therapy.
Aims and Methods: We compared the efficacy, adverse events, and drug compliance of standard triple, sequential, and concomitant therapy for *H. pylori* eradication. This was a prospective study involving 750 patients diagnosed with *H. pylori* infection between January 2014 and July 2016 in Yeouido St. Mary's Hospital. Diagnosis was made by rapid urease test (CLO test) or histological evidence of *H. pylori* via modified Giemsa staining. We compared 3 treatment regimens: the standard triple therapy (250 patients enrolled) consisted of rabeprazole 20 mg, amoxicillin 1 g, and clarithromycin 500 mg twice a day for 7 days; the sequential therapy (250 patients enrolled) consisted of rabeprazole 20 mg, amoxicillin 1 g twice a day for the initial 5 days, followed by rabeprazole 20 mg, clarithromycin 500 mg, and metronidazole 500 mg twice a day for the subsequent 5 days; the concomitant therapy (250 patients enrolled) consisted of rabeprazole 20 mg, amoxicillin 1 g, clarithromycin 500 mg, and metronidazole 500 mg twice a day for 7 days. 6 weeks following completion of therapy, successful *H. pylori* eradication was defined by a negative ^{13}C-urea breath test result. Adverse events and drug compliance were evaluated by physicians via direct questioning. 103 patients did not complete the study because of loss of follow-up or withdrawal of consent.
Results: A total of 647 patients (209, 211, and 227 patients in the standard triple, sequential, and concomitant therapy groups, respectively) were analyzed. The mean age of the patients was 55.7 years. There were 365 male and 282 female patients (male:female ratio = 1.29). The baseline characteristics were not significantly different between the 3 groups. The eradication rate was significantly higher in the concomitant group (89.4%, 203/227) than in the standard group (78.5%, 146/209) and the sequential group (85.3%, 180/211) ($p = 0.006$). Drug compliance and adverse events were not statistically different among the 3 groups.
Conclusion: Concomitant therapy appears to be more effective for *H. pylori* eradication compared to standard triple therapy and sequential therapy. There were no statistically different adverse events among the three groups.
Disclosure: Nothing to disclose

P0579 SUSCEPTIBILITY-BASED TAILORED VS. EMPIRIC AMOXICILLIN MODIFIED BISMUTH QUADRUPLE THERAPY AS *HELICOBACTER PYLORI* THERAPY: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: The increase in *Helicobacter pylori* (*H. pylori*) resistance to antibiotics and unsatisfactory efficacies of common empirical eradication regimens suggest that susceptibility-based tailored therapy may be required to achieve high efficacy.[1,2] Previous studies showed that substitution of amoxicillin for tetracycline was highly effective making modified bismuth quadruple therapy an option for first line therapy in China. [3,4]
Aims and Methods: This randomized, open-label, superiority, multi-center trial aimed to compare the eradication rates, safety and adherence of susceptibility-based tailored therapy with empiric bismuth quadruple therapy in treatment-naive patients with *H. pylori* infection. Subjects were randomized in 2 groups by 3:1 ratio: a) tailored therapy, according to antibiotic resistance pattern included esomeprazole 20mg bid, amoxicillin 1g bid, with a third drug (clarithromycin 500mg bid, metronidazole 400mg bid, or levofloxacin 500mg qd) for susceptible strains, or with bismuth 220mg bid plus metronidazole 400mg qid for triple-resistant strains; b) empiric therapy included esomeprazole 20mg bid, bismuth 220mg bid, amoxicillin 1g tid, and metronidazole 400mg tid. All regimens were given for 14 days. Antimicrobial susceptibility was assessed by the agar dilution method. Primary outcomes were *H. pylori* eradication rates. This trial was registered with ClinicalTrials.gov, NCT02935010.
Results: Between February 2017 and March 2018, 491 subjects were screened for eligibility; 382 were randomized in the study. The baseline characteristics were balanced between the 2 groups (Table 1). The intention-to-treat and per-protocol cure rates were 91.6% (262/286, 95% CI 88.4–94.8%) and 97.7% (250/256, 95.8–99.5%) for tailored therapy vs. 85.4% (82/96, 78.4–92.5%) and 97.6% (81/83, 94.3–100%) for empiric therapy. Tailored therapy was not superior to empirical therapy either in ITT analysis (Difference 6.2%, 95% CI −0.3–12.7%, $p = 0.059$) or in PP analysis (Difference 0.1%, −3.1–3.2%, $p = 0.486$). According to antimicrobial susceptibility, tailored therapy eradicated 99.4% (159/160) clarithromycin, 100% (11/11) metronidazole, 100% (27/27) levofloxacin susceptible strains, and 91.4% (53/58) triple-resistant strains respectively. Empiric therapy eradicated 100% (13/13) metronidazole susceptible and 97.1% (68/70) resistant strains. Both tailored therapy and empirical therapy achieved high adherence and low adverse event rates. The eradication rate of subjects with poor adherence was lower than subjects with good adherence, but a significate difference was only observed in empiric therapy (25%, 1/4 vs. 97.6%, 81/83, $p < 0.001$) but not in tailored therapy (85.7%, 12/14 vs. 97.7%, 250/256, $p = 0.058$).
Conclusion: In settings of high and multiple antibiotic resistances of *H. pylori*, susceptibility-based tailored therapy provided excellent results with 14-day PPI triple therapies being optimal choices for susceptible strains. However, empiric

Abstract No: P0579: Baseline characteristics and therapeutic outcomes in patients with anticoagulant therDOAC, direct oral anticoagulants; HBT, heparin bridge therapyapy

Variables	Tailored therapy (n = 286)	Empiric therapy (n = 96)	p value
Age, years (range)	43.0 ± 13.5 (18–72)	45.5 ± 13.6 (18–75)	0.112
Gender (male/female)	124/162	41/55	0.912
Diagnosis (Dyspepsia/PUD)	247/39	82/14	0.816
Clarithromycin/ Metronidazole/ Levofloxacin Resistance, n(%)	104 (36.4%) / 233 (82.2%) / 132 (46.2%)	30 (31.3%) / 81 (84.4%) / 47 (49.0%)	0.364 / 0.621 / 0.634
Took less than 80% of drugs, n	17	5	0.789
Loss of follow-up, n	16	9	0.195

[Table 1. Baseline characteristics]

modified bismuth quadruple therapy (three times daily of amoxicillin and metronidazole) was also proven to be highly effective for subjects with good adherence even in areas of high metronidazole resistance.
Disclosure: Nothing to disclose

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P0580 TRIPLE THERAPY OF VONOPRAZAN, AMOXICILLIN AND SITAFLOXACIN IS USEFUL FOR THE THIRD-LINE *HELICOBACTER PYLORI* ERADICATION THERAPY IN JAPAN

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Introduction: Vonoprazan (VPZ) is a novel potassium-competitive acid blocker, which has higher eradication rates comparing with PPI-based therapy. However, in Japan, there are still many patients who failed both first-line therapy using clarithromycin and second-line therapy using metronidazole. Sitafloxacin (STFX) has been shown as a preferable agents in third-line therapy in combination with amoxicillin (AMOX) and PPI. The aim of this study was to investigate the efficacy of triple therapy of VPZ, AMOX and STFX for the third-line therapy.
Aims and Methods: During April 2015 and December 2017, a total of 74 patients who had failed both first-line and second-line therapy were enrolled. If agreed, patients underwent endoscopy to obtain *H. pylori* strains to test the susceptibility to antibiotics if they agreed. VPZ (20 mg bid), AMOX (750 mg bid) and STFX (100 mg bid) were administered for 1 week and the result was tested by ^{13}C-UBT or stool antigen test 6–10 weeks after finishing the treatment.
Results: No major adverse effects were seen and all patients completed the regimen except for 1 patient who did not visit again for the evaluation. Eradication rate of VPZ-AMOX-STFX was 90.5% (67/74; 95% CI, 83.9–97.2%) and 91.8% (67/73; 85.5–98.1%) in ITT and PP analysis, respectively. Antibiotics susceptibility test was available in 29 patients. Eradication was not successful in 3 patients whose strains had MICs of STFX 0.5≤ mg/mL. In contrast, eradication was successful in 26 patients infected with strains which had MICs of STFX < 0.5 mg/mL.
Conclusion: Triple therapy of VPZ, AMOX and STFX would be an effective third-line *H. pylori* eradication therapy in Japan. Low susceptibility to STFX would be a major cause of the treatment failure.
Disclosure: Nothing to disclose

P0581 CHANGE IN HALITOSIS VALUE AFTER *HELICOBACTER PYLORI* ERADICATION: A SINGLE INSTITUTIONAL PROSPECTIVE ANALYSIS

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Introduction: Eradication therapy for *Helicobacter pylori* (*H. pylori*) infection is widely performed. Although patients may report that their halitosis has either improved or worsened after eradication therapy, these complaints are subjective. In addition, there are no objectively evaluated reports of changes in halitosis after *H. pylori* eradication.
Aims and Methods: The aim of this study was to investigate changes in halitosis after *H. pylori* eradication. Between February 2015 and March 2016, a total of 5,514 patients visited the Kudo Clinic. Of these, 174 were found to be infected with *H. pylori*. Informed consent for participation in this study was obtained from 71 patients. We assessed halitosis before and 2 months after eradication, and compared the changes. If primary eradication was unsuccessful, secondary therapy was performed. Halitosis values were measured after successful eradication was confirmed with urea breath testing. Halitosis values were evaluated with a Total Gas Detector^{TM} System (Refres HR BAS-108; Adonis Electronics Co., Ltd., Osaka, Japan). The ethics committee of the Kudo Clinic approved this study protocol (Approval number; 2015-01).
Results: Among the 71 patients (18 [25.4%] males and 53 [74.6%] females), 68 completed treatment and had successful eradication. The average age was 64.2 ± 10.5 years old. The Breath Refres Values were 49.4±21.4 before eradication and 52.2±26.4 after successful eradication, and did not decrease significantly (p = 0.55). Within the 27 patients whose Breath Refres Values showed more than 60, those improved significantly form 73.0±10.7 to 61.3±28.2 (p = 0.037).
Conclusion: Among the patients whose Breath Refres Values was high, their halitosis improved after successful eradication. Further examination will be necessary by increasing the number of cases.
Disclosure: Nothing to disclose

P0582 HOW TO GET RELIABLE INFORMATION ABOUT THE EFFICACY OF A *H. PYLORI* REGIMEN IN PATIENTS HARBOURING RESISTANT STRAINS?

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Introduction: Amongst the several factors that can affect the efficacy of anti *H. pylori* therapy, resistance to antimicrobials remains the most critical one. Despite this, in only few studies has antimicrobial susceptibility testing performed and there is uncertainty regarding the minimum number of resistant strains that need to be tested in order to get reliable information on the effectiveness of a given eradication regimen in patients harboring those strains.
Aims and Methods: During a 5-year study, we tried to identify a minimum number of patients to study to get a reliable estimate of effectiveness of a given treatment (namely sequential therapy) in patients harboring resistant strains. Consecutive 1682 naïve *H. pylori*-positive patients were studied between 2010 and 2015, and resistances to clarithromycin, metronidazole and levofloxacin assessed by E-test according to the EUCAST guidelines. Sequential therapy was offered and effectiveness evaluated 6 weeks after the end of the treatment. To identify a minimum number of patients to study to get a reliable estimate of effectiveness of sequential therapy in patients harboring resistant strains, a bootstrap analysis was firstly performed. Patients who completed the follow-up were sub-grouped according to the pattern of antimicrobial susceptibility/resistance, considering clarithromycin and metronidazole. For each of these groups, the effect of sampling across the range 10–300 patients was explored based on 500 samples drawn. This allowed the calculation of the variance in eradication estimates to be made for each level of sampling. These parameters were then used to calculate the power of each sample to detect the parent population eradication rate with a margin of error of +/- 1%, assuming a two-sided a-value of 0.05. Afterwards, the estimated minimum sample needed to give consistent results was calculated for theoretical eradication rates ranging from 50% to 95% assuming that the results would follow a standard binomial distribution and choosing a margin of error of +/- 5%, and a value of alpha of 0.05.

Abstract No: P0582: Bootstrap analysis

Characteristics of the Parent Populations

	Cla-S & Metro-S (n = 527)	Cla-S & Metro-R (n = 152)	Cla-R & Metro-S (n = 151)	Cla-R & Metro-R (n = 236)
Eradication rate	97.3% (95% CI: 95.6 to 98.4)	96.1% (95% CI: 91.7 to 98.2)	93.4% (95% CI: 88.2 to 96.4)	83.1% (95% CI: 77.7 to 87.3)
	Sample Size Estimated for each Pattern of susceptibility/resistance evaluated with the bootstrap analysis			
Power	Sample Size (n)			
99%	39	49	71	97
90%	25	30	40	61
80%	19	21	32	43

Results: 45.0% (95% CI: 42.3–47.7) of strains were susceptible to both agents. In the remaining 55% (95% CI: 52.3–57.7), resistance to 1 or 2 agents was present. However, 22.6% (95% CI: 20.5–25.0) of patients were resistant to both antimicrobials. The results of the bootstrap analysis (Table 1) show that the higher the eradication rate in the parent population, the lower the minimum number of strains required to evaluate, at any given power. For therapies whose eradication rates range between 75% and 85%, it could be estimated that a sample size ranging between 98 and 144 patients should be enrolled to get a reliable and consistent estimate of eradication rate.
Conclusion: Our large data set provided evidence showing that a large number of strains needs to be assessed to give reliable estimates of the effectiveness of a given eradication regimen in patients harboring resistant strains.
Disclosure: Nothing to disclose

P0583 THE EFFICACY OF A SIMPLE 14-DAY MODIFIED QUADRUPLE THERAPY CONTAINING AMOXICILLIN, TETRACYCLINE AND HIGH DOSE METRONIDAZOLE AND PROTON-PUMP INHIBITORS AS EMPIRICAL THIRD LINE ERADICATION TREATMENT IN TAIWAN

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Introduction: Studies had shown that low antibiotics resistances to amoxicilln, tetracycline even after failed *H. pylori* treatment and high dose metronidazole appeared to be able to overcome antibiotics resistance in Taiwan [(1,2).]
Aims and Methods: We assessed the efficacy of a simple 14-day modified quadruple therapy containing amoxicillin, tetracycline and high dose metronidazole and PPI as an empirical third-line rescue *H. pylori* treatment and the clinical factors influencing the success of eradication.
Methods: This study was conducted by analyzing 70 consecutive prospectively registered patients who failed 2 times *H. pylori* eradication by using the 1st line standard clarithromycin-based triple therapy and 2nd line levofloxacin-based therapy. 7 patients were lost to follow up. All of them received endoscopy for *H. pylori* culture. They were then treated according to the antibiotic susceptibility testing reports (Cultured group, n = 39). Those who failed *H. pylori* culture were prescribed with a simple modified 14-day quadruple therapy containing esomeprazole 40 mg twice daily, amoxicillin 1 g twice daily, tetracycline 500 mg four times daily and metronidazole 500 mg three times daily (empirical group, n = 24).). Follow-up urea breath test was performed 8 weeks later to assess treatment response.
Results: The eradication rates attained by Cultured group and empirical group were 89.7% and 58.3%, respectively in the per protocol analysis (p = 0.004) and 81.4% and 51.8%, respectively, in the intention-to-treat analysis (P = 0.014). Antibiotics resistances after 2 treatment failures were: Clarithromycin (79.5%); Levofloxacin (94.9%); Metronidazole (66.7%); Amoxicillin (2.6%); Tetracycline (0%). Eighty-four percent of patients with Metronidazole resistance were successfully eradicated. Culture-guided therapy was the clinical factors influencing the efficacy of *H. pylori* eradication (OR: 0.16; 95% *confidence interval*: 0.043–0.596, p = 0.006).
Conclusion: Empirical 14-day modified quadruple therapy is not sufficient as an alternative third-line rescue *H. pylori* treatment in spite of the low amoxicillin and tetracycline resistances after 2 treatment failures. Culture guided therapy is still recommended.
Disclosure: Nothing to disclose

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P0584 USING A NOVEL DEVELOPED HIGH RESOLUTION MELT CURVE ASSAY FOR THE ANALYSIS OF PREDOMINANCE OF *HELICOBACTER PYLORI* CLARITHROMYCIN RESISTANCE

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Introduction: *Helicobacter pylori* (HP) is the most common pathogen found in humans. Its resistance to clarithromycin is increasing continuously and it is one of the main reasons for eradication failure. The resistance is attributed to 3 point mutations (PM): A2142G, A2142C and A2143G within the peptidyl-transferase encoding region of the 23S rRNA gene. We aimed to analyze the predominance of HP clarithromycin resistance by using our novel high resolution melt (HRM) assay.
Aims and Methods: A total of 151 HP stool samples were collected from naïve patients with general gastric discomfort who also performed $^{13}CO_2$ breath tests (BTs). Stool antigen test (SAT) was also performed on 126 of the 151 stool samples collected HP DNA was extracted from the stool and was analyzed by HRM. The results were compared to the BTs and SATs. The HRM positive results were further analyzed by comparing them to 4 reference plasmids incorporating the three mutations and the WT sequences.
Results: The HRM results presented 106 positive and 45 negative samples. Of the 106 positive samples, 52 had PM - demonstrating a 34% clarithromycin resistance. When compared to the 151 BTs and the 118 SATs, the HRM had a sensitivity of 100% and 99% and specificity of 82% and 78% respectively. Of the 106 positive HRM samples, 54 (51%) had a WT sequence, 10 (9%) had an A2142G PM, 13 (12%) had an A2142C PM, 18 (17%) had an A2143G PM and 11 (10%) were heterozygote (multiple peaks).
Conclusion: Our study is consistent with other reports suggesting an increasing *H. pylori* clarithromycin resistance worldwide, yet further investigation is required in order to determine its prevalence in Israel. Moreover, our HRM assay may be used for screening prior to administration of clarithromycin eradication therapy.
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00-17:00
Small Intestinal I - Hall X1

P0585 THE PROTECTIVE EFFECT OF ANGIOTENSIN(1-7) ON NSAID-INDUCED SMALL INTESTINAL INJURY IN RATS

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Introduction: Non-steroidal anti-inflammatory drugs (NSAIDs) are some of the most commonly prescribed drugs in the world. However, recently its gastroduodenal complications, especially small intestine injury, has attracted people's attention. The pathogenesis is not yet completely clear, therefore there is no effective treatment measures. RAS is an important regulation system, which plays an important role in maintaining water and electrolyte balance. Ang(1–7) is one of the most important components of the system, which mainly synthesized by ACE2, bypassing the synthesis of Ang II. Studies have shown that Ang(1–7) can reduce the degree of inflammation in colitis and pancreatitis. However, there is few researches on whether Ang(1–7) has a protective effect on NSAIDs induced intestine injury.
Aims and Methods: We aimed to investigate the effect and mechanism of Angiotensin(1–7) on NSAID-induced intestinal injury.
40 Male SD rats weighing 180–200 g were randomly divided into 4 groups. The control group was given 1ml100 $g^{-1}d^{-1}$ saline by gavage; the experimental group was given diclofenac sodium 10 $mgkg^{-1}d^{-1}$ by gavage; the Ang(1–7) intervention group was given diclofenac sodium as the experimental group, meanwhile received Ang(1–7) which was given continued subcutaneously at 24 μg/kg/h from the day before gavage of diclofenac sodium; the Ang(1–7) +MasR antagonist group was treatment as the Ang(1–7) group, meanwhile received MasR antagonist A779 $1mgkg^{-1}d^{-1}$ which was intraperitoneally injected the day and half an hour before gavage of diclofenac sodium. The rats were sacrificed 5 days later. Assessed the injury of the intestine;Mas, AngII, *p*-p38MAPK and NF-κB were measured by western blot; TNF-α were detected by ELISA.
Results: 1. Injury of small intestine: Multiple ulcers were seen in the intestine mucosa of the experimental group, Ang(1–7) can significantly reduced the injury,

while the protect effect was blocked by MasR antagonist ($p < 0.05$). 2. Expression of Mas and AngII in the intestine: Mas in the Ang (1–7) group was significantly higher than that in the experimental group, while the AngII was significantly reduced ($p < 0.05$); the MasR antagonist significantly reduced the expression of MAS, while the AngII was significantly increased ($p < 0.05$). 3. The expression of *p*-p38MAPK, NF-κB and TNF-α in experimental group were much higher than control group, while in the Ang(1–7) group, they were much lower than that in the experimental group, the Ang(1–7) + MasR antagonist group were significantly higher than both the Ang(1–7) group and the experimental group ($p < 0.05$). 4. Pearson correlation analysis: The score of small intestine injury was highly negatively correlated with Mas ($p < 0.05$), and highly positively correlated with AngII, p-p38MAPK, NF-κB, and TNF-α ($p < 0.05$).

Conclusion: Ang(1–7) has a protective effect on NSAID-related small intestinal injury in rats. The protective effect mainly mediated by Mas receptor, then down-regulating the AngII, and inhibiting the activation of p38MAPK, NF-κB and TNF-α.

Disclosure: Nothing to disclose

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P0586 INTESTINOTROPHIC EFFECTS OF GLEPAGLUTIDE FOLLOWING CHRONIC EXPOSURE IN RATS AND DOGS

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Introduction: Glepaglutide is a novel, long-acting GLP-2 analog being developed for the treatment of Short Bowel Syndrome. Nonclinical pharmacology studies have shown that glepaglutide is a potent and selective GLP-2 receptor agonist, with activity across species.

Aims and Methods: The objective of these studies was to assess the systemic chronic toxicity and toxicokinetic (TK) profile of glepaglutide in the Wistar rat and the Beagle dog. In addition, pharmacodynamic effects were compared to subchronic exposure in Wistar rats.

In chronic studies, rats were dosed subcutaneously (SC) with vehicle, 1, 3 and 10 mg/kg glepaglutide on a daily basis for 26 weeks. Furthermore, sub-groups of control and high-dose animals were allowed a 6-week recovery period following completion of the dosing period. Dogs were dosed SC with vehicle, 0.25, 1 and 5 mg/kg glepaglutide on a daily basis for 39 weeks. Sub-groups of control and high-dose animals were allowed a 6-week recovery period following completion of the dosing period. Blood samples were taken at regular intervals during the studies for determination of TK profile. In addition to standard toxicology parameters measured during the studies (data not presented), the length and the weight of the small and large intestines were measured at necropsy as indicators of intestinotrophic effects and the intestinal tract was evaluated histologically. In sub-chronic studies, rats were dosed SC with vehicle 1, 4 and 10 mg/kg glepaglutide on a daily basis for 7 days. The length and weight of the small and large intestines were measured at necropsy as indicators of intestinotrophic effects.

Results: At steady state, the TK profiles of glepaglutide within the dosing interval were relatively constant in rats and dogs, and therefore an accurate half-life could not be determined. In chronic studies, glepaglutide induced dose-related significant ($p < 0.01$) increases in length and weight of the small intestines in both rats and dogs (Table 1). Furthermore, the length and weight of the large intestine was also slightly increased in rats. At all dose levels, macroscopic thickening of the duodenum, jejunum and ileum was present. Histologically, glepaglutide produced a dose-related increase in mucosal hyperplasia of the duodenum, jejunum and ileum. Interestingly, at the end of the recovery period significant intestinotrophic effects were still present in the high-dose groups although partial recovery was seen. Sub-chronic treatment in the rat induced significant dose-related increases in small intestinal mass, similar to those observed after chronic dosing.

Species	Rat				Dog			
	Main study animals		Recovery		Main study animals		Recovery	
Dose (mg/kg)	1	3	10	10	0.25	1	5	5
Small intestinal length	21/19	27/34	38/47	39/45	21/19	6/35	46/37	16/19
Small intestinal weight	115/85	155/164	190/238	85/101	71/25	74/91	103/80	78/34

[Table 1: Percentage (%) increase relative to control group (males/females)]

Conclusion: A significant dose-related intestinotrophic effect was seen following 26 and 39 weeks of glepaglutide exposure in rats and dogs, respectively. This response was similar to findings after 7 days of dosing in rats. At all doses, increased length and weight as well as macroscopic thickening and villous hypertrophy were noted in all segments of the small intestine. These findings were still present following a 6-week recovery period, indicating prolonged intestinotrophic effects of glepaglutide.

Disclosure: Nothing to disclose

P0587 EMERGING ROLE OF RIFAXIMIN IN THE MANAGEMENT OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS ON CHRONIC PPI TREATMENT

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Introduction: Despite their well-established efficacy, emerging studies are evaluating the effect of Proton Pump Inhibitor (PPI) drugs on gut microbiota composition and on a consequent possible causative role in inducing Small Intestinal Bacterial Overgrowth (SIBO). However, these analyses have so far produced mixing results. Moreover, therapeutical options for SIBO patients are still not well established.

Aims and Methods: The aim of our study was to assess the prevalence of SIBO and CH4 producers consequent to chronic PPI therapy using Lactulose Breath Test (ULBT). Secondary aim was to explore the possible role of Rifaximin in treating PPI-induced SIBO and CH4 producers patients.

125 consecutive GERD patients (>18 years old) constantly treated with PPI (PPI) for at least 6 months were enrolled and underwent ULBT. An age-matched control population (Control) of 100 patients, which had not used PPI in the last 6 months, was also enrolled. 25 Italian General Practitioners and one university hospital participated to the enrollment. Exclusion criteria were: liver and kidney diseases, prior antibiotic treatment in the last month, pregnancy and/or breast-feeding, diabetes, BMI > 29, alcohol abuse disorder, IBS, IBD, neurological/muscle diseases, celiac disease, lactose intolerance, previous gastric/intestinal surgery.

North American Consensus (Rezaie et al, *The American Journal of Gastroenterology* 2017) was used to define SIBO diagnosis and CH4 producers. ULBT samples were centrally read and interpreted. Among PPI, 22 SIBO positive patients and 42 CH4 producers were treated with Rifaximin 1200mg/daily for 14 days and rechecked with ULBT after 1 month. The area under the curve (AUC) before and after treatment was also calculated for both SIBO positive patients and CH4 producers.

Results: In the PPI group, 38/125 (30.4%) had a positive ULBT for SIBO vs. 27/100 (27%) of the Control group ($p < 0.05$). Interestingly, 77/125 (61.6 %) PPI patients were found to be CH4 producers vs. 21/100 (21%) controls ($p < 0.05$). In particular, among SIBO patients in the PPI group, 34 (89.4%) were also CH4 producers vs. 17/27 (63%) controls ($p < 0.05$). After Rifaximin treatment, ULBT resulted negative in 15/22 SIBO patients (68.1%) ($p < 0.05$) and in 23/42 CH4 producers (54.8%) ($p < 0.05$). At the AUC analysis, an overall reduction of 54.2% for H2 in SIBO patients and of 47.7% for CH4 in CH4 producers was assessed after Rifaximin treatment ($p < 0.05$).

Conclusion: Our data showed that chronic use of PPI could be able to increase the prevalence of SIBO and to shift the intestinal microbial composition towards a CH4-producing flora. Rifaximin could represent a useful therapeutical option for PPI-induced SIBO and for modulating CH4-producing flora.

Further studies are underway to determine the exact implications that sustain these findings.

Disclosure: Nothing to disclose

P0588 THE IMBALANCE OF THE HOMEOSTASIS SERINE PROTEASES-INHIBITORS IN INFLAMMATORY BOWEL DISEASE NAIVE PATIENTS: A HORIZON FOR NEW PERSPECTIVES THERAPIES?

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Introduction: The pathogenesis of chronic inflammatory bowel disease (IBD) suggest an inappropriate activation of the intestinal immune system against the intestinal host's flora of genetically predisposed persons. The intestinal microbiota can be involved in different ways in this pathogenesis. Indeed, an excessive proteolytic activity of the intestinal microbiota of IBD subjects was one of the recent and demonstrated hypothesis.

Aims and Methods: A prospective comparative study was enrolled in our medical center from January 2015 to December 2015. Were included to the study all the hospitalized new cases of IBD and a second group of healthy voluntary people. All the subjects (controls and patients) treated with an antibiotic, anti-inflammatory or pro-biotic in the 6 months prior to inclusion were excluded. All patients have benefited of a physical and biological examination and colonoscopy. Stool samples were collected for fecal water extraction. At the first step we measured the global proteolytic activity of fecal water using azocasein or casein as a substrate in both groups. To highlight the nature of the proteases involved, we studied the inhibitory effect of specific serine proteases inhibitors on fecal proteolytic activity. We used PMSF and SBTI as chemical serine protease inhibitors and Serpin ES expressed by a commensal bacterium of the intestinal microbiota. This Serpin was previously purified and optimized in the Ife laboratory, Metagenopolis at INRA Jouy-en-Josas in France using recombinant strain of *E. coli* (plasmid pDEST17). The final step was to search a natural serpin deficit in

IBD group so we studied in both groups the proteolytic activity of the fecal water after using proteases which degraded all the protein except serpins. For the statistical analysis we used Spss software (20.0) (significant difference for $p < 0.05$).
Results: Were included in the first group of IBD 28 patients vs. 15 in the second group of controls. The middle age was 46 years vs. 48 years in the second group. The sex ratio [H/F] was 1.33 vs. 1.14. The IBD group were divided in 15 cases of Crohn disease and 13 cases of Ulcerative colitis (UC) disease. The activity of the disease was variable from minimal to severe. Proteolytic activity was greater in patients vs. healthy controls (294.3 U/ml vs. 22.9U/ml, $p < 0.05$). Particularly high activity has been observed in the severe forms of both UC and Crohn's disease. We found a significant decrease in protease activity in the presence of both inhibitors: PMSF (1mM) (294.3 ml/l vs 63.60 U/ml $p < 0.01$) and SBTI (1mM) (294.3 U/ml vs 79.6 U/ml $p < 0.05$). Using the serpin ES (14 μg/μml) non-significant decrease in the proteolytic activity was found (294.3U/ml vs 242.2 U/ml, $p > 0.05$). In reverse zymography only one band was found in the first group vs. three bands in the healthy groups.
Conclusion: Our study demonstrated a higher proteolytic activity of fecal water in IBD group comparing to healthy people and this activity was concordant to the severity of the thrust. Serine inhibitors were able to decrease the proteolysis. Thus, majority were serine proteases. The lower concentration of serpin ES may explain the lesser inhibition. Finally, in IBD patients there is a natural deficiency in serpins therefore an imbalance in the homeostasis can be suggested as hypothesis to the pathophysiology of the IBD disease. Restoring this balance proteases-inhibitors can lead to new therapeutic perspectives especially by manipulating the microbiota using genetically modified probiotics.
Disclosure: Nothing to disclose

P0589 FREQUENCY OF SERONEGATIVE VILLOUS ATROPHY IN FUNCTION OF THE DEFINITION USED: DIAGNOSTIC UTILITY OF TRANSGLUTAMINASE DEPOSITS AND GAMMADELTA+ CELL COUNTING

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Introduction: Seronegative villous atrophy (SNVA) can be caused by coeliac or non-coeliac causes. Despite several international consensus on coeliac disease (CD), there is no agreement on how to approach the diagnosis of subjects with SNVA.
Aims and Methods: Evaluate 1) The diagnostic accuracy for CD of different tTG cut-offs with or without EmA and 2) The frequency of SNVA of coeliac cause in our geographical area.
Between April 2010 and November 2017 all consecutive patients with villous atrophy (VA) were prospectively registered. Coeliac serology (tTG and EmA), tTG subepithelial deposits, and gammadelta+ intraepithelial cells (by flow cytometry) were measured. CD was diagnosed based on the Catassi criteria (rule 4 of 5). Three definitions of positive serology were used: 1. Definition based on NICE guidelines: tTG> 8 U/ml (recommended by the manufacturer: Elia Celikey, Phadia) *plus* EmA+ for titres of tTG between 8 and 20 U/ml; 2. Given that >98% of the individuals in the general population of our health area have serum tTG < 2 U/mL, titres of tTG between 2 and 8 U/mL with EmA+ were considered positive; 3. tTG+ >2 U/mL (even with negative EmA). For each cut-off definition, sensitivity (S) and specificity (E) for the diagnosis of CD were calculated.
Results: 238 VA were diagnosed (225 CD, 13 non-CD) (age, 18±1.2 years, limits 0 to 84, 70% women). 24 of the 225 (11%) patients with CD presented serum tTG < 8 U/ml or between 8 and 20 U/ml with negative EmA (< 17 years, 5% *vs.* ≥17 years, 21%; $p < 0.001$). All had positive tTG deposits (19/24) or gammadelta+ cells (22/24) and clinical response to a gluten-free diet, confirming the diagnosis of CD. Using the NICE definition as a cut-off point, 37/238 patients had SNVA (24 CD, 13 non-CD) (S, 89%; E, 100%). Considering also as tTG+ titres between 2–8 U/mL with EmA+, 26/238 had SNVA (13 CD, 13 non-CD) (S, 94%; E, 100%) (S, $p < 0.001$ vs. NICE). Finally, considering tTG+ >2 U/mL, 17/238 had SNVA (5 CD and 12 non-CD) (S, 98%; E, 92%) (S, $p < 0.001$ vs. NICE).
Conclusion: CD is the most frequent cause of SNVA in our area. Based on the definition of negative serology used, the frequency of seronegative CD varies from 2 to 11%. Both the tTG deposits and the gammadelta+ cells analysed by flow cytometry are complementary diagnostic tools of great value in these patients. The serum tTG cut-off in clinical practice should be reconsidered.
Disclosure: Nothing to disclose

P0590 TISSUE TRANSGLUTAMINASE DEPOSITS COMPARED TO THE SCORE 'COELIAC-LITE' IN THE DIAGNOSIS OF COELIAC DISEASE WITHOUT VILLOUS ATROPHY

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Introduction: Recently, we have described a diagnosis scoring system (Score 'Coeliac-lite') that allows diagnosing the forms of coeliac disease (CD) without atrophy. The Score is based on the assessment of the intraepithelial lymphocyte count, the gammadelta+ cell count, coeliac serology, and HLA-DQ2.5/8 (UEG 2017), and has a good accuracy to predict GFD response (AUC, 0.83). The ESPGHAN 2012 CD diagnostic criteria support the use of tTG mucosal deposits in doubtful cases.
Aims and Methods: To assess whether the determination of tTG deposits in the duodenal mucosa can improve the diagnostic accuracy of the Score 'coeliac-lite'. 119 patients with symptoms of the CD spectrum without villous atrophy were included (age, 39.6±1.5 years; 71% women), who were treated with a gluten-free diet (GFD) based on positive serology and/or compatible histology (lymphocytic enteritis) and/or a positive coeliac genetics and/or CD IEL cytometry pattern. In all of them, the Score coeliac-lite (cut-off ≥10) and the presence of subepithelial tTG IgA deposits (confocal immunofluorescence) were analysed. 28 patients (15%) with inconclusive results of the tTG deposits assay were excluded. Response to GFD was defined as clinical *plus* histological (or serological when positive) remission. The diagnosis of CD was based on the rule of '4 of 5' by Catassi. The relationship between presence of deposits and Score positivity and GFD response was analysed using a binary logistic regression analysis.
Results: The response to a GFD was 86% in patients with a Score≥10 and 29% for a Score<10 ($p < 0.001$). The tTG deposits were positive in 55% of patients, being more frequently positive in patients with a Score≥10 ([<10], 38%; [10–16], 74%; [≥17], 87.5%; $p < 0.001$). There was a non-significant trend to a higher response rate to GFD in patients with a Score≥10 and positive tTG deposits (Score<10: tTG+ 23% vs. tTG- 33%, $p = 0.39$; and Score≥10, tTG+, 91% vs. tTG- 67%, $p = 0.06$). This trend was likely due to that tTG deposits were positive in 87% of patients with positive serology (serum tTG >2 U/mL in 30% of patients, being those with a Score ≥17). The logistic regression analysis showed that only the Score 'coeliac-lite' (OR, 14; $p < 0.001$) had an independent predictive value for GFD response (tTG deposits: OR, 1.08, $p = 0.9$).
Conclusion: The assay technique of tTG deposits was inconclusive in 15% of the patients, which limits its routine use. As well, a positive result does not seem to provide important additional information with respect to the Score 'coeliac-lite'.
Disclosure: Nothing to disclose

P0591 COELIAC DISEASE IN SELECTIVE IGA DEFICIENCY. SAME PATHOLOGY, DIFFERENT APPROACH TO DIAGNOSIS AND SURVEILLANCE

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Introduction: Selective IgA deficiency (sIgAd) is the most common primary humoral immunodeficiency in the Caucasian population.
Patients with sIgAd have a 10- to 20-fold increased risk of developing coeliac disease (CD), especially silent forms.
CD in patients with sIgAd must be tested with Immunoglobulin G (IgG) antibodies (Ab).
There is a paucity of literature on this topic and international clinical guidelines do not establish which Ab, IgG tissue transglutaminase (tTG) or IgG deaminated gliadin peptide (DGP), should be used for the screening and surveillance of sIgAd-CD patients.
Aims and Methods: The 3 main objectives of our study were to identify which IgG-Ab in sIgAd-CD patients should be preferably chosen for the screening, to study their clearance once a gluten free diet (GFD) has been established and to show if a correlation does exist between Ab levels and villous atrophy grading. For this purpose, individuals tested in order to dismiss CD between December 2012 and December 2017, were revised retrospectively.
All sIgAd patients with positive results for one or more IgG-Ab were included. A group of CD patients without sIgAd with same characteristics as those above were randomly selected as a control group.
Results: 29 patients were included. 26/29 CD (17/26 group A: CD newly-diagnosed. 9/26 group B: CD follow-up). 3/29 had isolated IgG DGP and were not CD (false positive). In group A at diagnosis 25% were IgG DGP negative (false negative). The totality of confirmed CD (26/26) had IgG tTG and IgG endomysial positive. It was observed that the more severe the atrophy was, the higher the Ab levels were. After 5 months, (±3) of GFD, no reduction of IgG tTG was proved. However, among controls, IgA tTG showed 60% reduction by this time. In GFD-adherent at long-term follow-up (26 months) IgG tTG remained positive in >70% despite villous recovery.
Conclusion: Our results suggest the importance of a screening strategy based on IgG tTG in sIgAd patients.
This study demonstrates the lower rate of Ab clearance with the long-term persistent Ab in spite of GFD.
In line with EPSGHAN recommendations, levels associated to villous atrophy are assay-dependant also among sIgAd-CD patients.
Disclosure: Nothing to disclose

P0593 PREDICTIVITY OF AUTOIMMUNE STIGMATA FOR GLUTEN SENSITIVITY IN SUBJECTS WITH MICROSCOPIC ENTERITIS: A RETROSPECTIVE STUDY

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Introduction: Non celiac gluten sensitivity (NCGS) is an emerging gluten-related disorder most likely characterized by a selective involvement of innate immune system. Some reports suggested a possible association with other autoimmune diseases. We aimed to investigate whether the presence of autoimmune stigmata in a group of patients with both clinical suspicion of NCGS and histological picture of microscopic enteritis could be predictive factors of NCGS.

Aims and Methods: Patients with microscopic enteritis were followed up by means of periodical laboratory and clinical examinations. At baseline, we collected data about previous clinical history, including existence of autoimmune diseases, and patients were tested for autoantibody assay. NCGS was diagnosed according to Salerno criteria, while other causes of microscopic enteritis were diagnosed according to well-established protocols. Patients with celiac disease were excluded from the final analysis. Student's t and chi-square test were applied in univariate analysis for continuous and binary variables, respectively. Kaplan-Meier curves were drawn and Cox regression was used to estimate hazard ratios (HR).

Results: 63 patients were included in our final analysis. 22 had a final diagnosis of NCGS, while the remaining 41 had non gluten-related causes of microscopic enteritis (irritable bowel syndrome was found in 34). The prevalence of autoimmune thyroiditis was higher among NCGS (40.1%) than in other microscopic enteritis (14.6%, $p = 0.03$). Furthermore, we found in NCGS a higher positivity rate for IgG anti-gliadin antibodies (AGA) (27.3% versus 2.5%, $p = 0.006$) and anti-nucleus autoantibodies (ANA) (45.4% versus 12.2%, $p = 0.005$). Autoimmune thyroiditis was associated to an increased risk of NCGS diagnosis (HR = 2.4), but with a not significant trend ($p = 0.06$). Both ANA (HR = 2.4, $p = 0.04$) and AGA (HR = 2.7, $p = 0.04$) were directly associated to NCGS diagnosis.

Conclusion: NCGS may have a cohort of autoimmune stigmata that can precede its diagnosis and may have a predictive value.

Disclosure: Nothing to disclose

P0594 COGNITIVE IMPAIRMENT IN COELIAC DISEASE: NORMALIZATION FOLLOWING GLUTEN-FREE DIET

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Introduction: Patients with coeliac disease commonly report symptoms of 'brain fog'. The mechanisms are poorly understood, but disease-related cognitive deficits and psychological problems have been suggested.

Aims and Methods: The aim of the study was to register self-reported symptoms of inattention and concentration impairment in coeliac disease before and after treatment with gluten-free diet, compared to a healthy control group.

Patients with newly diagnosed coeliac disease were included consecutively from 2 out-patient clinics (Oslo University Hospital and Lovisenberg Diaconal Hospital). The patients completed the questionnaires Adult ADHD Self-Report Scale v1.1 Symptoms Checklist (ASRS) and Hospital Anxiety and Depression Scale (HADS) prior to start of a gluten-free diet and after at least 12 months on the diet. Health care personnel at Oslo University Hospital served as healthy controls.

Results: A total of 33 newly diagnosed coeliac patients (median age 38, range 19–72, 24 women, 9 men) were included in the study. Of these, 27 patients met for follow up after minimum 12 months and repeated the questionnaires. 60 healthy controls (median age 45, range 24–69, 41 women, 19 men) completed the same questionnaires.

Coeliac patients had significantly higher scores than healthy controls on ASRS (median 27.0, IQR 20.0–35.5 vs. median 22.5, IQR 19.0–26.0, $p = 0.007$) and HADS (median 8.0, IQR 5.0–13.0 vs. median 5.0, IQR 2.0–8.0, $p = 0.0008$). After minimum 12 months on a gluten-free diet, coeliac patients improved their results on both ASRS (median 23.0, IQR 17.0–28.0, $p = 0{,}013$) and HADS (median 6.0, IQR 2.0–10.0, $p = 0{,}003$). There was no difference between coeliac patients on a gluten-free diet and healthy controls.

Conclusion: Coeliac patients reported significantly more symptoms than healthy controls on ASRS and HADS. The difference in regard to healthy controls disappeared after introduction of a gluten-free diet.

Disclosure: Nothing to disclose

P0595 DO CLINICAL SYMPTOMS OR SEROLOGY CORRELATE WITH CAPSULE ENDOSCOPY FINDINGS IN COELIAC DISEASE?

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Introduction: Small bowel capsule endoscopy (SBCE) has a useful role in detecting macroscopic changes and identifying complications of coeliac disease (CD).

Aims and Methods: In this study, we aimed to identify the relationship between clinical parameters to SBCE findings in patients with CD in comparison to a control group.

Patients with a history of histology confirmed CD (Marsh 3 grade) who underwent a SBCE were included in this study. A group of age matched patients undergoing SBCE for other indications were selected as a control group. Demographic data, clinical symptoms, serology and SBCE findings were collected.

Results: 86 patients (mean age 53.8 years; SD±14.8) with CD who underwent a SBCE were included. These were compared to 85 healthy, age (52.8 years; SD±1.17; $p = 0.630$) and gender-matched controls with a normal SBCE. Indications for SBCE in the CD group included: anaemia (16.3%), ongoing clinical symptoms (100%). Indications for controls included: anaemia (3.5%), gastrointestinal symptoms (100%), raised faecal calprotectin (17.6%).

Patients with CD had a mean duration of disease of 9.75 years SD±14.4. Histology at time of SBCE was Marsh: 0 (16.0%), 1 (12.0%), 2 (2.0%), 3a (24.0%), 3b (18.0%), 3c (28.0%). Areas of small bowel (SB) affected on SBCE were: proximal (55.8%), mid SB (1.2%), distal (3.5%), diffuse (4.7%), proximal and mid SB (5.8%), proximal and distal SB (1.2%). 14% of patients had a normal SBCE.

There was a significant correlation between small bowel transit (SBT) and length of abnormal SB ($p = 0.004$) in patients with CD. There was a significant longer SBT in CD patients than in controls (271.1 SD±13.1 vs 220 SD±97.6 minutes, $p = 0.006$).

There was a significant correlation between anti-gliadin IgA ($p = 0.001$), anti-gliadin IgG ($p = 0.0001$) and SBT and anti-gliadin IgA ($p = 0.038$), anti-gliadin IgG ($p = 0.001$) and length of abnormal SB. There was a significant correlation between anti-gliadin IgG and percentage of SB affected ($p = 0.017$).

There was no significance in mean SBT ($p = 0.462$), length of abnormal SB ($p = 0.194$) and percentage of affected SB ($p = 0.285$) across Marsh classifications. Those with scalloping on SBCE were more likely to be of Marsh 3B (30.0%) and 3C (45.0%) ($p = 0.020$). Patients with villous blunting were also more likely to be of Marsh 3B (28.6%) and 3C (57.1%) ($p = 0.013$).

There was no significance in SBT, abnormal length and percentage SB affected across presenting symptoms.

Conclusion: SBCE findings in CD correlate with serology (anti-gliadin IgA, anti-gliadin IgG). We have shown that SBT correlates with length of abnormal SB, thus confirming that SBT is affected by abnormal SB. This is the first study confirming a longer SBT in CD patients by SBCE.

Disclosure: Nothing to disclose

P0596 WHAT IS THE ROLE OF CAPSULE ENDOSCOPY IN EVALUATING PATIENTS WITH REFRACTORY COELIAC DISEASE?

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Introduction: Small bowel capsule endoscopy (SBCE) is used in refractory coeliac disease (RCD) to assess the extent of disease and ensure there are no complications (lymphoma or ulcerative jejunitis). However there are no published reports on SBCE in RCD following immunosuppressive therapy.

Aims and Methods: Patients with histologically confirmed refractory coeliac disease (RCD) who underwent a SBCE at baseline and after treatment were enrolled in this study. These were compared to a group of control CD patients with no underlying RCD.

Results: 19 patients (median 53 years) with RCD (12 patients; 63.2% - type 1) were compared to 28 patients with control CD (median 48 years). There was no statistically significant difference in duration of disease, gender, age at SBCE and serology between the 2 groups.

Patients with RCD were more likely to have worse histology (Marsh 3a-c) than SBCE control CD who had a higher percentage of normal histology at the time of SBCE ($p = 0.002$) Those with RCD had a longer abnormal small bowel (SB) mucosa (185 SD±167.6 vs 29.5 SD±73 minutes $p = 0.0001$) and longer percentage of abnormal SB (53.9 SD±38.0 vs 6.9 SD±15.2 minutes $p = 0.0001$) when compared to those with control CD.

A repeat SBCE was carried out after a mean of 9.63 SD±6.6 months in patients with RCD following treatment. There was no statistical significant difference in histology and serology at the time of the first and second SBCE. Patients received the following treatment: 36.8% steroids, 26.3% immunosuppressants, 36.1% combination of mycophenolate / azathioprine and steroids. However, there was an improvement in the length of abnormal SB mucosa (185 vs 116 minutes; $p = 0.035$) and the percentage of abnormal SB (50.8 vs 32.9%; $p = 0.027$). 7 patients (36.8%) had diffuse mucosal involvement on the first SBCE but only 4 (21.1%) had diffuse disease on repeat SBCE ($p = 0.007$). There was no statistical correlation between coeliac serology and small bowel passage time, length of mucosal abnormality and percentage of affected SB at first and second SBCE. The same findings were also true for histology.

Conclusion: More severe SB involvement on SBCE can be found in patients with RCD. This is the first study that shows an improvement in SB abnormality on SBCE following treatment of RCD patients. Histology is useful in distinguishing RCD from non-RCD but not for assessing improvement in patients with RCD following treatment. SBCE might potentially be regarded as a less invasive, more accurate way of following up these patients.

Disclosure: Nothing to disclose

P0597 FREQUENCY AND DIFFERENTIAL CHARACTERISTICS OF ULTRASHORT CELIAC DISEASE

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Introduction: Ultrashort celiac disease (USCD) is a novel CD subtype limited to the duodenal bulb (D1), with recently conflicting frequency rates (0.1% to 10%). Compared to conventional CD (CCD), a mild clinic and histologic phenotype with minimal laboratory abnormalities has been reported. However, we currently lack data on flow cytometry findings in these patients.
Aims and Methods: Unicenter prospective study conducted from February 2015 to February 2018, including patients with a new diagnosis of CD. A systematic biopsy protocol (separate biopsies for flow cytometry and histologic study from D1 (1–2) and D2 (2–4)) was performed in all patients undergoing duodenal biopsies to rule out CD. CD diagnosis was defined by Catassi and Fasano criteria plus compatible duodenal flow cytometry (CD103+ > 90, TCR gammadelta > 16, and NK-CD3 < 8), either in D1 or both D1+D2. Baseline characteristics were compared between CCD and USCD patients.
Results: A total of 66 patients (54% pediatric) with a new diagnosis of CD were included, of whom 7 (10%) showed USCD. No significant differences were observed between CCD and USCD regarding demographic, clinic, laboratory or CD serology parameters. Of note, 71% of USCD showed intermittent positive CD serology titres within a 5-yr period before diagnosis, and CD had been previously ruled out in 54% of them by means of normal D2 biopsies. Marsh I-II lesions on D1 histology were significantly higher in USCD compares to CCD patients (60 % vs. 15%, p 0.04). As for flow cytometry, no relevant differences in D1 were observed regarding IELs or TCR gammadelta between groups, whereas typical NK-CD3 count was significantly less diminished in USCD patients (CCD 1.2 ± 0.9 vs. USCD 7.57 ± 5.52, $p < 0.001$).
Conclusion: Up to 10% of pediatric and adult CD patients in our series showed USCD. No villous atrophy was documented in up to 57% of patients with USCD and flow cytometry was instrumental for an adequate diagnosis. A immunophenotype with a minimal decrease in NK-CD3 cells, mimicking that of CD patients on a gluten-free diet, was observed in USCD patients.
Disclosure: Nothing to disclose

Reference

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P0598 MICRORNA PROFILING AS A GUIDE TO PERSONALIZED MEDICINE IN ENTEROPATHY ASSOCIATED T-CELL LYMPHOMAS AND REFRACTORY CELIAC DISEASE

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Introduction: Peripheral T-cell lymphomas (PTCL) are considered orphan diseases and develop in the setting of chronic inflammation as celiac disease (CD). A small proportion of CD patients develops refractory celiac disease (RCD), associated with an increased risk of enteropathy associated T cell lymphoma (EATL), In this context our group has focused on EATL in CD patients with the aim to profile microRNA contents in CD, RCD and EATL patients to obtain molecular biomarkers useful to classify and stratify CD patients according to their 'neoplastic risk'.
Aims and Methods: Clinical series were composed by 7 RCD, 24 EATL, 10 AITL, 10 ALCL, 21 PTCL-NOS. EATL and lymphocytic infiltrate of RCD II (RCD-TIL), were obtained by Laser MicroDissection (LMD6000, Leica) from FFPE blocks. The expression profile of 301 miRNA was determined using TaqMan Array Microfluidic Cards (Thermo Fisher Scientific). Statistical analysis was performed using BRBArray Tools, GenePattern and R Software Packages.
Results: Our data show that miRNA profiling distinguished EATLs from other PTCLs. Specifically, EATL are characterized by a subset of miRNAs significantly up-or down-modulated compared to PTCLs. When RCD patients were considered in the analysis, our data showed that RCD II TILs are more similar to EATLs than to other PTCLs (by PCA analysis). Therefore these results suggest that unique miRNA signatures are conserved by RCD and EATL. On the other hand, our results show that specific oncosuppressor miRNA families are lost in EATL compared to RCD patients, such as the miR-200, let-7 and miR-192-215 families.
Conclusion: These data suggest that the identification of such signatures could trace the evolution of the inflammatory response of CD into a carcinogenetic process. The availability of accurate biomarkers could implement surveillance and early EATL diagnosis. CD patients' stratification according to their neoplastic risk could address follow-up and screening program, pursuing a 'personalized medicine' approach for CD patients.
Disclosure: Nothing to disclose

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P0599 PRIMARY GASTROINTESTINAL FOLLICULAR LYMPHOMA: A PROSPECTIVE, LONG TERM FOLLOW-UP CLINICAL STUDY OF 27 CASES

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Introduction: Primary gastrointestinal follicular lymphomas (PGFL) represent a rare entity whose clinical characteristics, management and prognosis after a long term follow-up, have not been well described.
Aims and Methods: Our aim was to prospectively analyse the clinical, biological, endoscopic and pathological features, as well as treatment outcome, of a series of consecutive patients with PGFL. All adult patients with PGFL, consecutively enrolled into the multicenter French national study between 1990 and 2014, were evaluated and followed up prospectively. Diagnosis was based on histomorphological criteria according to the WHO classification (confirmed by a reference pathologist). Follow-up comprised at least annual clinical, biological and endoscopic evaluation for all patients.
Results: Among 27 patients with PGFL included in the study, there were 13 men and 14 women, median age at diagnosis was 61 years (extremes: 33–79). The median follow-up was 88 months (6–190). The most frequent circumstances of diagnosis were fortuitous diagnosis (n = 11), followed by abdominal pain (n = 6), rectal bleeding (n = 5), and dyspepsia (n = 4). The duodenum was the most common site of involvement (n = 13) and multifocal localizations were observed in 7 patients (26%). Endoscopic aspect was the most frequently micronodular or polyposis type or mixture of both. Surveillance was the most frequently adopted attitude (low tumour mass) (n = 18, 66%), followed by chemotherapy (n = 7, 26%). The overall 5-year survival rate was 93%. Out of 16 patients receiving only surveillance, 6 (22%) reached a spontaneous complete remission. On the other hand, in 3 patients a transformation into high-grade lymphoma was observed. Moreover, in 3 patients secondary tumours were observed.
Conclusion: This study is the biggest series of PGFL including clinical and endoscopic results with a long term follow-up, published so far. It shows that PGFL are frequently fortuitously diagnosed by gastroenterologist during endoscopy, most frequently localized in the duodenum, and usually of an indolent course and good prognosis. However, in rare cases, their transformation into more aggressive high-grade lymphoma may be observed. An appropriate characterization and follow-up of these lymphomas is mandatory.
Disclosure: Nothing to disclose

P0600 NEUROENDOCRINE TUMORS OF THE GASTROINTESTINAL TRACT ARISING IN INFLAMMATORY BOWEL DISEASES: MORE THAN A COINCIDENCE?

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Introduction: The risk to develop gastro-intestinal malignancies is higher in patients affected by inflammatory bowel diseases (IBD). Apart from colorectal cancer, associated with grade and duration of the active inflammation, there is a growing evidence of neuroendocrine tumors (NETs) development in these patients and a correlation between these two diseases has been postulated. Enteroendocrine cells seem to be involved in the innate immune system machinery that is damaged in IBD: studies performed in IBD patients and experimental murine models proved that subtypes of interleukin-17 and Toll-like receptors (TLR) are expressed in neuroendocrine cells. In addition, defects of density, differentiation and hormonal production in enteroendocrine cells have been described in an experimental study and microcarcinoids have been detected in up to 10% of patients affected by long standing ulcerative colitis.
Aims and Methods: We report a series of 5 NETs developed in 4 IBD-affected patients. Histological parameters and immunophenotype of the neoplastic lesions were reviewed by an expert pathologist. The neoplastic lesion immunophenotype was assessed using A-chromogranin (CgA), synaptophysin (Syn), serotonin and somatostatin receptor type 2A (SSTR2A).
Results: We evaluated 4 patients (3 M, 1 F), aged between 32 and 63 years, affected by Crohn's disease (3 cases) and ulcerative colitis (1 case) with a diagnosis of gastro-intestinal NET. In 3 cases diagnosis was incidental after surgery for severe IBD relapse (1 was located in the appendix, 2 in the ileum), whereas in 1 case NET was discovered in the duodenum during an endoscopic examination. 4 G1 (ki67 < 3%, well differentiated, WHO 2017) NETs and a mixed epithelial - neuroendocrine tumor (MANEC) were detected in the resection specimens of the

four cases (Table 1). In 3 cases active IBD was found in specimens, with focal, slight increase of neuroendocrine cells, but no evidence of nodular hyperplasia. None of our patients showed evidence of loco-regional or at distance metastatic disease and no one experienced neoplastic relapse over the years of follow-up.
Conclusion: Although it was suggested that well recognized modulators of inflammatory response in IBD, such as interleukins, could modify the growth and functions of neuroendocrine cells, our results did not confirm these data, at least from a quantitative standpoint. In 3 of our cases, in fact, only a moderate increase of endocrine cells with no evidence of pre-neoplastic lesions was detected in the bowel mucosa with active disease, suggesting that IBD-induced inflammatory response may not be able to activate, via local or systemic signals, the carcinogenetic pathways of neuroendocrine lesions. NETs were incidentally diagnosed during surgery in 3 of the 4 cases. Considering that these lesions are often undetectable at endoscopy because of the submucosal - parietal location, a follow up including more specific imaging tests, such as Computed Tomography/ Magnetic Resonance Imaging (CT/MRI) and endoscopic ultrasonography (EUS), could improve early detection of these neoplasms. Larger studies are needed to confirm this hypothesis.
Disclosure: Nothing to disclose

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P0601 FEASIBILITY OF DOUBLE-BALLOON ENDOSCOPY-ASSISTED ENDOSCOPIC BALLOON DILATION OF STRICTURES SECONDARY TO PRIMARY SMALL INTESTINAL LYMPHOMA

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Introduction: Primary small intestinal lymphoma usually has a good prognosis, and is treated with chemotherapy alone. However, some patients with primary small intestinal lymphoma need surgery because of strictures before or after chemotherapy. Endoscopic balloon dilation (EBD) is a safe alternative in some patients with benign small intestinal strictures. However, there is no evidence of the efficacy or safety of EBD for small intestinal strictures secondary to primary small intestinal lymphoma. We retrospectively analyzed the clinical features of primary small intestinal lymphoma in patients treated with EBD to evaluate its efficacy and safety.
Aims and Methods: A total of 2081 patients underwent double-balloon enteroscopy (DBE) from April 2005 to January 2017 at Jichi Medical University Hospital. Five consecutive patients with small intestinal strictures secondary to primary small intestinal lymphoma treated with DBE-assisted EBD (four males, mean age 61±7.8 years) were retrospectively reviewed.
Results: All patients had a single stricture causing obstruction. Three of the five strictures formed before chemotherapy, including two follicular lymphomas and one marginal zone lymphoma, which were localized lesions, corresponding to Lugano classification stage I-II1. 2 of the 5 strictures occurred post-treatment, and included 1 follicular lymphoma and 1 diffuse large B-cell lymphoma, which were advanced lesions corresponding to Lugano classification stage IV. A total of 13 DBE-assisted EBD were performed for these 5 strictures. The diameter at the first dilation was limited to 10mm or less to avoid perforation before remission, and then gradually increased up to the largest possible size (12–18mm) to facilitate long-term patency. 4 of the 5 strictures required multiple DBE-assisted EBDs (2 lesions: 2 EBDs, 2 lesions: 4 EBDs). The median follow-up after the final DBE-assisted EBD was 22 months (9–94 months). 1 patient developed bowel obstruction during follow-up, due to adhesions (no recurrent stenosis). No adverse events associated with DBE-assisted EBD were observed.
Conclusion: DBE-assisted EBD provides favorable short-term outcomes in patients with small intestinal strictures secondary to primary small intestinal lymphoma. DBE-assisted EBD for the strictures associated with primary small intestinal lymphoma has the potential to be a safe and effective treatment to avoid surgery.
Disclosure: Hironori Yamamoto has patents for double-balloon endoscopy produced by Fujifilm Corporation. He also has a consultant relationship with the Fujifilm Corporation and has received honoraria, grants, and royalties from the company. Tomonori Yano, Yoshikazu Hayashi, and Keijiro Sunada have received honoraria from Fujifilm Corporation.

P0602 CHARACTERISTICS OF THE SMALL INTESTINAL GIST DIAGNOSED BY BALLOON-ASSISTED ENDOSCOPY

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Introduction: Small intestine GIST is regarded as roughly 20% of GIST on the whole, and while endoscopy is spreading and diagnostic opportunities are increasing. However, its clinical features are still unclear.
Aims and Methods: To clarify the clinical features of small intestinal GIST cases diagnosed by double balloon endoscopy (DBE), 32 consecutive cases, who were diagnosed as GIST from June 2003 until March 2018, were enrolled in this study. The clinical characteristics such as, sex, age, examination motive, endoscopic diagnosis, and other examination methods were analyzed, and the usefulness of biopsy diagnosis was evaluated retrospectively. Furthermore, the overall survival rate was also elucidated as a single-centre cohort study.
Results: There are 17 males and 15 females. Average age is 66 ± 14 (30–83) years old. Number of lesions is 27 cases (84.4%) with single occurrences and 5 cases with repeated occurrences.
Lesion sites is 4 cases of deep duodenum, 25 cases of jejunum and 3 cases of ileum.
Motives for examination is 27 cases of Gastrointestinal bleeding (16 cases of black feces, 7 cases of anemia, 4 cases of bloody stools), 2 cases of abdominal pain, 2 cases found while following up on other diseases, 1 case of positive PET scan.
Abdominal CTs were performed before DBE in 28 cases, and 4 cases (14.3%) of those unable to identify lesions via CT scan, but 2 of those 4 cases were identified via capsule endoscopy, and the remaining 2 cases identified only through DBE. On the other hand, in 3 cases (9.4%) where lesions were identified beforehand in the CT scan, the lesions could not be rendered in the DBE, but in 1 case where the scope could not be inserted into the lesion site, the lesion site was able to be identified through contrast radiography. Capsule endoscopy was performed in 15 cases, with 4 cases (26.7%) failing to identify the lesion, but in all 4 cases it was possible to identify the lesion via DBE. In 20 (69.0%) of the 29 cases where lesions were able to be observed via endoscopy, endoscopic observation revealed accompanying apex ulceration.
DBE biopsy diagnosis was performed in 18 (56.3%) cases, 12 (66.7%) of which histological diagnosis was possible. Post-biopsy bleeding was observed in 6 cases (33.3%). The overall 1-, 3-, and 5-year survival rates were 96.2% (95% CI, 89.0% to 100%), 96.2% (95% CI, 89.0% to 100%), and 77.5% (95% CI, 59.6% to 100%).
Conclusion: With small intestine GIST, there are rare cases where CT scan and capsule endoscopy are unable to identify lesions, and especially when bleeding is in doubt, it is suggested that balloon-assisted endoscopy should be performed with the possibility of GIST in mind. The diagnostic rate of biopsy by DBE cannot be said to be sufficient, and with a high frequency of post-biopsy bleeding, it goes without saying that safety can also be regarded as insufficient. In cases where biopsy diagnosis is commensurate with the risk of bleeding and diagnosis by endoscopic imaging is difficult, we think that this should be performed with caution.
Disclosure: Nothing to disclose

P0603 TUMOUR DETECTION RATES AT CAPSULE ENDOSCOPY PERFORMED FOR THE INVESTIGATION OF IRON DEFICIENCY ANAEMIA

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Introduction: Iron deficiency anaemia (IDA) is a common problem seen by gastroenterologists and a key aim in its investigation is the diagnosis or exclusion of malignancy. Currently the BSG guidelines only suggest small bowel imaging if there is an inadequate response to iron therapy post non-diagnostic upper and lower gastrointestinal endoscopy1.
Aims and Methods: The aim of this study was to review the role of capsule endoscopy (CE) in the investigation of IDA, with a focus on the detection of neoplasms. All CEs were undertaken over a 5-year period at a medium sized district general hospital for recurrent IDA or obscure GI bleeding (208 of a total of 471) were reviewed. The results were divided into neoplastic findings, clinically significant but non neoplastic findings and insignificant or normal findings. For those cases that detected a potential neoplasm, electronic records were reviewed to ascertain the final diagnosis.
Results: 208 CEs were reviewed. The patients had an age range of 19 to 91 years with a median age of 68. 115 of the patients were women and 98 men. Of these 208, 10 (4.8%) were found to have a potential neoplasm, 148 (71.2%) were found to have clinically significant but non neoplastic findings, 50 (24%) were found to have insignificant or normal findings. Of the 10 that were found to have a suspected neoplasm; 1 was a tumour in the third part of the duodenum, 3 were Gastro Intestinal Stromal Tumours (GIST), 1 was a neurofibroma, 1 was a small bowel lymphoma, 1 an ileal neuroendocrine tumour, 1 was a caecal tumour and 2 had non-malignant findings (duplication cyst and small bowel Crohn's disease). The mean age of those with malignancy was 68 versus 64 in those without malignancy. The mean haemoglobin of those with malignancy was 79. Of the other significant pathology detected; Angioectasia was the primary diagnosis in

114 (54%), small bowel Crohns in 14 (6.7%), NSAID enteropathy in 11 (5.2%) and miscellaneous causes in 7 (3.4%). This series has a detection rate of 3.4% (7 out of 208) for neoplasia. The tumour detection rate of 3.4% in our series of 208 IDA patients with a mean age of 68 is compared with a rate 4.5% from a series of 220 IDA patients with a mean age of 40.5. 2

Conclusion: In our series the diagnostic yield of CE for IDA is 76.0%. 3.4% were diagnosed with malignancy. Patients with malignancy were older than those without. While small bowel tumours are rare, our experience suggests that they are more common than previous data suggests. CE is a beneficial tool in the investigation of IDA with negative bi-directional endoscopies, particularly in the investigation for malignancy

Disclosure: Nothing to disclose

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P0604 PROGRAMMED CELL DEATH LIGAND-1 EXPRESSION IS ASSOCIATED WITH MICROSATELLITE INSTABILITY IN NON-FAMILIAL SMALL BOWEL CARCINOMAS: RESULTS FROM THE SMALL BOWEL CANCER ITALIAN CONSORTIUM

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Introduction: Small bowel carcinomas (SBC) are rare neoplasms, often associated with poor prognosis and limited therapeutic challenges. Several predisposing conditions for SBC development are known, including immune-mediated intestinal disorders, such as coeliac disease (CD) and Crohn's disease (CrD). CD-associated SBC (CD-SBC) harbor much more frequently microsatellite instability (MSI) in comparison with both CrD-associated SBC (CrD-SBC) and sporadic SBC (spo-SBC).[1] In colorectal and gastric cancers MSI is associated with expression of programmed cell death ligand-1 (PD-L1),[2,3] a crucial immune checkpoint aimed at inhibiting and escaping immune system response, thus leading to responsiveness to PD-L1/programmed cell death protein-1 (PD-1) pathway blockade treatment.[4]

Aims and Methods: Aim of this study was to investigate PD-L1 expression in a large cohort of non-familiar SBC, either or not associated with CD or CrD, and correlated it with MSI status. We assessed PD-L1 by immunohistochemistry (clone E1L3N, Cell Signaling) in a total of 82 non-familial SBC, i.e. 32 CrD-SBC, 23 CD-SBC and 27 spo-SBC. We correlated PD-L1 expression with MSI, which was evaluated using a pentaplex panel of monomorphic mononucleotide repeats.

Results: PD-L1 positivity (>5% of tumour or immune cells) was seen in 22 (27%) cases, including 8 CrD-SBC (25%, 3 MSI and 3 non-MSI cases), 8 CD-SBC (35%, 7 MSI and one non-MSI) and 6 spo-SBC (22%, 3 MSI and 3 non-MSI). In all positive cases, PD-L1 was essentially expressed on stromal immune cells, which were predominantly macrophages restricted to the tumour invasive margin, while PD-L1 reactivity on tumour cells was found only in two, both MSI cases, i.e. one CrD-SBC (tumour cell membrane) and one CD-SBC (tumour cell cytoplasm). The frequency of PD-L1 expression did not differ significantly among the 3 groups. PD-L1 positivity was more frequently observed in MSI SBC (13/27, 48%) in comparison with non-MSI SBC (9/55,16%). The association between PD-L1 immunoreactivity and MSI status was statistically significant ($p = 0.0035$). The single CrD-SBC case with PD-L1-positive tumour cells had a lymphoepithelioma-like morphology and was positive for Epstein-Barr virus latent phase markers.

Conclusion: Our study showed an association between PD-L1 immunoreactivity and MSI status, similar to that reported in colorectal and gastric cancers. Interestingly, an Epstein-Barr virus positive case of CrD-SBC also expressed PD-L1 on tumour cells. These findings could be relevant in selecting patients affected by SBC in whom therapeutic PD-1/PD-L1 inhibition could be beneficial.

Disclosure: Nothing to disclose

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MONDAY, OCTOBER 22, 2018 09:00-17:00

Nutrition I - Hall X1____

P0605 GUT MICROBIOTA COMPOSITION AND OBESITY IN APPARENTLY HEALTHY INDIVIDUALS FROM MOSCOW

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Introduction: The diversity of microbes living within us, a large proportion of which reside within our gut, has been increasingly appreciated. Recent evidence suggests that the gut microbiota (GM) plays a role in energy harvest, storage, and expenditure. E.g. GM transplantation from obese to germ-free mice had been shown to induce obesity [1]. The purpose of the present study was to evaluate the differences between GM composition in lean and obese subjects.

Aims and Methods: The study included untreated subjects aged 25 to 76 years carefully selected through exclusion of chronic diseases by means of clinical and laboratory evaluation, abdominal US, ECG, treadmill test, ECHOCG.

Microbiota composition was studied by sequencing of the V3-V4 variable regions of the 16S rRNA gene according to recommended protocol of 16S metagenomic sequencing Library Preparation. Diet - by quantitative assessment. Statistical analysis was performed using the R3.1.0., generalized linear models (FDR, age, and sex adjusted).
Results: 104 participants were included (38 men). BMI obesity (O) was determined in 26%, abdominal obesity (AO) in 55%. O and AO were associated with high abundance of gram-negative opportunistic genera Serratia (FDR 0.003; 0.004) and Prevotella (FDR < 0.001; < 0.001). Low Oscillospira abundance was strongly correlated with AO (FDR < 0.001). This genus is a 'central enigmatic component' of the gut microbiome, which reduce inflammation and associated with leanness and high physical activity level. The average caloric intake was 2156±545 kcal. Average daily intake of carbohydrates 210±91g; proteins 79±20 g; fat 107±32g. Bifidobacterium (FDR 0.008) representation was increased and Serratia decreased (FDR 0.008) in those who consumed more starch. High fat consumption was associated with high Serratia (FDR 0.014) and low Oscillospira (FDR 0.004) abundance. Thus, high representation of opportunistic bacteria was associated with O and AO. In addition, the bacteria were more presented among those who consumed smaller amounts of starch, and beneficial bacteria abundance was lower in those who consumed a lot of fat.
Conclusion: We concede that GM composition is strongly associated with obesity and GM modification by diet may be a relevant therapeutic avenue for obesity.
Disclosure: Nothing to disclose

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P0606 STRESS RESPONSE IN HIGH-FAT DIET-INDUCED OBESE MICE: FOCUS ON INTESTINAL PERMEABILITY

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Introduction: Obesity is a major public health issue; it may have different impacts depending on its grade. Indeed, grade I/II obese subjects seem to be protected from irritable bowel syndrome (IBS) while IBS prevalence is increased by a factor of six in morbid obesity patients than to the general population.
Aims and Methods: The aim of the present study was to evaluate the response of obese mice to a stress model, the water avoidance stress (WAS), which is frequently used to study the pathophysiology of IBS.
Male C57Bl/6 mice fed a high fat diet (60% kcal as Fat; HFD) or not (standard diet; SD) for 12 weeks (W12). At W12, WAS (1h/day for 10 consecutive days) was performed (SD-WAS and HFD-WAS, $n = 15$) or not (SD-CC and HFD-CC, $n = 15$). Body composition was assessed by EchoMRI (at W0, W12 and after WAS). The intestinal permeability was evaluated *in vivo* by oral gavage with FITC-dextran. Colonic permeability was assessed *ex vivo* by using Ussing chambers. Expression of tight junction proteins and plasma corticosterone were evaluated by westernblot and ELISA, respectively.
Results: HFD mice had a higher body weight than SD mice, related to increased fat mass without altering lean mass. In response to WAS, only HFD mice lost weight. A strong increase in plasma corticosterone was observed among HFD-WAS mice compared to SD-CC and SD-WAS mice. HFD-WAS mice also showed an increase in intestinal permeability compared with the other groups. There was a positive correlation between intestinal permeability and corticosterone levels ($r = 0.51$, $p = 0.021$). Finally, *in vivo* colonic permeability was increased in SD-WAS, HFD-CC and HFD-WAS groups compared with SD-CC group but in more pronounced manner in HFD-CC and HFD-WAS groups. Occludin expression was reduced in SD-WAS, HFD-CC and HFD-WAS compared with SD-CC.
Conclusion: High-fat diet obesity modifies the response to stress in mice with an increased sensitivity and enhanced intestinal permeability. The involved mechanisms and the impact on the functional bowel disorders remain to be determined.
Disclosure: Nothing to disclose

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P0607 OVERNIGHT OR MORNING ONLY SPLIT DOSING WITH 1 L POLYETHYLENE GLYCOL NER1006 CAN DELIVER 92% OR HIGHER RATES OF SUCCESSFUL OVERALL COLON CLEANSING IN NORMAL WEIGHT AND OBESE PATIENTS

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Introduction: Adequate bowel cleansing is essential for effective colonoscopy, but may be hard to achieve in overweight or obese patients.[1] The ESGE minimum performance standard rate for adequate colon cleansing success is 90%, a measure which includes overweight or obese patients.[2] NER1006 is a novel 1 L polyethylene glycol (PEG)-based bowel preparation. It was evaluated in the two phase 3, randomized, treatment-blinded central reader-assessed trials MORA[3] and NOCT.[4] This post hoc analysis of MORA and NOCT assessed the cleansing efficacy of 2 split dosing regimens of NER1006 in patients according to body mass index ranges (BMI).
Aims and Methods: Patients aged 18–85 years were randomized to receive a split-dosing regimen of either evening/morning (PM/AM) NER1006, or same day morning only (AM/AM) NER1006. Overnight split dosing started at ~6:00 pm (± 2 h) with dose 2 at ~6:00 am (± 2 h). Morning only dosing started at ~5:00 am (± 2 h) with dose 2 at ~7:00 am (± 2 h). The percentage of patients with overall bowel cleansing success (Harefield Cleansing Scale (HCS) grades A and B) was analysed for normal weight patients (BMI 18.5–24.9), overweight patients (BMI 25.0–29.9) and obese patients (BMI ≥30.0), respectively. Data were analysed using the modified full analysis set 2 (mFAS2) population, which comprised all patients who received at least 1 dose of study drug and who had documented primary endpoint data from a central reader.
Results: The mFAS2 population had 787 patients. Data from 776 (227 normal weight, 310 overweight, 239 obese) were included in the analysis (Table 1). 11 patients were excluded for missing or low (< 18.5) BMI data (insufficient sample sizes). Among normal weight and obese patients, both dosing regimens NER1006 PM/AM and NER1006 AM/AM attained overall cleansing success rates of 92% or higher. For overweight patients, NER1006 PM/AM attained overall cleansing success rates of 90–98%.
Conclusion: Overnight or morning only split dosing with NER1006 delivered overall HCS cleansing success (e.g. adequate level cleansing) in at least 92% of normal weight or obese patients and for overweight patients, NER1006 overnight split dosing was successful in 90–98%. NER1006 therefore meets the ESGE minimum performance standard for colon cleansing in these weight groups.
Disclosure: Bharat Amlani and Lucy Clayton, employees of Norgine Ltd

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Abstract No: P0607

Overall HCS cleansing success, per BMI category	NER1006 PM/AM	NER1006 AM/AM	NER1006 PM/AM
Phase 3 trial	MORA	MORA	NOCT
Patients (mFAS2), N	262	270	255
Normal weight patients (BMI 18.5–24.9), n (%)	83/87 (95%)	84/91 (92%)	47/49 (96%)
Overweight patients (BMI 25.0–29.9), n (%)	95/97 (98%)	100/114 (88%)	89/99 (90%)
Obese patients (BMI ≥30.0), n (%)	69/72 (96%)	58/62 (94%)	98/105 (93%)
Patients with missing BMI data or BMI < 18.5, n	6/262	3/270	2/255

[Table 1. Overall HCS colon cleansing success using split dosing with NER1006 in normal weight, overweight and obese patients]

P0608 DUODENO-JEJUNAL BYPASS LINER FOR THE TREATMENT OF DIABETES MELLITUS IN OBESE PATIENTS: COMPLETENESS OF DUODENAL BLINDING AS THE KEY FACTOR FOR EFFICACY

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Introduction: The global increase in obesity incidence results in an increase of type 2 diabetes mellitus (T2DM). Surgical treatment has proven to be effective, however it carries a high risk of complications. The duodenal-jejunal bypass liner (EndoBarrier®, GI Dynamics, EB) is an endoscopic implant that mimics the intestinal bypass portion of the Roux-en-Y Gastric Bypass. It results in weight loss and improvements in glucose control in obese patients with T2 diabetes mellitus (T2DM).

Aims and Methods: This is a analysis of a prospective, controlled, multicentre study aimed to identify factors associated with an outcome of EB for T2DM. Seventy subjects (45 with an implant, 25 controls) were included in the study. The groups were comparable with respect to age, gender, BMI (mean 41.7 vs. 39.5 kg/m2), T2DM duration (7.8 vs. 8.3 years), HbA1c level (88 vs 86 mmol/mol) and T2DM treatment. In the EB group, all devices were successfully implanted. Only 6 devices had to be explanted prior to the end of the 10 months study period (bleeding, dislocation and need for ERCP because of choledocholithiasis). At 10 months there was significantly greater weight loss and %EWL (19% vs. 7% and 43 vs. 12) and significantly improved long term compensation of T2DM marker HbA1c (decreased by 25 vs. 10 mmol/mol) in the EB group. T2DM medicinal treatment could be reduced in more device subjects than controls. There was no serious adverse event. Deepness of anchor ingrow, lower initial BMI and lower body height were identified as positive factors for efficacy of EB for T2DM compensation.

Conclusion: The EB is safe when implanted for 10 months, and results in significant weight loss and HbA1c reduction. Deepness of anchor ingrow, lower initial BMI and lower body height could be positive factors for efficacy.

Disclosure: Nothing to disclose

P0609 THE EFFECT OF THE DIETICIAN SUPPORT AND BEHAVIOURAL THERAPY IN PATIENTS UNDERGOING INTRAGASTRIC BALLOON TREATMENT FOR OBESITY

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Introduction: Obesity is an important public health problem that has reached epidemic proportions in the world. The placement of intragastric balloon (IGB) is nowadays widely accepted as a main endoscopic procedure to lose weight. Other than the endoscopist, the dietician is the only professional considered essential in the multidisciplinary team for IGB patient management. He is considered to play an important educational role just before and after the endoscopic procedure, but his real role during the follow up when IGB is in site has not been investigated. The aim of this study is to evaluate the impact of dietician support and behavioural therapy in patients treated with IGB while the device is in site.

Aims and Methods: We retrospectively reviewed records of 170 obese patients subjected to IGB treatment in Gastroenterology Unit, University Hospital of Udine, Italy, from 2003 to 2015. Their epidemiological characteristics were also evaluated. Patients were treated with nonadjustable fluid-filled (700 ml average filling, mean residence time 204±23 days) IGB. During the follow-up patients were interviewed regarding their diet and calories intake and a weight check-up was conducted in order to calculate % total body weight loss (%TBW) and Δ Body Mass Index (ΔBMI). According to our protocol, during the frame of IGB in site, patients were invited to undergo a dietician check-up (DC) every 1.5 months accompanied by cognitive behavioural therapy in order to obtain a behaviour-change intervention. According to their adherence to DCs, patients were grouped in not adhering (0 DC), partially adhering (1–2 DCs) and totally adhering ($\geq$ 3 DCs) to the protocol. A comparison was made among the three groups regarding %TBW and ΔBMI at 180±15 days during IGB in site. To compare quantitative variables the Kruskal-Wallis test was used.

Results: Among the 170 patients (58 males, 112 females, mean age 44±12 years) included in the study, mean initial weight was 123.6±27.7 kg and mean baseline BMI was 44±9 kg/m.^{2} Body weight data at 180±15 days during IGB in site, as well as adherence to DCs were available for 146 out of 170 patients. There was no difference between the patients adhering, partially adhering and not adhering to DCs regarding %TBW at 180±15 days ($p = 0.17$). However not adhering patients had a higher ΔBMI at 180±15 days in comparison to those adhering or partially adhering to CDs ($p = 0.03$). Mean pre-procedural weight and BMI were lower in patients who were treated with psychotropic drugs prior to IGB treatment ($p = 0.002$ and $p = 0.025$, respectively); however no difference was observed in %TBW and ΔBMI at 180±15 days during IGB in site ($p = 0.20$; $p = 0.51$). Mean pre-procedural BMI was higher in patients with obese first degree relatives ($p = 0.03$) and a significant difference was observed in relation to %TBW and ΔBMI at 180±15 days during IGB in site ($p = 0.03$; $p = 0.048$).

Conclusion: Dietician support accompanied by behavioural therapy seems not to be effective in lowering weight as an addition to the obesity treatment using IGB when the device is in site. Prospective studies including a greater number of subjects are needed in order to further enlighten this issue.

Disclosure: Nothing to disclose

P0610 ADHERENCE TO VITAMIN SUPPLEMENTATION AND NEW LIFESTYLES AFTER BARIATRIC SURGERY

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Introduction: Over the past decade, several studies have demonstrated that bariatric surgery (BS) is the gold standard for the treatment of morbid obesity and weight-related comorbidities and is far more effective than nonsurgical interventions. However, it permanently alters the gastrointestinal anatomy and might induce long-term deficiencies and absorption issues. Adherence to treatment recommendations such as multivitamins, iron tablets, Vitamin B and D supplementations is a crucial aspect in the management of patients submitted to bariatric surgery.

Aims and Methods: The aim of this study was to evaluate the adherence to treatment recommendations in a large population of obese patients submitted to BS using a new validated web-based instrument.

An anonymous web survey by a new validated questionnaire consisting of 23 items evaluating: a. Bariatric procedures performed; b. Individual reasons underlying BS; c. Lapse of time since last BS, d. the frequency of follow-up (FU) visits post BS, e. Perception of well-being post BS; f. Adherence to recommendations post BS; g. Changes in lifestyles, was launched through e-methods. Participants have been invited among patients who underwent BS from 1996 to 2016. A single surgeon (L. A). performed all procedures.

Results: We received an automatic notification of delivery from 1100 out of 1600 obese subjects and 290 (81.4 % female, mean age 39.5 ± 10.1) filled in the questionnaire. 59% underwent Sleeve gastrectomy (SG), 31 % Roux-enY- gastric Bypass (RYGB), 7.2 % adjustable gastric banding (AGB), 2.8% other procedures such as mini gastric-one anastomisis gastric bypass (MGB-OAGB) and duodenal switch (DS), 6.2% had a revisional procedure and only one underwent three bariatric operations. The time interval from surgical procedures was < 1 yrs in 20.9%, 1 to 3 yrs in 25.1%, 4 to 6 yrs in 29.6% and 7 to 10 yrs in 24.4 %. The last FU visit was < 1 yrs in 51%, < 2 yrs in 18 %, < 3 yrs in 6.9%, < 4 yrs in 5.9%, < 5 yrs in 4.5 % and > 5 yrs in 11.7% obese subjects. Only 31.4% adhere to treatment recommendations. The risk of non-adherence to treatment recommendations was around two times higher in malabsorptive (RYGB, DS, MGB-OAGB) than restrictive procedures (AGB and SG) and decreases with age and strict follow-up. (OR = 1.96, 95%CI: 1.256–3.058). It is also independent of sex, the time interval from BS and basal BMI. Moreover, 72% of subjects showed an improvement of their quality of life (QoL) due to a significantly stronger self-identity.

Conclusion: Adherence to treatment recommendations in our obese patients is low especially after malabsorbtive bariatric procedures possibly since in Italy, vitamin supplementation and micronutrient blood tests are not reimbursed by the national health insurance. Conversely, QoL strongly improved.

Disclosure: Nothing to disclose

P0611 THE EFFECTS OF OAT β-GLUCAN CONSUMPTION AT BREAKFAST ON APPETITE AND FOOD INTAKE, AS WELL AS BLOOD GLUCOSE, PLASMA INSULIN AND PLASMA GLP-1 CONCENTRATIONS IN HEALTHY SUBJECTS

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Introduction: High fibre consumption is associated with lower body weight (1), and improved postprandial glycemia (2). There is evidence that oat β-glucan lowers appetite and exerts an inhibitory effect on eating; however, not all studies are consistent and the underpinning mechanisms are not entirely understood.

Aims and Methods: We investigated the effects of 4 g high molecular weight (MW; 2.213 x10^6 g mol^{-1}) oat β-glucan on *ad libitum* eating, subjective appetite, glycaemia, insulinaemia and plasma GLP-1 responses in 33 normal-weight subjects (22 female/11 male, mean age (years): 26.9 ± 1.0, BMI (kg/m^2): 23.5 ± 0.4). The study followed a double-blind, cross-over design with subjects fed two different test breakfasts with and without oat β-glucan on two different days in random order, followed by an *ad libitum* test meal. Blood samples and ratings for subjective appetite were collected postprandially at regular time intervals. Viscosity of test meals were measured using a constant shear rheometer, Bohin Rheometer C-VOR 150 (Malvern Bohin Instruments) at a shear rate of 50 s^{-1}, representative of gastric conditions.

Results: Oat β-glucan increased feelings of fullness ($p = 0.046$) and satiety ($p = 0.021$), but did not affect energy intake or amount eaten at the *ad libitum* test meal. There was a treatment by time interaction for plasma GLP-1, plasma

insulin and blood glucose. GLP-1 was significantly reduced at 90 min ($p = 0.021$), blood glucose at 30 min ($p = 0.008$) and plasma insulin at 30 and 60 min ($p = 0.002$ and 0.017, respectively) following the oat β-glucan breakfast when compared with the control breakfast. Viscosity of test breakfast containing oat β-glucan was significantly greater compared to control ($p < 0.05$).
Conclusion: Four grams of high MW oat β-glucan lowers appetite but not *ad libitum* eating and beneficially modulates postprandial glycaemia and insulinaemia, however, it does not increase plasma GLP-1 secretion.
Disclosure: Robert. E. Steinert is an employee of DSM Nutritional Products, Basel, Switzerland.

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P0612 VARIABILITY IN THE NIGHT PROFILE OF TOTAL GHRELIN IN OBESE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Ghrelin is a hormone produced in the gastrointestinal tract. The main functions of ghrelin are the initiation of food intake and the stimulation of gastrointestinal motility. Obstructive sleep apnea is the most common sleep breathing disorder in which occurs repetitive upper airway obstruction causing fragmentation of sleep and decreasing sleep quality. The most important cause of sleep apnea is overweight. In the literature, we find reports that both inefficient sleep and obesity affect ghrelin but the results concerning their impact, especially on the night ghrelin profile, still require research[1,2].
Aims and Methods: Patients evaluated for sleep breathing disorders were divided into the study group with diagnosed obstructive sleep apnea and into control group. During sleep, blood samples were collected at 23, 1, 3, 5, 7. Total serum ghrelin was measured with a radioimmunoassay test, according to the manufacturer's instructions. Statistical analyses were performed to find correlations between total ghrelin levels and score in Epworth sleepiness scale and selected sleep parameters from polysomnography- apnea hypopnea index (AHI) and % snoring time during sleep were chosen. Moreover, the correlations between total ghrelin levels and parameters of obesity (BMI, abdominal circumference) were assessed.
Results: The study included 59 patients (49 men and 10 women), 46 patients were diagnosed with sleep apnea (OSA group). Most of the patients included in the study were overweight (20.3%) or obese (74.6%). After analysis of results in both groups, we observed a tendency towards lower ghrelin values in OSA group. However, only for values measured at 5 am this correlation was statistically significant, the trend in the other assays were close to statistical significance. There was no substantial relationship between ghrelin values and sleep parameters (AHI, % snoring time) and severity of daytime sleepiness (ESS). After analysis between obesity parameters and total ghrelin concentrations we found a statistically significant negative correlation between obesity parameters (stronger for BMI) and ghrelin levels in the first hours of sleep- at 23 and 1, while at 3 this correlation was close to statistical significance [Table 1]

	OSA group		Control		
Ghrelin	BMI	Waist circumference	BMI	Waist circumference	Both BMI
23:00	**−0.41(0.0050**)**	**−0.36 (0.0135*)**	0.32 (0.2799)	0.41 (0,1618)	**−0.31 (0.0185*)**
1:00	**−0.40(0.0069**)**	**−0.37 (0.0125*)**	0.21 (0.4936)	0.24 (0.4371)	**−0.30 (0.0203*)**
3:00	**−0.26 (0.0869)**	**−0.25 (0.0959)**	0.21 (0.4821)	0.22 (0.4706)	**−0.24 (0.0710)**
5:00	−0.21 (0.1739)	−0.21 (0.1707)	0.14 (0.6545)	0.23 (0.4481)	−0.21 (0.1219)
7:00	−0.21 (0.1637)	−0.23 (0.1371)	0.23 (0.4481)	0.28 (0.3538)	−0.18 (0.1749)
Mean	**−0.32 (0.0312*)**	**−0.28 (0.0561)**	0.26 (0.3839)	0.30 (0.3156)	**−0.26 (0.0485*)**

[Table 1. Correlation between obesity parameters and total ghrelin values.]
Conclusion: During sleep, in group with obstructive sleep apnea, we observed a trend towards lower total ghrelin values. There was no significant relationship between total ghrelin values and sleep parameters and severity of daytime sleepiness. We found a statistically significant, negative correlation between obesity parameters (stronger for BMI) and total ghrelin levels in the first hours of sleep. These results indicate that lower values of total ghrelin at night are probably not the effect of inefficient sleep, but the result of being overweight. Further research should focus on understanding the clinical significance of these results.
Disclosure: Nothing to disclose

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P0613 EXCESSIVE BODY FATNESS AT YOUNG AGE INCREASES RISK OF COLORECTAL CANCER: META-ANALYSIS AND DOSE-RESPONSE ANALYSIS

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Introduction: Colorectal cancer (CRC) was thought to be associated with overweight and obesity, and the CRC development may be due to early life exposures. However, the relationship between BMI at young age (age ≤30 years) and CRC remains less defined. We hypothesized that overweight and obese at young age were independent risk factors for later-life CRC risk.
Aims and Methods: We conducted a meta-analysis and dose-response analysis to quantify the association betwen colorectal cancer risk and overweight and obesity.
We searched Pubmed, Embase, Medline and Cochrane Library biomedical literature databases before Nov 16, 2017. Fourteen articles with 2 455 416 participants were included. The WHO definition was used to classify the BMI categories: overweight (≥25.0–29.9 kg/m^2) and obesity (≥30.0 kg/m^2) compared with normal weight (≥18.5–24.9 kg/m^2) as the reference category. Where non-standard categories of BMI and reference category were used, Hamling method was used to generate the adjusted risk ratios according to standard BMI categories and same reference category (normal). Random effect models and a dose-response analysis were used in this meta-analysis.
Results: Compared with normal weight people, overweight and obese young adult had a significant 16% (95% CI: 1.06–1.26) and 32% (95% CI: 1.11–1.56) higher risk of CRC, respectively. However, the association between BMI at young age and CRC risk may not exist for obese women (RR: 1.22 (95%CI: 0.99, 1.51)); Overweight, but not obese, may not a risk factor for rectal cancer (RR 1.12 (95% CI: 0.97, 1.29)). In dose-response analysis, we observed a linear relationship between BMI at young age and CRC risk. Each 1 kg/m^2 increment was associated with a 2% increased risk. Moderate heterogeneity was observed.
Conclusion: In conclusion, our meta-analysis, included 14 original studies, reveals that a 16% and a 32% higher risk of CRC for overweight and obese people separately when compared with normal weight people at their young age. Dose-response analysis indicates a 2% increase in risk of CRC for each 1 kg/m^2 increase in BMI at young age. These results indicate that reducing body fat at young adulthood could help prevent later life CRC risk.
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00-17:00

Paediatric: Upper GI - Hall X1____

P0615 SAFETY AND EFFECTIVENESS OF PER-ORAL ENDOSCOPIC MYOTOMY IN CHILDREN WITH ACHALASIA: A COMPARISON OF THE RESULTS IN PAEDIATRIC AND ADULT PATIENTS

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Introduction: Achalasia is a primary motility disorder characterized by incomplete lower oesophageal sphincter relaxation. It has a relatively low incidence among children. Endoscopic balloon dilation and laparoscopic myotomy were the available treatments for achalasia regardless of age until the introduction of per-oral endoscopic myotomy (POEM). POEM is demonstrated to be effective and safe for the treatment of adult patients with achalasia as a novel incision-free endoscopic surgery, however, it is rarely performed in children.
Aims and Methods: The objective of this study was to review the safety and effectiveness of POEM in paediatric patients by comparing the results of paediatric and adult patients. The data of 218 consecutive patients with achalasia who underwent POEM at our institution between September 2011 and June 2017 were retrospectively reviewed. The patients were classified into two groups: (A) paediatric patients, and (B) adult patients. Age, previous treatments for achalasia, duration of symptoms, pre- and post-POEM Eckardt scores, manometry findings, and treatment outcomes, including duration of hospitalization and occurrence of complications, were compared between the groups using the chi-square and Student's *t*-tests.
Results: There were 7 patients in group A and 211 in group B. The median age was 15.0 ± 3.1 years (range: 9–18 years) in group A and 52.0 ± 17.8 years (range: 19–93 years) in group B. The mean duration of symptoms was significantly longer for group B than for group A (122.9 months [range: 3–840 months] vs. 30.7 months [range: 1–84 months]; $p = 0.001$). The length of myotomy was statistically different between the groups (14.0 cm [range: 7–24] in group A and 15.0 cm [range: 5–28] in group B; $p = 0.046$) There were no statistically significant differences among the groups with respect to previous treatments for achalasia, median operation times, mean hospitalizations, or occurrence of complications. The median follow-up periods were 39.6 months [range: 18–54 months] for group A and 38.4 months [range: 10–79 months] for group B. Significant Eckardt scores

and integrated relaxation pressure reductions were achieved in both groups. No perioperative mortality or major postoperative complications occurred.
Conclusion: POEM is a minimally invasive, incisionless operation. POEM is a safe and effective operation for both paediatric and adult patients. POEM may be a useful treatment method for both paediatric and adult patients with achalasia. Long-term follow-up studies would be helpful to determine whether POEM could become an appropriate therapy for paediatric patients with achalasia in the near future.
Disclosure: Nothing to disclose

P0616 CHANGES OF MORPHLOGICAL DISORDERS OF GASTRIC MUCOSA IN CHILDREN WITH CHRONIC GASTRITIS CO-INFECTED WITH HELICOBACTER PYLORI AND EPSTEIN-BARR VIRUS AFTER A COURCE OF ANTIHELICOBACTER THERAPY

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Introduction: The persistence of Epstein-Barr virus in the gastric mucosa in Hp-associated chronic gastritis increases the prevalence, severity and activity of inflammation.
Aims and Methods: The aim of the work is to estimate the dynamics of morphological disorders of the gastric mucosa in children with chronic gastritis co-infected with *Helicobacter pylori* and Epstein-Barr virus after course of anti helicobacter therapy.
69 children aged 7–17 with chronic Hp-associated gastritis were observed. According to the study of gastrobiopsy there was a chronic inflammatory process in all cases. Via polymerase chain reaction Epstein-Barr virus (EBV) persistence in the gastric mucosa was detected in 46 out of 69 patients (66.7 %), highly pathogenic strains of *Helicobacter pylori* containing CagA gene were detected in 47 cases (68.1 %). In addition to the standard morphological study, morphometric analysis of the cellular composition of gastric glands was performed. Patients were examined twice: before and six months after the course of anti helicobacter therapy.
Results: Morphological study of gastrobiopsy materials conducted 6 months after the course of anti helicobacter therapy has allowed us to find out that none of the patients had eradication of *Helicobacter pylori*. In most cases, a decrease in severity of the process in the body of the stomach (62.5 %) and in the antral region (73.9 %) was recorded. However, every third patient was found to have no regression or progression of disorders of morphology of gastric mucosa. This dynamics of the pathological process in associated with co-infection with highly pathogenic strains of *Helicobacter pylori* and EBV (31.9 % against 13.6 % in patients with no co-infection, $p < 0,01$). The morphometric analysis of the cellular composition of fundum glands found that severe hyperplasia endocrinocytes remained in group of EBV- positive patients after 6 month, while the number of parietal cells increased by 56.3 %, in the pyloric glands. In EBV - negative patients their number did not change, there was a significant decrease in the number of endocrinocytes (39.0 % of the original figures, $p < 0,05$.
Conclusion: Co-infection of gastric mucosa of highly pathogenic strains of *Helicobacter pylori* and Epstein-Barr virus is a factor in the absence of eradication, regression of pathogenic changes and disorders of the cellular composition of gastric glands.
Disclosure: Nothing to disclose

P0617 SEVERITY OF HISTOLOGICAL DAMAGE IN COELIAC DISEASE: ASSOCIATED FACTORS AND LONG-TERM SIGNIFICANCE

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Introduction: Recent paediatric guidelines allow non-invasive diagnosis of coeliac disease in selected patients. However, besides diagnostic purposes, there might be other reasons for the duodenal biopsy. For example, it is unclear whether patients with severe villous atrophy have higher risk to develop long-term complications and should therefore be followed up more closely. We investigated if the severity of intestinal lesion affects other disease features and long-term prognosis.
Aims and Methods: Comprehensive medical data of 835 children diagnosed with coeliac disease in 1966–2014 were collected. Furthermore, questionnaires evaluating overall health, coeliac disease-related symptoms (GSRS questionnaire), quality of life (PGWB questionnaire), lifestyle and gluten-free diet were sent to 559 currently adult patients. All study variables were compared between patients divided to three groups based on the severity of diagnostic histopathology.
Results: Altogether 284 (34%) patients had partial, 332 (40%) subtotal and 219 (26%) total villous atrophy. Those with more severe lesion were born (1996 vs 1996 vs 1991, $p < 0.001$) and diagnosed (2007 vs 2006 vs 1999, $p < 0.001$) during earlier years and had higher median endomysium antibody titers (1:200 vs 1:500 vs 1:500, $p < 0.001$), and lower haemoglobin (126 vs 124 vs 121, $p = 0.005$) and body mass index (16.6 vs 16.1 vs 16.1, $p = 0.005$). They were also less often screen-detected (33% vs 25% vs 17%, $p < 0.001$) and had more anaemia (16% vs 22% vs 35%, $p < 0.001$) and growth disturbances (20% vs 38% vs 54%, $p < 0.001$), whereas there was no difference in gender distribution or the overall frequency of symptoms at diagnosis. Differences between the groups at diagnosis persisted after adjustment with birth and diagnosis year. The groups had similar short-term (6–24 months) dietary adherence and treatment response. At total, 237 (42%) adults responded the questionnaires median of 18.5 years after the diagnosis. After adjustment of the groups, there were no differences in working full-time, presence of children or coeliac disease in the family, smoking or frequency of physical exercise, adherence to gluten-free diet, experience of dietary treatment, self-perceived health, presence of associated diseases, quality of life or gastrointestinal symptoms in adulthood.
Conclusion: Severe villous atrophy at childhood diagnosis was associated to more difficult clinical presentation. However, the degree of mucosal damage did not affect the long-term treatment outcomes in adulthood.
Disclosure: Nothing to disclose

P0618 DIAGNOSTIC DELAYS IN CHILDREN WITH COELIAC DISEASE IN THE CENTRAL EUROPEAN REGION IN 2016

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Introduction: Coeliac disease (CD) is a lifelong immune-mediated systemic disorder affecting about 1% of the population. The majority of adult and paediatric patients remain undiagnosed and diagnostic delays in many regions reach up to 10 years.
Aims and Methods: The aim of our study was to identify the diagnostic delays in children with CD in Central European region.
We retrospectively analysed medical records of children and adolescents diagnosed with CD in 2016 from five Central European countries as a part of a multicentre web-based survey, focusing on the age at the diagnosis and the duration between first CD related symptoms, first visit to paediatric gastroenterologist and confirmation of the diagnosis. Differences between preschool (< 6y) and school-age children were also studied. Statistical analysis was performed using SPSS for Windows.

Abstract No: P0618: Table 1. Diagnostic delays in children with Coeliac disease in Central Europe

	No of centres	No of patients	Age at diagnosis ($p < 0.05$)	Symptoms to visit at PaedGI (duration; median (range))	PaedGI to diagnosis ($p < 0,001$) (duration; median (range))	Symptoms to diagnosis (duration; median (range))
Croatia	6	43	10y	3m (0–4y)	2m (0–7y)	7m (0–8y)
Germany	5	39	6.5y	6m (0–5y)	0m (0–8m)	8m (0–5y)
Hungary	21	283	7y	6m (0–14y)	1m (0–8y)	8m (0–14y)
Italy	2	59	5y	6m (0–5.5y)	1m (0–8m)	7m (0–6y)
Slovenia	7	35	7.5y	6m (0–7y)	1m (0–5y)	7m (0–7y)
TOTAL	41	459	7y	6m (0–14y)	1m (0–8y)	8m (0–14y)

Abstract No: P0621: Table 1. Clinical presentation of CD in different regions of Central Europe.

SYMPTOM		TOTAL (N = 652)	CROATIA (N = 66)	GERMANY (N = 69)	HUNGARY (N = 381)	ITALY (N = 82)	SLOVENIA (N = 54)
Asymptomatic		20.2%	12.1%	23.2%	20.7%	24.4%	16.7%
Abdominal pain	As a leading sy. (as all symptoms)	33.1% (51.5%)	36.4% (47.0%)	36.2% (56.5%)	24.4% (41.2%)	14.6% (23.2%)	33.3% (40.7%)
Growth retardation		13.8% (21.9%)	9.1% (16.7%)	17.4% (18.8%)	10.5% (17.8%)	13.4% (19.5%)	5.6% (11.1%)
Diarrhoea		12.9% (30.6%)	15.2% (25.8%)	4.3% (27.5%)	10.2% (23.9%)	12.2% (24.4%)	9.3% (22.2%)
Iron deficiency		10.2% (24.0%)	7.6% (15.2%)	2.9% (4.3%)	9.4% (24.9%)	6.1% (11.0%)	9.3% (14.8%)
Abdominal distention		7.1% (32.1%)	3.0% (9.7%)	5.8% (20.3%)	6.6% (31.5%)	3.7% (11.0%)	5.6% (20.4%)
Constipation		5.4% (13.8%)	3.0% (9.1%)	1.4% (5.8%)	3.9% (9.4%)	7.3% (19.5%)	7,4% (18.5%)
Unexplained fatigue		3.3% (11.7%)	1.5% (9.1%)	4.3% (14.5%)	2.4% (6.8%)	4.9% (14.6%)	0.0% (13.0%)
Other symptoms		4.0% (4.2%)	0.0% (0.0%)	0.0% (0.0%)	4.7% (5.0%)	3.7% (3.7%)	0.0% (0.0%)

*Study was co-financed by Interreg CE programme (CE 111, Focus IN CD).

Results: Data from 459 children and adolescents (66% female, 41% preschool) from Croatia, Hungary, Germany, Italy and Slovenia, were available for further analysis.
Median age at the time of diagnosis was 7 years (range 7m–18.5y) and more than two thirds of children were diagnosed before the age of 10 years. There was significant difference between regions regarding the median age at the diagnosis, being the lowest in Italy, and the highest in Croatia ($p < 0.05$).
Median duration from first CD related symptoms to the first visit of paediatric gastroenterologist was 6 months (range 0–14y; preschool 5m (0–5y), school-age 6m (0–14y)), with no significant regional difference.
Median duration from the first visit of paediatric gastroenterologist to the confirmation of the diagnosis was 1 month (range 0–8y; preschool 1m (0–8m), school-age 1m (0–8y)) and significant difference was found between regions ($p < 0.001$), being the highest in Croatia and Slovenia.
Median delay from the first symptoms to diagnosis was 8 months (range 0–14y; preschool 6m (0–5y), school-age 9m (0–14y)) without regional differences.
Conclusion: Our data showed that diagnostic delays in children with CD in five Central European countries are lower in comparison with the available data from other regions. Within the Central Europe, we did not find important differences in delays between the onset of symptoms and final diagnosis. However, the delay between the first visit of paediatric gastroenterologist and the final diagnosis was significantly higher in Slovenia and Croatia. This could be attributed to regional differences in the availability of diagnostic methods and/or capacity of paediatric gastroenterology service, as well as to the older age at diagnosis in Slovenia and Croatia, which is correlated with longer diagnostic delays, however it also could be caused by lower number of patients from some countries.
Regardless of relatively short diagnostic delays that we found, there is still a room for further improvement. Undiagnosed and/or untreated CD is associated with severe complications; therefore, it is very important to raise the awareness about the disease prevalence, changes in clinical presentation, and the use of reliable diagnostic methods in order to further reduce delays and the unnecessary burden of undetected and thus untreated disease.
*Study was co-financed by Interreg CE programme (CE 111, Focus IN CD).
Disclosure: Nothing to disclose

P0619 NATURAL HISTORY OF POTENTIAL CELIAC DISEASE: FACTORS PREDICTING EVOLUTION TO VILLOUS ATROPHY

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Introduction: Potential celiac disease (PCD) is still a controversial clinical condition: there is not yet agreement on prognosis and treatment.
Aims and Methods: Aim of our study was to investigate the natural history of the disease and to identify risk factors associated with possible development of villous atrophy.
We prospectively enrolled 340 PCD children (twice positive anti-tTG IgA and anti-endomisyum antibodies + duodenal mucosa Marsh 0 or 1): 67.1% females, most asymptomatic (86.7%). They were followed till 144 months (median 76.1) with serial clinical, serological and histological evaluations. 208 are still on gluten-containing diet, the remaining being on GFD because of symptoms or parental choice.
Results: During FU 88/340 (25.8%) became anti-tTG negative. 42 (20.2%) children developed villous atrophy: cumulative survival at 12 years was 42% and 61% for males and females, respectively. A cluster of events (children developing villous atrophy) was observed in the first 2 years of FU with no difference between sex. The best predictors of evolution to villous atrophy at the time of enrollment were: intraepithelial lymphocyte infiltration ($p = 0.001$), age >10 years ($p = 0.001$), HLA homozygosity ($p = 0.021$), intensity of anti-tTG2 intestinal deposits (p .049). Familiarity for CD and other autoimmune disease did not impact the natural history of this condition.
Conclusion: PCD is confirmed to be an heterogeneous condition, but it seems possible to identify risk factors at the time of diagnosis and in first years of follow-up to discriminate children who will develop eventually villous atrophy.
Disclosure: Nothing to disclose

P0621 CLINICAL PRESENTATION OF COELIAC DISEASE IN CHILDREN AND ADOLESCENTS FROM CENTRAL EUROPEAN REGION IN 2016

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Introduction: Coeliac disease (CD) is a lifelong immune-mediated systemic disorder, affecting genetically susceptible individuals after ingestion of gluten. It occurs approximately in 1% of the population and has a diverse clinical presentation, ranging from classical gastrointestinal manifestation of malabsorption to subclinical and asymptomatic forms.
Aims and Methods: The aim of our study was to present clinical manifestations of CD among the children and adolescents in Central European (CE) region.
41 centres from five CE countries (Croatia (CRO) - 6, Germany (GER) - 5, Hungary (HUN) - 21, Italy (ITA) - 2 and Slovenia (SLO) - 7) provided data as a part of a multi-centre web-based survey. We retrospectively analysed medical records of children and adolescents diagnosed with CD in 2016, focusing on a single leading symptom indicative of CD and other associated symptoms. We compared clinical presentation at the time of diagnosis of preschool (< 6y) and school-age children and analysed regional differences in clinical picture. Statistical analysis was performed using SPSS for Windows.
Results: Data from 652 children and adolescents (64.0% female, 37.0% preschool) from CRO (N = 66), GER (N = 69), HUN (N = 381), ITA (N = 82) and SLO (N = 54) with the diagnosis of CD, confirmed in 2016, were available for further analysis.
Median age at the time of diagnosis was 7 years (range 7m–18.5y). 20.2% of children were asymptomatic, out of which 64.4% belonged to a known risk group (73% with positive family history of CD).
The most common leading symptom at the time of diagnosis was abdominal pain (33.1%), followed by growth retardation (13.8%) and diarrhoea (12.9%). We did not find any regional differences regarding the most common leading symptom. Abdominal pain was also found to be the most common leading symptom in both, preschool (20.9%) and school-age (41.1%) children. In preschool children, the second most common leading symptom was diarrhoea (17.0%), followed by growth retardation (16.0%) and in school-age children the opposite was found (growth retardation - 12.4%, diarrhoea - 10.2%).
Conclusion: Our data showed that clinical presentation of CD is diverse in children in CE. Although classical clinical presentation is not so frequent, gastrointestinal symptoms, especially abdominal pain, remain the leading symptom in all compared groups of children and adolescents. In school-age children, abdominal pain was twice as common in comparison to preschool children. In Germany it was a leading complaint in almost half of the included children.
Also becoming increasingly common is for CD to present as an asymptomatic disease. Our data showed that one fifth of included children had no symptoms before the diagnosis was confirmed with asymptomatic group being the largest in Italy and Germany compared to other regions.

It is very important to raise the awareness about the changes in clinical presentation of childhood CD shown by our data and by other studies in order to prevent diagnostic delays and negative consequences of undetected/untreated disease.
Disclosure: Nothing to disclose

P0622 UTILISATION OF DIAGNOSTIC TOOLS FOR COELIAC DISEASE IN CHILDREN IN 2016-2017 - A NATION-WIDE SURVEY

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Introduction: ESPGHAN allowed in 2012 to confirm the diagnosis of coeliac disease (CeD) without biopsy in children with CeD-relevant symptoms (as defined in Husby, JPGN 2012) and serum anti-transglutaminase antibody levels exceeding 10 times the upper limit of normal (High TGA+) in whom endomysial antibodies (EMA) are positive and who carry HLA-DQ2 or DQ8. In this study we explored how these criteria are followed in clinical practice.
Aims and Methods: Paediatric gastroenterologists in Hungary were asked to upload medical data of their patients diagnosed with CeD between January 2016-April 2017 concerning disease presentation, antibody, histology and DQ results into an anonymised web database developed during the Interreg Central Europe 'Focus in CD' project and utilised before in Croatia, Germany, Italy and Slovenia. Here we present the results of the Hungarian subgroup.
Results: 27 gastroenterology services representing all counties in Hungary uploaded altogether 654 patients' data diagnosed in the last year with CeD, of whom 566 were children and adolescents below 18 years of age (median 8 years [range 1–18]). Biopsy was performed in 435 children (76.8%), which showed Marsh 2–3 lesions or villous atrophy by other grading in 413 (95%), Marsh 0–1 in 12 (2.7%), or the biopsy specimen was not evaluable in 10 (2.3%). In 26 children biopsy was not possible because of the parents' refusal or other medical reasons. In other 105 patients (18.5%) the no-biopsy approach was applied, in whom EMA was tested in 92/105 (87%) and HLA-DQ was determined in 94 (89.5%). The most frequent reasons for the lack of genetic testing were high costs not supported by insurance, and for replacement of EMA the use of DGP in 2 centers. Altogether 75% of children (79/105) had all the criteria required by the 2012 ESPGHAN guidance for the non-invasive diagnosis, while 84% (88/105) fulfilled the protocol of having CeD-relevant symptoms, High TGA+ and EMA+ result. In these cases, HLA-DQ testing did not add to the diagnosis, indicating a safe diagnosis even without genetic testing. Also in the group where biopsy was not possible because of parental refusal, 65% of children (17/26) fulfilled these criteria and the same was true for 43% of children (188/435) who eventually received endoscopy.
Conclusion: The majority of practising paediatric gastroenterologists in Hungary follow well ESPGHAN criteria in making the no-biopsy diagnosis of CeD. As omitting HLA-DQ testing does not compromise accuracy, this would make the no-biopsy approach more broadly available also in countries with less financial resources. Of note is that also 43% of children who currently undergo biopsy already do qualify for these less strict criteria even before the endoscopy, but a final diagnosis also must depend on collaboration and acceptance by parents.
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Disclosure: Nothing to disclose

P0623 EXPRESSION OF IRON TRANSPORTER PROTEINS IN THE SMALL BOWEL MUCOSA OF CHILDREN WITH CELIAC DISEASE

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Introduction: Anemia is a common finding in untreated celiac disease, but the mechanisms behind this association are obscure. Abnormal expression of small intestinal iron transport proteins could provide a possible explanation but the existing research is scarce and contradictory. We investigated whether aberrant expression of the transporter proteins is associated with anemia in pediatric celiac disease.
Aims and Methods: Duodenal cytochrome B (DcytB), divalent metal transporter 1 (DMT1), ferroportin, hephaestin and transferrin receptor 1 (TfR1) were stained immunohistochemically in duodenal biopsies of 27 celiac disease patients with villus atrophy and 16 children with normal mucosal morphology. Twenty of these 43 individuals had anemia. The expressions of the proteins were investigated as regards to intensity (negative/weak, strong) and the results were compared between the groups. Subgroup analyses were made between children with positive celiac serology but normal villi (potential celiac disease) and seronegative controls.
Results: In celiac disease patients, no differences in protein expressions between anemic and non-anemic patients were seen. The expressions of DcytB ($p = 0.036$) and hephaestin ($p = 0.040$) were significantly lower in celiac disease patients than individuals with normal mucosal morphology (Table 1), and there was a similar but non-significant trend in the expression of DMT1 ($p = 0.060$). In the subgroup analysis of the morphologically normal patients, there were no differences between seropositive or -negative patients.
Table 1. The intensity of the iron transporter proteins in duodenal biopsies 43 children.

	Celiac disease N = 27 %	No villous atrophy N = 16 %	P-value
DcytB			
Negative/Weak	82.5	56.3	0.036
Strong	14.8	43.8	
DMT1			
Negative/Weak	77.8	50.0	**0.060**
Strong	22.2	50.0	
Ferroportin			
Negative/Weak	74.1	75.0	0.946
Strong	25.9	25.0	
Hephaestin			
Negative/Weak	88.9	63.5	**0.040**
Strong	11.1	37.5	
TfR1			
Negative/Weak	70.4	50.0	0.182
Strong	29.6	50.0	

DcytB, duodenal cytochrome B; DMT1, divalent metal transporter 1, TfR1, transferrin receptor 1

[The intensity of the iron transporter proteins in duodenal biopsies 43 children.]
Conclusion: We conclude that anemia in celiac disease is not associated with abnormal expression of iron transporters. Instead, the expressions of DcytB and hephaestin, enzymes catalyzing the reduction and oxidation of iron, respectively, are decreased in patients with villous atrophy. These changes might lead to insufficient absorption of iron in the small intestine and thus predispose to the development of anemia in untreated celiac disease.
Disclosure: Nothing to disclose

P0624 THE RELATIONSHIP BETWEEN THE STATUS OF VITAMIN D AND P53 PROTEIN IN CHILDREN WITH CELIAC DISEASE

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Introduction: The presence of antibodies reacting with the p53 tumor suppressor protein has been described in patients with some autoimmune disorders.
Aims and Methods: Our purpose was to explore the relationship between the level of vitamin D and the content of p53 proteins in the mucous membrane of the

duodenum in children with celiac disease (CD). In 42 children with CD at the age from 7 to 15 years in the biopsy samples of the duodenum was determined the level of p53 protein expression by monoclonal mouse antibodies to human proteins (clone DO-7) Dakopatts, (Denmark). Level of 25 D (OH) was determined in serum by ELISA (Elecsys-2010).
Results: Vitamin D deficiency was diagnosed in 33 children with CD (13.3 ± 3 ng / ml), 9 patients have vitamin D insufficiency (24 ± 4ng / ml). In the group of children with vitamin D deficiency, the amount of p53 protein in the mucous membrane of the duodenum was $6.5 \pm 0.3\%$, and in the case of vitamin D deficiency it was $3.1 \pm 0.3\%$. The number of interepithelial lymphocytes of the small intestinal mucosa was $83.3 \pm 5.4\%$ in cases of vitamin D deficiency, at vitamin D insufficiency it was $38.0 \pm 3.9\%$.
An inverse strong correlation was found between the values of vitamin D and the values of tissue protein p53 ($r = -0.759$, $p < 0.001$).
Conclusion: Immunohistochemical methods established a relationship between vitamin D deficiency and increase of the p53 protein in the mucosa of the small intestine in sites of atrophy of the epithelium in children with CD, which is an indirect confirmation of the delay in the regeneration of the small intestine at vitamin D deficiency.
Disclosure: Nothing to disclose

P0625 *H. PYLORI* INFECTION MAY EXACERBATE SMALL INTESTINAL MUCOSAL INJURY IN CONCOMITANT NON-SELECTIVE NSAIDS AND PPI TREATMENT

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Introduction: *Helicobacter pylori* (HP) infection is a primary cause of gastric and duodenal ulcers. Most HP uninfected gastroduodenal ulcers are caused by NSAIDs. Many capsule endoscopic studies of healthy volunteers revealed that concomitant administration of non-selective NSAIDs and PPI can induce small intestinal mucosal injuries in over 50% of subjects.
Aims and Methods: As HP infection is the main cause of duodenal ulcers, the impact on small intestinal mucosa is clear. Therefore, the aim of the study was to investigate any association between HP infection and small intestinal mucosal injury. Two RCTs evaluated small intestinal mucosal injury in healthy volunteers after NSAIDs treatment, all subjects were checked for HP infection by breath test or serum antibody before treatment to evenly distribute subjects with HP infection in both RCT groups. From the studies, 213 subjects (38 subjects treated with diclofenac plus PPI, 34 treated with diclofenac plus PPI and rebamipide, 72 treated with loxoprofen plus PPI, and 69 treated with celecoxib only), whose entire small intestine was evaluated before and after NSAIDs treatment by capsule endoscopy were included in the analysis. Numbers of small intestinal mucosal breaks were compared between subjects infected with HP and those without HP infection before and after NSAIDs treatment.
Results: In all subjects prior to NSAIDs treatment, there were more mucosal breaks in 46 subjects infected with HP than 167 subjects without HP infection; however, there were no significant differences (0.44 ± 1.9 vs 0.22 ± 1.0; $p = 0.30$). In all subjects following NSAIDs treatment, mucosal breaks were statistically greater in subjects infected with HP than subjects without HP infection (16.0 ± 68 vs 2.25 ± 8.6; $p = 0.011$). After treatment, there were more mucosal breaks in subjects infected with HP than those not infected in subgroups that were treated concomitantly with non-selective NSAIDs plus PPI. In the subgroup treated with celecoxib only, there was little difference in the number of mucosal breaks for HP infection.
Conclusion: There is a high possibility that *H. pylori* infection exacerbates small intestinal mucosal injury in concomitant non-selective NSAIDs treatment with PPI.
Disclosure: All authors have declared no conflicts of interest.

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P0626 EVALUATION OF QUALITATIVE AND QUANTITATIVE SMALL BOWEL BACTERIAL OVERGROWTH SYNDROME IN CHILDREN WITH CHRONIC DIARRHEA USING JEJUNAL FLUID BACTERIAL CULTURE AND BREATH TESTS

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Introduction: 24% of chronic diarrheas in older children are of unknown etiology. Small bowel bacterial overgrowth syndrome (SBOS) is an underdiagnosed disorder in children usually suspected where no etiology has been ascertained after an extensive workup. Existing literature on SBOS in children have used study designs that are not full-proof. Most studies are based on breath test analyses and response to empirical antibiotics. Limited studies have used small bowel intubation and aspiration as the primary modality for diagnosis of SBOS in children which is considered gold standard.
Aims and Methods: This was a prospective longitudinal interventional study. We aimed to assess a) the prevalence of SBOS, b) the specific microbiological profile and antibiotic sensitivity in SBOS in the jejunal cultures, c) correlation of bacteriological confirmation with yield of breath tests, and d) response to antibiotics and outcome after stopping the therapy. Chronic diarrhea $\pm$ bloating patients of >3months with undetermined etiology underwent glucose and lactulose hydrogen breath tests on days 1 and 2. Jejunal aspirate by jejunoscopy for culture and sensitivity was performed on day 3. Those with bacterial confirmation on jejunal culture were subjected to 2 therapeutic phases (primary: day 1–14; secondary: day 28–42) of two sensitive oral antibiotics with a wash out phase of 2 weeks (day 14–28) in between. Co-trimoxazole was emperically chosen in primary antibiotic failure. SBOS was defined as all of the following: a) jejunal aspirate bacteriological count of $\geq 10^5$ CFU/mL, b) positive hydrogen breath test (glucose or lactulose) and c) response (clinical and breath test) within 2 weeks of completion of antibiotic therapy. Their long-term outcome over 6 months was noted.
Results: Of the 48 children aged 14.6 ± 3.3 y, 8 did not satisfy all the SBOS criteria. Another 5 were excluded as they had a specific disease later at follow-up (celiac disease, $n = 2$; giardiasis, $n = 2$; combined variable immunodeficiency, $n = 1$). SBOS as per the above criteria was present in 16/35 (46%) cases. The jejunal cultures ($n = 16$) yielded *Pseudomonas* ($n = 8$), *Eschericia coli* ($n = 7$) and *Klebsiella* ($n = 4$) and *Steptococcus* ($n = 3$). 7/16 cultures grew >1 organism. 2/4 *Klebsiella* were resistant to all antibiotics and treated with empirical choice of antibiotics. Of the positive glucose ($n = 12$) and lactulose ($n = 7$) hydrogen breath tests, dual positivity was seen in three. In the first therapy phase, primary antibiotics administered as per sensitivity pattern were cefixime ($n = 10$), norfloxacin ($n = 6$) and co-trimoxazole ($n = 2$). 5/10 of cefixime group did not show response after 2 weeks. In the second therapy phase after wash out period, secondary antibiotics administered were co-trimoxazole ($n = 8$), norfloxacin ($n = 4$), cefixime ($n = 2$) and nitrafurantoin ($n = 2$). Cefixime resistant organisms ($n = 5$) and multi-antibiotic resistant *Klebsiella* ($n = 2$) responded clinically to co-trimoxazole. All patients responded by hydrogen breath tests. Over a follow-up period of 3 (2–9) months, 5 patients (31%) had recurrence of symptoms. All 5 were primary antibiotic responsive and responded (clinical and breath test) to the same antibiotics during recurrence.
Conclusion: SBOS (jejunal culture and breath test positivity) is seen in 46% of chronic diarrhea with no discernable etiology. Gram negative organisms are the commonest flora in 80%; multibacterial in 43%. Primary antibiotic response is seen two-third. Co-trimoxazole is a favourable drug for primary antibiotic failure and antibiotic resistant groups. One-third have relapse of SBOS and are respond to primary antibiotics.
Disclosure: Nothing to disclose

P0627 A FIRST APPROACH FOR AN EVIDENCE-BASED METHOD TO ADJUST PANCREATIC ENZYME REPLACEMENT THERAPY IN CYSTIC FIBROSIS

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Introduction: The aim of this project was to assess the effectiveness of a method to adjust pancreatic enzyme replacement therapy (PERT) in Cystic Fibrosis (CF) based on the prediction of the optimal dose according to food properties, by means of modelling of results of *in vitro* digestion studies.
Aims and Methods: Prospective interventional study with 43 patients from 5 European centres. During 24h they followed a fixed diet (5 meals), along with the optimal dose of enzymes for each meal previously characterised or determined by *in vitro* digestion. Fat in stools was determined after samples collection, which was carried out using colorimetric markers for a precise identification of stools corresponding to the study meals. Beta regression models were applied to explain the relationship of study variables with coefficient of fat absorption (CFA).
Results: Median CFA was 90% (95% CI 84, 95%) with no differences among centres. Patients' compliance with protocol was 99% and median Bristol stool scale was 3–4. No association of CFA with age, mutation or BMI z-score, but a significant effect was found with transit time ($p < 0.05$). Findings suggest that these variables do not play as an important role as food characteristics do on lipids digestion (on the basis of which the study doses were established).
Conclusion: Applying the *in vitro* predicted recommended PERT dose for each meal, the clinical target of CFA is reached with low variability among patients. The proposed approach can be considered a first step towards an evidence-based method to adjust PERT in CF.
Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00-17:00
Liver & Biliary II - Hall X1____

P0628 IMPACT OF *CYP2R1*, *CYP27A1* AND *CYP27B1* GENETIC POLYMORPHISMS CONTROLLING VITAMIN D METABOLISM ON SUSCEPTIBILITY TO HCV INFECTION IN A HIGH-RISK CHINESE POPULATION

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Introduction: CYP2R1 and CYP27A1 hydroxylases involve in the hydroxylation from vitamin D_3 to 25-hydroxyvitamin D_3 ($25[OH]D_3$), and CYP27B1 hydroxylase further catalyzes the conversion of $25(OH)D_3$ to $1,25(OH)_2D_3$, the most active vitamin D metabolite, which plays a role in the immune regulation and pathogenesis of hepatitis C virus (HCV) infection. The present study aims to investigate the relationship between the polymorphisms of vitamin D pathway genes (*CYP2R1*, *CYP27A1* and *CYP27B1*) and HCV infection outcomes in Chinese population.

Aims and Methods: Nine single nucleotide polymorphisms (SNPs) from *CYP2R1*, *CYP27A1* and *CYP27B1* were genotyped in a Chinese population with high risk of HCV infection. The distributions of these SNPs were compared among groups of different HCV infection outcomes, including 863 HCV persistent infection cases, 524 spontaneous clearance subjects and 1079 uninfected controls.

Results: Logistic regression analyses showed that *CYP2R1* rs12794714-G, rs10741657-A, rs1562902-C, and rs10766197-G alleles were significantly associated with increased susceptibility to establishment of HCV infection (all $p_{FDR} < 0.05$, in additive/dominant models), and the combined effect of the four unfavorable alleles was related to an elevated risk of HCV infection in a locus-dosage manner ($p_{trend} = 0.008$). The risk effects of the four unfavorable alleles were more distinct among drug user or subjects aged < 50 years. Moreover, haplotype analyses suggested that compared with the most frequent $A_{rs12794714}G_{rs10741657}T_{rs1562902}A_{rs10766197}$ haplotype, the haplotype containing the four unfavorable alleles GACG indicated a risk effect of HCV infection (adjusted odds ratio [OR] = 1.243, p = 0.006). However, no links were found between these SNPs and viral clearance, and also no associations of the other two genes with infection outcomes were found.

Conclusion: Our study implicated that genetic variants in *CYP2R1* may be marker SNPs for risk of HCV infection susceptibility in Chinses population.

Disclosure: Nothing to disclose

P0629 INHIBITION OF CYCLOOXYGENASE-2 AMELIORATES LIVER CIRRHOSIS BY TARGETING SPLENIC ABNORMALITIES

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Introduction: Splenomegaly is always observed in patients with liver cirrhosis. As an important immunological organ, the spleen plays a crucial role in regulating immunological response. Besides, spleen directly connected with the liver via the portal circulation. The immune cells and cytokines derived from spleen may affect the progression of liver cirrhosis. However, the abnormalities of splenic immune function with liver cirrhosis have not been fully characterized.

Aims and Methods: To fully assess the changes of immune cell subsets in the spleen of liver cirrhotic rats and explore whether cyclooxygenase-2 (COX-2) is involved as a potential modulator in these change. Twenty-four male Sprague-Dawley rats weighing 200–250g were randomly assigned into 3 groups with 8 rats in each group. The control group: received intraperitoneal injection of normal saline (1ml, twice a week); the TAA group: received intraperitoneal injection of thioacetamide (TAA, 200 mg/kg, twice a week for 16 weeks); the TAA+celecoxib group: received TAA intraperitoneally and celecoxib via gastric gavage (20 mg/kg/day). Sections from paraffin-embedded livers were stained with hematoxylin and eosin and Sirius Red. The expression of collagen III was tested by immunohistochemistry. Besides, Protein expression of a-SMA and COX-2 was evaluated by Western blot. Flow cytometry was used to detect the number of total T cell, CD4+ T-cell, CD8+ T-cell, Treg (CD4+CD25+FOXP3+), total B cell (B220+), follicular B cell (B220+CD21+CD23+), marginal B cell (B220+CD21+CD23-) and the activated B cell (B220+CD38+) in the spleen of each group. The enzyme-linked immunosorbent assay was performed to evaluate the expression of IgG and IgM both in the spleen and serum.

Results: A considerable amount of collagen was visualized in the liver of TAA group compared with that of the control group. While reduced fibrotic area was found in liver of the TAA+celecoxib group. The hepatic protein expression of a-SMA increased significantly by 2.3-fold compared with that in the control group. While the hepatic a-SMA protein expression decreased significantly in the TAA+celecoxib group. Elevated protein expression of COX-2 was detected in the spleen of the TAA group compared with that in the control group. But celecoxib significantly reduced the expression of COX-2 in spleen of the TAA+celecoxib group. Besides, compared with the control group, the protein expression of IgM and IgG in spleen and serum were found to be greatly increased in the TAA group. While they were significantly reduced in TAA+celecoxib group compared with that in TAA group. Moreover, the number of splenic total T cell, CD8+ T-cell, Treg, total B cell and the activated B cell (B220+CD38+) were all increased in TAA group compared with the control group, while dramatically reduced in TAA+celecoxib group. Interestingly, compared with the control group, the number of splenic marginal B cell (B220+CD21+CD23-) were decreased in TAA group, while increased in TAA+celecoxib group. And no obvious changes of splenic CD4+ T-cell and follicular B cell (B220+CD21+CD23+) were observed in each group.

Conclusion: The present study indicates that COX-2 may be involved in regulating the development and differentiation of immune cell subsets in spleen of liver cirrhosis. And the inhibition of COX-2 by celecoxib could attenuate the liver cirrhosis and the relevant immune dysfunction. Furthermore, the study shed light on the fact that Celecoxib may ameliorate liver cirrhosis partly through the targeting splenic abnormalities.

Disclosure: Nothing to disclose

P0630 CELECOXIB ATTENUATES HEPATOCYTE APOPTOSIS THROUGH INHIBITION OF ENDOPLASMIC RETICULUM STRESS IN CIRRHOTIC RATS

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Introduction: Endoplasmic Reticulum Stress (ERS) is an important mechanism in the process of liver disease and chronic progression. ERS is involved in the progression of liver fibrosis and its recovery. Excessive and prolonged ER stress triggers apoptosis to eliminate dysfunctional cells. Apoptosis induced by ER stress is is considered to be important way on the origin and development of liver fibrosis. Cox-2 induction is closely related to endoplasmic reticulum stress. Our previous studies have found that the Cox-2 inhibitor, Celecoxib, can improve hepatic fibrosis and portal hypertension. But the role of Celecoxib in alleviating liver fibrosis is related to alleviating ERS, and there is no research report.

Aims and Methods: To investigate whether celecoxib could alleviate the development of liver fibrosis by reducing hepatocyte apoptosis via inhibition of endoplasmic reticulum stress (ERS) response. Methods: Peritoneal injection of thioacetamide (TAA) was employed to induce liver cirrhosis for 16 weeks (200 mg/kg/3 days before 8 weeks, 100 mg/kg/3 days after 8 weeks). 45 male Sprague-Dawley rats were randomly assigned to the control, TAA, and TAA+celecoxib groups. TAA-cirrhotic rats received celecoxib (20 mg/kg/day) or its vehicle by gastric gavage for last 8 weeks. rats were put to death after 16 weeks, and serum AST, ALT and ALB content in rats were detected. The degree of fibrosis was assessed by visible hepatic fibrotic areas (Sirius red) and hydroxyproline contents. The stress level of endoplasmic reticulum was evaluated by detecting its marker protein GRP78 and CHOP. Apoptosis level is evaluated by the detection of Caspase-12 and Caspase-3, hepatic expression of PERK, IRE1 and ATF6 is related to ERS.

Results: Celecoxib administration significantly decreased serum AST and ALT levels in the liver, without significant changes in ALB. The degree of fibrosis in liver fibrosis and hydroxyproline was significantly reduced to celecoxib (−38% and −25.7%, $p < 0.01$). Compared with the TAA group, celecoxib ameliorated endoplasmic reticulum stress by lowering the level of GRP78 ($p < 0.05$). Consistently, the up-regulation of hepatic apoptosis-level (Caspase-12, Caspase-3) and CCAAT/enhancer binding protein homologous protein(CHOP)induced by TAA was significantly inhibited after celecoxib administration. Furthermore, the expressions of critical molecules in ERS (PERK,IRE1,ATF6) was reduced after celecoxib management ($p < 0.05$).

Conclusion: Therapeutic administration of celecoxib can efficiently reduce hepatic apoptosis in TAA-cirrhotic rats. These effects may be due to the suppression of CCAAT / enhancer binding protein homologous protein (CHOP) expression, which are subsequent to the inhibition of endoplasmic reticulum stress.

Disclosure: Nothing to disclose

P0631 THE PREDICTIVE ABILITY OF LABORATORY INDICES IN ASSESSING ADVANCED HEPATIC FIBROSIS AMONG CHRONIC HEPATITIS C PATIENTS WITH DIFFERENT STATUSES OF ANTI-VIRAL TREATMENT AND BODY MASS INDEX

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Introduction: Histological staging is essential for prognostication and treatment decision among patients with chronic hepatitis C. Liver biopsy is the gold standard in assessing liver fibrosis but is invasive with potential complications. Therefore, many non-invasive methods to predict liver fibrosis have been reported. Aspartate aminotransferase (AST)/platelet ratio index (APRI) and fibrosis-4 (FIB-4) are well-known serum markers and have been widely used to predict histological results. However, in clinical settings, serum biomarkers might rapidly fluctuate over time and be influenced by many factors, such as anti-viral treatment, steatohepatitis status, and other comorbidities. It is not well established how these factors influence the diagnostic accuracy of APRI and FIB-4 in evaluating liver fibrosis. Therefore, this study aimed to investigate the predictive ability of two laboratory indices for liver fibrosis in patients with different statuses of anti-viral treatment, body mass index (BMI), and other comorbidities.

Aims and Methods: A total of 96 patients (men, 53.1%) with chronic hepatitis C infection who underwent liver biopsy between September 2015 and December 2017 at Tatung Mackay Memorial Hospital, Taiwan were retrospectively reviewed. The histological appearance of fibrosis was assessed using the Ishak scoring system (range, 0–6) and several laboratory values were evaluated. The APRI was calculated as AST [IU/L] / upper limit of normal AST [IU/L]) × 100 / platelet count [109/L]. The FIB-4 index was calculated as AST [IU/L] × age [years] / platelet count [109/L] × alanine aminotransferase (ALT) [IU/L]1/2. The predictive performance of two indices was assessed using receiver operating characteristic (ROC) analysis, and the area under the ROC curve (AUROC) was evaluated.

Results: The mean age was 59.3 (range, 35–83) years. The proportion of diabetes, hyperlipidemia, and hypertension was 27.1%, 69.8%, and 47.9%, respectively. A total of 29 (30.2%) patients were hepatitis C treatment naïve, 18 (18.8%) had virological breakthrough during interferon-based anti-viral treatment, and the remaining patients completed anti-viral treatment. The APRI and FIB-4 AUROCs were both higher in patients who completed the treatment than those who did not. Furthermore, patients with BMI $\leq$25 kg/m^2 had higher predictive ability of the two laboratory indices than those with BMI $>$25 kg/m^2 (Table).

Conclusion: The laboratory indices, APRI and FIB-4, can predict advanced fibrosis in the liver in patients with hepatitis C infection. The diagnostic accuracy seems better in patients who received anti-viral treatment and those with BMI $<$ 25 kg/m^2. These indices will be useful in estimating liver fibrosis.

	AUROC	Cut-off	Sensitivity	Specificity	PPV	NPV
Total 96 patients						
APRI	0.747	0.66	64.9%	71.2%	58.5%	76.4%
FIB-4	0.739	2.63	62.2%	78.0%	63.9%	76.7%
Treatment naïve or virological breakthrough (n = 47)						
APRI	0.691	1.26	60.0%	77.3%	75.0%	63.0%
FIB-4	0.635	4.18	48.0%	81.8%	75.0%	58.1%
Treatment completion (n = 49)						
APRI	0.757	0.52	58.3%	83.8%	53.9%	86.1%
FIB-4	0.784	1.91	75.0%	78.4%	53.0%	90.6%
BMI $\leq$ 25 (n = 43)						
APRI	0.890	1.11	83.3%	80.6%	62.4%	92.6%
FIB-4	0.796	2.69	75.0%	74.2%	53.0%	88.5%
BMI $>$ 25 (n = 53)						
APRI	0.699	0.44	76.0%	60.7%	42.8%	86.7%
FIB-4	0.740	1.78	80.0%	64.3%	46.5%	89.3%

APRI = aspartate aminotransferase / platelet ratio index; AUROC = area under the receiver operating characteristic curve; BMI = body mass index; FIB-4 = fibrosis-4; NPV = negative predictive value; PPV = positive predictive value.

[Analysis of two laboratory indices in identifying advanced (Ishak 4–6) liver fibrosis.]

Disclosure: Nothing to disclose

P0632 DENDRITIC CELL CONTRIBUTES TO AUTOIMMUNE HEPATITIS VIA AUTOPHAGY INHIBITION

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Introduction: Dendritic cells (DC) is a pivotal cell participating in various kinds of autoimmune diseases and plays an important role in autoimmune hepatitis (AIH). However, the mechanism used by DCs to take part in the development of AIH *in vivo and vitro* remains unclear.

Aims and Methods: The study was aimed to investigate the functions of DCs and mechanisms of DCs alteration in AIH. Peripheral blood samples were collected from 12 patients with biopsy-proven AIH and 6 healthy controls (HC). Mature DCs (CD11C+HLA-DR+) and activated T lymphocytes (CD4+CD3+ and CD8+CD3+, respectively) were detected by flow cytometry (FCM). In concanavalin A (Con A, 20mg/kg for 12h) induced AIH mice, the percentage of mature DCs (CD11C+CD80+) and activated T lymphocytes (CD4+CD69+ and CD8+CD69+, respectively) in the blood, spleen and liver were detected by FCM. Circulating TNF-α, IFN-γ, and IL-6 were assessed by ELISA. *In vitro*, immature DCs were generated from mice bone marrow (BMDC) cultured with GM-CSF (10ng/ml) and IL-4 (10ng/ml). We then treated the immature BMDCs with Con A (10, 20, 40μg/mL) and LPS (1μg/ml) for 24 hours respectively. The expression of major histocompatibility complex II (MHC-II), CD80 and CD86 was determined by FCM. The expression of autophagic related proteins were determined by western blot.

Results: The percentage of mature DCs in the peripheral blood of AIH patients was obviously higher than that in HCs, accompanied by the elevation of activated T lymphocytes. Similarly, the percentage of mature DCs and activated T lymphocytes in blood, spleen and liver were also increased in the Con A-induced hepatitis mice. Moreover, the inflammatory cytokines, such as TNF-α, IFN-γ, and IL-6 were significantly up-regulated in the Con A-treated group. Further study showed that the percentage of LPS-induced mature BMDCs from AIH mice was increased than that from control mice. *In vitro*, Con A stimulation promoted the maturation of BMDCs as evidenced by higher levels of MHC-II, CD80 and CD86 as compared with control cells. Interestingly, Con A markedly decreased autophagy level (decreased LC3 protein expression) in BMDCs.

Conclusion: We provided a strong evidence that abnormal maturation of DCs mediated the progression of AIH. Furthermore, the impaired autophagy activity could be an important mechanism for DCs to promote the development of AIH.

Disclosure: Nothing to disclose

P0633 ROLE OF ADIPOCYTE FATTY ACID BINDING PROTEIN (AFABP) IN THE DIAGNOSIS OF NAFLD

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Introduction: NASH diagnosis and the need for reliable noninvasive methods to distinguish it from simple steatosis and allow for grading and staging of disease are of high necessity. Adipocyte fatty acid binding protein (AFABP) is adipokine involved in the inflammation and insulin resistance.

Aims and Methods: We aimed to evaluate efficiency of AFABP in diagnosis and quantification of histopathological status of NAFLD in Egyptian patients.

A total of 90 subjects (45 male and 45 female) were included in the study and were divided into 3 groups: NASH, steatosis and control. All participants were subjected to calculation of HOMA-IR, NAFLD score, BARD score, complete blood counts, lipid profile, fasting and post-prandial blood glucose level, liver function tests, HCV-Abs, HBsAg, serum AFABP, liver biopsy and abdominal ultrasound.

Results: A significant increase was detected in fasting insulin, HOMA-IR, serum AFABP level and NAFLD score in NASH group ($p < 0.01$) and there was significant increase in BMI in both NASH and steatosis groups compared to control ($p < 0.05$).

The AUROC cut off level (pg/ml), sensitivity, specificity and accuracy of AFABP in diagnosis of fibrosis according to Brunt score in NASH were (0.838, 10.6, 75, 72.7 and 83.8 respectively) ($p = 0.005$ and 95% CI: 0.686–0.991). Also, AUROCs of non invasive markers for diagnosis of NASH have been showed highly significant value of BARD score, NAFLD score and HOMA-IR. Highly significant value of AFABP in diagnosis of significant histological grade (A2-A3) according to Brunt score in NASH was found ($p = 0.001$).

While in steatosis, AUROCs showed highly significant value of BARD score, NAFLD score, HOMA-IR and AFABP. As regards AFABP, the AUROCs, cut off level (pg/ml), sensitivity, specificity and accuracy were (0.928, 9.36, 100, 80 and 92.8 respectively) ($p = 0.003$ and CI: 0.830- 1).

Conclusion: AFABP proved to be a promising marker in predicting fibrosis stages, histological grades and activity.

Disclosure: Nothing to disclose

P0634 ANGIOCRINE HGF SIGNALING PLAYS A CRUCIAL ROLE IN THE EARLY STAGE OF LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

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Introduction: Hepatocyte growth factor (HGF) is a hepatic mitogen and is considered an initiator of liver regeneration. Liver regeneration following partial hepatectomy (PHx) is a complex process where liver sinusoidal endothelial cells (LSEC) play an important role. LSEC are regarded as one of the most important liver cell types that produce HGF, but the exact contribution of LSEC to liver regeneration remains to be defined.
Aims and Methods: To investigate the effects of hepatic angiocrine HGF signaling on liver regeneration, Stab2-Cre$^{tg/wt}$;HGF$^{fl/fl}$ (HGF-LSEC-KO) mice, where HGF is specifically knocked out in LSEC, were used. 70% PHx was performed on these mice and the kinetics of liver to body weight ratio, hepatocyte proliferation, HGF/c-MET signaling pathways, and cell-cycle-associated genes were analyzed at different time points after PHx.
Results: We observed that HGF-LSEC-KO mice have a significantly reduced liver to body weight ratio compared to the control group at 72 hours after PHx. HGF-LSEC-KO mice had a higer mortality after PHx and the proliferation of hepatocytes was significantly impaired at 48 hours after PHx in HGF-LSEC-KO mice.
Conclusion: Angiocrine HGF signaling plays a crucial role in the early stage of liver regeneration after PHx in mice. Hepatic angiocrine HGF signaling is not only essential for liver regeneration after injury but also for the growth of the liver and even the whole organism.
Disclosure: Nothing to disclose

P0635 EXTRACELLULAR VESICLES FROM AMNION-DERIVED MESENCHYMAL STEM CELLS AMELIORATE HEPATIC INFLAMMATION AND FIBROSIS IN RATS

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Introduction: There are no approved drug treatments for liver fibrosis and non-alcoholic steatohepatitis (NASH), an advanced stage of fibrosis which has rapidly become a major cause of cirrhosis. Therefore, development of anti-inflammatory and anti-fibrotic therapies are desired. Mesenchymal stem cell (MSC)-based therapy, which has been extensively investigated in regenerative medicine for various organs, can reportedly achieve therapeutic effect in NASH via paracrine action. Extracellular vesicles (EVs) encompass a variety of vesicles released by cells that fulfill functions similar to those of MSCs including induction of cell proliferation as well as anti-inflammatory, immunomodulatory, anti-fibrotic, and anti-apoptotic effects.
Aims and Methods: We herein investigated the therapeutic effects of EVs from amnion-derived MSCs (AMSCs) in rats with NASH and liver fibrosis.
AMSC-EVs were collected from supernatant of AMSCs with ultracentrifugation. NASH was induced by a 4-week high-fat diet (HFD), and liver fibrosis was induced by intraperitoneal injection of 2 mL/kg 50% carbon tetrachloride (CCl_4) twice a week for six weeks. AMSC-EVs were intravenously injected at weeks 3 and 4 in rats with NASH (15 μg/kg) and at week 3 in rats with liver fibrosis (20 μg/kg). The extent of inflammation and fibrosis were evaluated with quantitative reverse transcription polymerase chain reaction (qRT-PCR) and immunohistochemistry. The *in vitro* effect of AMSC-EVs on inflammatory and fibrogenic response was investigated using rat hepatic stellate cells (HSCs) and Kupffer cells (KCs). In addition, the effect of AMSC-EVs on lipopolysaccharide (LPS)/toll-like receptor (TLR) 4 signaling pathway was investigated in HEK293 and 293/hTLR4-MD2-CD14 cells.
Results: Dynamic light scattering demonstrated that the diameter distribution of AMSC-EVs ranged from 50 to 150 nm, with a single peak at approximately 100 nm. Additionally, the expression of the EV marker CD81 was observed by western blotting of AMSC-EVs. Animal experiments demonstrated that AMSC-EVs significantly decreased the number of KCs in the liver of rats with NASH and the mRNA expression levels of inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6, and transforming growth factor (TGF)-β. Furthermore, AMSC-EVs significantly decreased fiber accumulation, KC number, and HSC activation in rats with liver fibrosis. *In vitro*, AMSC-EVs significantly inhibited KC and HSC activation. AMSC-EVs dose-dependently suppressed the expression of *TNF-α*. In addition, the increase in LPS-induced NF-κB transcriptional activity was significantly suppressed by AMSC-EVs. Furthermore, LPS-induced phosphorylation of IκB-α and p65 was inhibited by AMSC-EVs. AMSC-EVs suppressed the LPS/TLR4 signaling pathway.
Conclusion: AMSC-EVs ameliorated inflammation and fibrogenesis in a rat model of NASH and liver fibrosis, potentially by attenuating HSC and KC activation. AMSC-EV administration should be considered as a new therapeutic strategy for chronic liver disease.
Disclosure: Nothing to disclose

P0636 INTRODUCTION OF CRYOPRECIPITATE INTO THE LIVER LEADS TO IMPROVEMENT OF PORTAL BLOOD FLOW

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Introduction: Liver cirrhosis is a very common pathology in the structure of gastrointestinal diseases. The amount of five-year survival rate is 62% in the compensation stage of cirrhosis whereas it decreases to 19% in the decompensation stage. However, the hepatic tissue has a unique ability for regeneration due to hypertrophy and hyperplasia of ultrastructure of hepatocytes. In this respect, we give preference to minimally invasive techniques with the use of agents influencing an inflammation process and liver regeneration such as cryoprecipitate. The cryoprecipitate is a highly concentrated solution of fibrinogen derived from donor plasma by cryoprecipitation, which consist of growth factors to decrease macrophage activity and cirrhosis progress.
Aims and Methods: To study the changes in portal blood flow in patients with liver cirrhosis after introduction of cryoprecipitate into cirrhotic liver tissue.
40 patients (28 men and 12 women) aged from 25 to 60 (the mean age 45 years) with liver cirrhosis were supervised from 2000 to 2017 in Faculty Surgery Clinic №1. 27 patients had alcoholic cirrhosis and 13 patients had mixed (viral and toxic) cirrhosis. Cirrhosis of Class A according to Child-Pugh was diagnosed in 8 patients, Class B in 13 patients, Class C in 19 patients. Cryoprecipitate was injected into liver tissue (1.5–2 ml in each segment) by percutaneous puncture under ultrasonic guidance. The portal blood flow study was conducted before and 6 and 12 months after the procedure using duplex ultrasound examination.
Results: Statistically significant changes were obtained after 6 months in 92% of patients.
Stagnation index (ratio of the linear velocity of flow to the diameter of the vessel) became normal in 6 months in all patients, which correlates with the risk of bleeding from esophageal veins. In patients with long-term cirrhosis of the liver class A, B and C, the circulation in the portal system was normalized, and the risk of bleeding from the esophageal veins was minimal in 6 months. The results obtained 12 months after the procedure did not changed.
Conclusion: Stimulation of liver regeneration with cryoprecipitate in patients with long-term cirrhosis reduces portal hypertension after 6 months in 92%.
Disclosure: Nothing to disclose

P0637 TOLL-LIKE RECEPTOR 3 PROMOTES LIVER REGENERATION AFTER PARTIAL HEPATECTOMY

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Introduction: Following two-thirds partial hepatectomy (PHx), the liver restores its organ mass due to compensatory growth of the remnant liver. Inflammation plays a crucial role inducing regeneration by stimulating adult G_0 hepatocytes to enter G_1 phase.[1] The endosomal Toll-like receptor 3 (TLR3) detects double-stranded RNA and activates signaling pathways that can either lead to cell survival or cell death. Further, it promotes inflammation via inducing the expression of pro-inflammatory cytokines (e.g. TNFa, IL-6).[2] Previous work has shown that TLR3 supports tissue regeneration during dermal wound repair, but seems to have either host-protective or detrimental effects in the intestine.[3] In contrast, the exact role of TLR3 in the process of liver regeneration needs further clarification.
Aims and Methods: The present study aims to evaluate the role of TLR3 in liver regeneration. Therefore, we examine TLR3-deficient mice (TLR3-/-) and wild type (WT) controls by applying a standardized PHx. With regard to distinct cell cycle phases, we demonstrate the biomolecular characteristics of both mouse strains. Male TLR3-/- on C57BL/6 background and C57BL/6 WT control mice were subjected to surgery. PHx in mice was performed according standard procedures.[4] Animal experiments were performed in accordance with Federal Animal Regulations and were institutionally approved by the District Government of Upper Bavaria. Assessment of liver regeneration was conducted by calculating the liver/body weight ratio. Hepatocyte proliferation was analyzed via IHC applying anti-BrdU monoclonal antibody. For cell cycle analyses Western blotting with following primary antibodies was applied: p-STAT3 (Tyr705), p-Rb (S807/811), p-CDK2 (T160), CDK1, GAPDH and ß-tubulin. The cell cycle inhibitor p21 was examined by quantitative real time-PCR and IL-6 concentrations in serum were measured by an ELISA assay. P values < 0.05 were considered significant.
Results: Liver regeneration was significantly reduced in TLR3-/- according to liver/body weight measurement at 72 hours, 168 hours and 336 hours. Further, TLR3-/- did not reach the WT ratio level at the end of the regeneration process. 4 hours after PHx serum levels of IL-6 were higher in TLR3-/- but no difference in

the protein levels of pSTAT3 was detectable. Cell cycle examinations via Western blotting revealed significantly lower levels of p-Rb protein and p-CDK2 at 32 hours and 40 hours, respectively. In line with G_1/S transition block, less BrdU-positive hepatocyte nuclei in S phase at 32 hours and 40 hours were detectable in TLR3-/- compared to controls. Supporting this finding, also CDK1 in G_2 phase was diminished in TLR3-/-. The cell cycle inhibitor p21 showed a significant increase at 32 hours after PHx in TLR3-/-.

Conclusion: According to our results, TLR3 appears to have a tissue growth promoting effect on the liver after PHx. This was shown by a diminished liver-to-body weight ratio in TLR3-deficient mice. Supporting this finding, the levels of proliferation promoting effector proteins such as CDK2 or Rb protein were reduced. Finally, these results were confirmed by IHC where less BrdU-positive hepatocyte nuclei were found in TLR3-/-. The elevated fold induction of cell cycle inhibitor p21 on mRNA level at 32 hours after PHx could explain the delay of cell cycle progression in our TLR3-/-. However, further investigation of TLR3 influencing liver regeneration is warranted. In this respect, the main objective continue to be the revelation of TLR3-associated signalling pathways inducing cell proliferation upon acute tissue loss in the liver.

Disclosure: Nothing to disclose

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P0638 DEVELOPMENT OF SELF-RENEWING 3D ORGANOIDS CULTURE FROM HUMAN FETAL BILIARY TREE STEM CELLS (HBTSCS) AS A POTENTIAL SYSTEM FOR REGENERATIVE MEDICINE AND DISEASE MODELLING

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Introduction: 3D organoids represent an advanced culture technology in the field of stem cells and regenerative medicine, recapitulating embryonic organ development. Adult or fetal biliary tree represent ideal cell sources of stem/progenitor cells to be used for the regenerative medicine of liver and pancreas. The aim of our study was to generate 3D organoid cultures of hBTSCs and differentiate them toward hepatocyte cells which are suitable for cell therapy and regenerative medicine of liver.

Aims and Methods: The fetal biliary tree (N = 3, obtained from elective pregnancy termination) was digested, mechanically and enzymatically, to isolate *EpCAM/LGR5*-enriched hBTSCs, we also used the fragments of undigested bile duct to cultivate the organoids. Cells and bile duct fragments were then embedded in Matrigel and cultured in an expansion organoid medium containing soluble factors typical of the stem cell niche (e.g. EGF, FGF, Noggin, R-Spondin1) that represent LGR5 ligands and Wnt agonists and favor the expansion of stem cells and maintenance of stemness. Culture medium was also supplemented with Forskolin, a cAMP activator, and with a TGFβR inhibitor to induce cell proliferation and arrest of differentiation. After 7 days the medium was changed to differentiation medium for a period of 10 days. We analyzed colony formation efficiency, organoid size and morphology, cell proliferation and gene expression by RT-qPCR. Also to assess hepatocyte function we used ELISA to analyze albumin secreted in medium of culture.

Results: An average of 85 ± 7 million (N = 3) *EpCAM/LGR5* enriched fetal hBTSCs were obtained. The cells isolated from fetal biliary tree showed a high tendency to generate organoids with high colony formation efficiency (> 60%). Cell proliferation and population doubling in organoids was significantly higher compared to 2D conditions ($p < 0.05$). Fetal biliary tree organoids were composed of single layered cuboidal epithelium and inner cell masses. RT-qPCR analysis demonstrated that organoids in expansion condition expressed multipotency stem cell markers (SOX2, NANOG, OCT4), endodermal stem/progenitor cell markers (LGR5, EpCAM, PDX1, SOX17), hepatic progenitors and ductal markers (CK19, CK7) and stem/progenitor surface genes (NCAM, CD133, CD44), recapitulating major processes of self-organization during embryonic development, whereas the differentiated organoids expressed high level of mature hepatocyte marker like CYP3A and ALB. Interestingly, LGR5 Expression reduced notably in organoids in differentiation condition compared to organoids in expansion condition ($p < 0.01$). Moreover differentiated organoids acquired a hepatocyte morphology, including polygonal cell shape and secreted significant high level of Albumin in to medium respect to the same cells in 2D culture.

Conclusion: We have demonstrated that organoids expand clonogenically stable *in vitro* for at least two months, maintaining a stable phenotype of multipotent stem cells and they can differentiate toward mature functional hepatocyte. This system has potential applications in regenerative medicine of liver and pancreas and in disease modeling.

Disclosure: Nothing to disclose

P0639 ORAL BRANCHED CHAIN AMINO ACID SUPPLEMENTATION INCREASES LIVER PROTEIN SYNTHESIS AND REGENERATION VIA MTOR/4E-BP1 AND AKT IN HEPATECTOMIZED MICE

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Introduction: Branched chain amino acid (BCAA) supplementation may benefit patients with liver cirrhosis and hepatocellular carcinoma. In this study, we attempt to elucidate the effects of BCAA on protein synthesis and hepatocyte regeneration in mice after hepatectomy.

Aims and Methods: Mice were subjected to hepatectomy and then supplemented with or without BCAA. The expression and activity of various proteins were evaluated to determine the mechanistic effects of BCAA supplementation. In addition, the effects of various doses of BCAAs on HepG2 cells were evaluated.

Results: BCAA supplementation for 1 day significantly increased the body weight, liver/body weight ratio, and epididymal fat weight of hepatectomized mice. BCAA intake for 7 days significantly increased serum albumin levels and increased the expression of phosphorylated mammalian target of rapamycin (p)-mTOR and p- eukaryotic translation initiation factor 4E binding protein 1 (4E-BP1), thereby promoting liver protein synthesis. BCAA supplementation for 1, 3, and 7 days increased DNA synthesis in mouse hepatocytes after liver hepatectomy and activated p-protein kinase B (Akt). In HepG2 cells, 1×, 2×, and 5× concentrations of BCAAs increased cell proliferation. All doses of BCAAs activated p-mTOR and p-Akt, while 2×, 5×, and 10× doses of BCAAs increased the protein expression of p-4E-BP1 and only 1× BCAA increased cyclin D1 protein levels.

Conclusion: These results suggest that BCAA supplementation may represent a therapeutic strategy for patients undergoing liver operation by increasing liver protein synthesis and may play a role in hepatocyte regeneration. The beneficial effects of oral BCAA supplementation may involve the mTOR/4E-BP1 and Akt pathways.

Disclosure: Nothing to disclose

P0640 NEW OPPORTUNITIES OF COMBINED DIAGNOSTICS OF HEPATIC FIBROSIS AND STEATOSIS IN CLINICAL PRACTICE

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Introduction: Non-invasive diagnoses of hepatic fibrosis (HF) have become a part of clinical practice over the past 10 years. Non-invasive techniques for quantification of hepatic steatosis (HS) remains not always available.

Meanwhile, the clinical importance of steatosis determination is great, since HS is the morphological substrate of alcoholic (ALD) and non-alcoholic liver disease (NAFLD), metabolic and drug-induced liver injury (DILI), HS accompanies chronic viral hepatitis (CVH) and aggravates the progression of HF.

Transient elastography using the FibroScan® 502 Touch with XL probe and CAP technology allows to reliably define HF and HS in obese patients.

Aims and Methods: We aimed to evaluate the capabilities of the FibroScan 502 TOUCH with XL probe and CAP technology in non-invasive diagnostics of the combined determination of HF and HS.

1265 outpatients with first gastroenterologist's appointment were included in the study. Men 728 (59%), mean age 36.4 ± 5.7 years, duration of the disease -1.0 ± 1.9 years, BMI ≥30–407 (33%), hepatic steatosis according to ultrasound in 456 (37%). Patients were divided into 3 groups:

1) with cytolysis more than 1.5 norms, 2) with the presence of steatosis by ultrasound; 3) patients with CVH. All participants underwent general examination to find out the etiology and activity of the disease.

Results: Patients from group 1 have had the following diseases: NAFLD (35%), ALD (28%), opisthorchiasis (5%), hypothyroidism and autoimmune thyroiditis (4%), primary biliary cholangitis (3%), DILI (25%). According to FibroScan 502 TOUCH with XL probe and CAP evaluation the HS was identified in 88% of cases (ALD, NAFLD, DILI).

In group 2: NAFLD (55%), ALD (28%), DILI (17%), all patients had HS. In group 3: CHC (100%), HS - in 75%, in half of cases HS was not associated with BMI ≥25. 82% of patients had genotype 3.

Conclusion: Transient elastography using the FibroScan® 502 Touch with XL probe and CAP technology allows to reliably define HF and HS in normal weight and overweight patients. It helps to prescribe the patients correct medications.

Disclosure: Nothing to disclose

P0641 DHEA-S LEVEL AS MARKER OF INFLAMMATION AND FIBROSIS IN NAFLD PATIENTS

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Introduction: NAFLD includes a pathological spectrum of phenotypes ranging from simple steatosis to steatohepatitis (NASH), the progressive from of fatty liver disease associated with inflammation and cellular injury. Dehydroepiandrosterone -s (DHEA-s), is a steroidal hormone present at highest concentration in the body, with an improving effect on insulin resistance, an antioxidant effect and antifibrotic effect. Aim of our study was to correlate DHEA-s level with presence of NASH and also with insulin resistance and leptin level.
Aims and Methods: We included 153 patients with NAFLD and we divided into 2 groups: 73 patients NASH group and 80 non- NASH group, age and sex-matched. The diagnostic criteria for NASH was fatty liver accompanied by the presence of steatohepatitis in biopsy samples. Severity of NASH was diagnosed by activity (grade) and fibrosis (stage). In all patients we determined BMI, aminotransferases, insulin level, HOMA -IR, leptin level and DHEA-s level.
Results: In NASH group BMI was 32.5 ± 3 and in non- NASH group BMI was 30.3 ± 3, without statistic significance. In NASH group, DHEA-s level was lower than normal value adjusted with age and gender and also lower compared with non- NASH group where the DHEA-s level was normal. In NASH group DHEA-s correlated with leptin level ($p = 0.038$) and insulin resistance ($p = 0.042$), but didn't correlated with fibrosis degree ($p = 0.282$), aminotrasferases (ASAT $p = 0.143$ and ALAT $p = 0.119$). If we selected from NASH-group only 52 patients with low degree of fibrosis (0–2) based on Brunt's Criteria, we observed that DHEA-s level correlated with fibrosis progression, in the others 21 patients with high degree of fibrosis or cirrhosis DHEA-s didn't correlated with progression of the disease. In non-NASH group DHEA-s didn't correlated with any parameters (aminotransferases, leptin, insulin or HOMA-IR).
Conclusion: In our study, decreased level of DHEA-s was associated with inflammation and progression of fibrosis in early stages of disease and, also, correlated with leptin and insulin resistance. In patients with simple steatosis or high degree of fibrosis/ cirrhosis DHEA-s didn't prove to be a marker for disease's evolution
Disclosure: Nothing to disclose

P0642 BERBERIS ARISTATA, ELAEIS GUINEENSIS AND COFFEA CANEPHORA EXTRACTS IMPROVE HEPATIC STEATOSIS THROUGH THE MODULATION OF THE METABOLIC PROFILE AND OF MIR-122 LEVELS IN AN ANIMAL MODEL OF NAFLD

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Introduction: NAFLD and metabolic syndrome seem to have insulin resistance as a common pathophysiological mechanism. Recently, a number of studies have described microRNAs (miRNAs) as mediators in the pathogenesis of both insulin resistance and NAFLD.
Aims and Methods: The aim of this study is to evaluate whether and how a mixture of plant extracts consisting of *Berberis Aristata*, *Elaeis Guineensis* and *Coffea Canephora* may affect the development of obesity, hepatic steatosis and insulin resistance, conceivably associated to the modulation of miRNAs levels, in an animal model of NAFLD induced by a high fat diet. Three groups of C57BL/6 mice ($n = 8$ each) were randomized into one of the following 24 week diets: 1) standard diet (SD); 2) high fat diet (HFD, 60% fat); 3) HFD enriched with plant extract (HFD+E) (140 mg/Kg/die). Body weight was monitored during the diet protocol. At the end of the treatment all mice were fasted for 4 hours and intraperitoneally injected with a bolus of insulin (0.75U/kg) to test the insulin tolerance by ipITT. Blood samples were used to measure glycaemia by a portable glucometer, insulinemia by ELISA essay, transaminases and lipid profile by a clinical chemistry benchtop analyzer. After sacrifice, liver biopsies were collected to examine the hepatic histology by H&E staining and to isolate total RNA and measure miRNA expression by q-PCR.
Results: The HFD+E mice show lower body weight (40±3.6 g vs 47.4±6 g, HFD+E vs HFD, $p = 0.008$), the amelioration of insulin sensitivity (10138±1620 mg/dl*120min vs 7529±1469 mg/dl*120min, iAUC of HFD+E vs HFD, $p = 0.008$) together with the reduction of insulinemia (725,8±270 pg/ml vs 1156.3±307.4 pg/ml, HFD+E vs HFD, $p = 0.04$), total cholesterol (178±17 mg/dl vs 209±19 mg/dl, HFD+E vs HFD, $p = 0.007$), low density lipoproteins (10.7±3.2 mg/dl vs 19.3±1.6 mg/dl, HFD+E vs HFD, $p < 0.001$), triglycerides (86.3±11 mg/dl vs 130.3±22 mg/dl, HFD+E vs HFD, $p < 0.001$) and alanine-aminotrasferase (38.7±24 U/l vs 81.3±47 mg/dl, HFD+E vs HFD, $p = 0.03$) compared to HFD mice. H&E staining show macro- and microvesicular steatosis with ballooning degeneration in mice fed with HFD, which is improved in mice fed with HFD+E. Moreover, a down-regulation of miR-122 hepatic levels is observed in HFD mice compared to SD mice (0.95±0.6 REU vs 2.17±1.5 REU, HFD vs SD, $p = 0.03$). Interestingly, this effect on the miRNA levels is prevented by the combination of plant extracts with HFD (1.39±0.03 REU vs 0.95±0.6 REU, HFD vs SD, $p = 0.03$).
Conclusion: In conclusion, the combination of *Berberis Aristata*, *Elaeis Guineensis* and *Coffea Canephora* added to HFD is able to ameliorate obesity, insulin resistance and hepatic steatosis, which are developed by C57BL/6 mice fed with a HFD. Moreover, this metabolic profile associates to the modulation of hepatic miR-122 levels, which are down-regulated in HFD mice and remain unchanged in mice fed with HFD+E compared to SD mice. These data suggest a possible role of miR-122 in the beneficial effects of Berberis Aristata, Elaeis Guineensis and Coffea Canephora combination on metabolic syndrome.
Disclosure: Nothing to disclose

P0643 MANAGEMENT THE PATIENTS WITH GALLSTONE DISEASE

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Aims and Methods: Development of a diagnostic and therapeutic algorithm for optimizing the treatment of gallstone disease based on ultrasound and CT of the gallbladder.
235 patients (31% of men) were included in the study, mean age (Mediana) = 48 years, mean duration of the disease (Mediana) = 1.8 years. In all cases gallstones have been diagnosed by abdominal ultrasound. Disease risk factors were identified: irregular meals - 78%, heredity - 40%, obesity - 35%; comorbid diseases of the gastrointestinal tract - 75%, heart ischemic disease and arterial hypertension −41%, diabetes mellitus and glucose intolerance-38%, urolithiasis and gout −11%. The technique of Philips CT scanner 'MX-8000 IDT-16CT' have been used to evaluate the stones density in Hounsfield *Units* (X-ray negative stones - < 100 Hounsfield *Units*). The same method has been used to evaluate steatosis of the liver and pancreas and atherosclerosis of the abdominal part of aorta.
Results: All patients were divided into 3 groups: 1) with biliary sludge (bile rheology disorder) −10% ($n = 24$), 2) with the gallstones density < 100 Hounsfield *Units (HU)*, 41% ($n = 98$), 3) with the gallstones density > 100 HU - 49% ($n = 113$). The patients from group 3 were recommended to perform cholecystectomy.
Patients with biliary sludge and gallstones < 100 HU ($N = 122$), which occupying < 1/3 of the gallbladder volume, were recommended to follow hypolipidemic diet, physical activity, body weight normalization, litholytic therapy with ursodeoxicholic acid (UDCA) was administered in daily dose of 15 mg / kg of body weight for 3 months. After the end of this period repeated CT was done. Depending on the result therapy with UDCA was either ended or continued. Steatosis of the liver was detected in 35% of cases ($n = 74$, $Me = 32$ units), pancreas - in 32% ($n = 70$, $Me = 28$ units). The gallstones density correlated ($r = 0.5$) with the degree of liver and pancreas steatosis, abdominal aorta atherosclerosis deformation and increased volume of gallbladder, liver cysts and hemangiomas, patients age.
After 6 months of UDCA administration biliary sludge resolved in 91.7%, gallstones with density < 100 HU resolved in 11.3%. After 9 months of such a treatment biliary sludge resolved in 100%, gallstones with density < 100 HU - in 52% of patients. After 12 months, the dissolution of stones reached 81.3%. In 18.7% of cases ($n = 18$) therapy was unsuccessful. The steatosis of the liver ($Me = 55$ units) and pancreas ($Me = 44$ units) decreased according to CT at month 6 and month 12 ($p < 0.05$).
Conclusion: Litholytic therapy with UDCA for 6 months resulted in biliary sludge resolution in 100% cases, the same therapy for 12 months resulted in resolution of gallstones < 100 HU in 82% cases which accompanied with regression of liver and pancreas steatosis. In other conditions cholecystectomy is indicated.
Disclosure: Nothing to disclose

P0644 DRUG HOLIDAY IN PATIENTS WITH POLYCYSTIC LIVER DISEASE TREATED WITH SOMATOSTATIN ANALOGUES: A NOVEL TREATMENT STRATEGY

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Introduction: Somatostatin analogues (SA) reduce liver volume in patients with polycystic liver disease (PLD). The effect tends to wear off after 6 months of therapy suggesting development of SA tolerance. Drug holidays, defined as an interruption of pharmacotherapy for a period of time, could be the answer to the development of tolerance. In this study we examined the liver volume reducing effect of SA rechallenge after a drug holiday.

Aims and Methods: We selected patients from the International PLD registry from two tertiary centers. Patients were included when treated with SA, octreotide or lanreotide, during two cycles (On-1 and On-2) separated by a drug holiday (Off-1). Each separate period lasted at least 3 months. For our primary outcome we compared the effect of SA between On-1 and On-2, expressed as percentage change in height adjusted liver volume (hTLV) assessed by computed tomography or magnetic resonance imaging. For our secondary outcomes we compared natural liver growth before SA treatment (Off-0) with liver volume change during drug holiday (Off-1).
Results: Out of 741 patients in the PLD registry, 45 patients were treated at least twice with SA. In 34 patients, the initial liver volume reducing effect was similar to that after rechallenge [−2.5% per 6 months (IQR -3.8-0.8) vs. −1.6% per 6 months (IQR -3.0-0.9), p = 0.521]. In patients who responded in On-1, defined as a decrease in liver volume, 86.4% again showed a decrease in On-2. In 25 patients, the increase in hTLV per 6 months was significant higher during the drug holiday (Off-1) compared with the natural growth (Off-0) before initial SA exposure (4.5% vs 1.6%, p = 0.009) suggesting a rebound effect. In the group of patients who responded in the first treatment cycle (On-1), hTLV decreased with 0.1% per 6 months in the total observation period (On-1, Off-1 and On-2) in which patients were treated for 53.1% of the time (−0.6% after 46.5 months).
Conclusion: These results postulate that a drug holiday resensitizes the liver to the beneficial pharmacological effects of SA. Our results support the concept of rechallenge after a drug holiday as a strategy for selected patients with PLD. This strategy avoids needless continuous therapy and reduces medical costs.
Disclosure: Nothing to disclose

P0646 SQLE DRIVES NON-ALCOHOLIC FATTY LIVER DISEASE AND SERVES AS A THERAPEUTIC TARGET

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases worldwide; however, the mechanisms involved in NAFLD development remains largely unknown. Cholesterol is increasingly recognized as a causative agent in NAFLD. SQLE is a one of the rate-limiting enzyme in the endogenous cholesterol biosynthesis pathway, but its role in the pathogenesis of NAFLD is unknown.
Aims and Methods: We aimed to evaluate the functional role and molecular mechanisms of SQLE in NAFLD and to assess the therapeutic efficacy of targeting SQLE in NAFLD. The biological function of SQLE and therapeutic efficacy of terbinafine (SQLE selective inhibitor) was assessed in hepatocyte-specific Sqle transgenic mice.
Results: SQLE mRNA expression was significantly up-regulated in NAFLD patients (N = 23) as compared to healthy controls (N = 16). We evaluated the biological function of SQLE in the evolution of NAFLD in SQLE transgenic (tg) animal models. Wild-type and hepatocyte-specific Sqle tg mice were fed with normal chow for 11 months. Compared to wild-type littermates, Sqle tg mice showed significant higher liver-to-body weight ratio and increased hepatic levels of triglyceride, cholesterol and free fatty acid, accompany with enhanced insulin resistance by insulin tolerance tests (ITTs). Moreover, Sqle tg mice displayed increased serum levels of aspartate transaminase (AST) and alanine transaminase (ALT). H&E staining confirmed the histological presence of steatohepatitis (NASH) in the livers of Sqle tg mice; whereas wild-type mice showed normal histology. These findings suggested for the first time that hepatocyte overexpressing SQLE in Sqle tg mice spontaneously leads NASH formation.
Additional experiments were performed to confirm the role of SQLE in NASH. Sqle tg mice and wild-type mice with fed with high fat high cholesterol (HFHC) diet for 15 weeks. Compared to wild-type mice, Sqle tg mice fed HFHC diet had a significant increased body weight, liver weight, liver-to-body weight ratio, enhanced hepatic free fatty acid, triglyceride, and cholesterol; and significantly induced serum levels of triglyceride, cholesterol, ALT and AST. ITTs and glucose tolerance test revealed the marked elevated insulin resistance in HFHC diet fed Sqle tg mice than wild-type mice. Liver histology demonstrated a pronounced steatohepatitis with fibrosis in Sqle tg mice compared to wild-type mice In keeping with this, mRNA expression of pro-inflammatory and pro-fibrotic factors including Tgfβ1, Tnfα, Ccl-20, Ccl-12, Col1α1 and Col1α2 were significanctly induced in tg mice fed HFHC diet. These data confirmed the effect of SQLE in promoting the development of NASH.
We finally evaluated the therapeutic efficacy of SQLE inhibitor (terbinafine) in NASH.
Terbinafine treatment significantly attenuated body weight, liver weight and liver-to-body weight ratio; decreased liver free fatty acid, triglyceride and cholesterol; reduced serum levels of ALT and AST; improved insulin resistance and markedly attenuated histological severity of steatohepatitis in tg mice fed HFHC diet compared to the untreated mice fed the same diet.
Conclusion: We identified for the first time that SQLE causes spontaneous NASH formation in hepatocyte specific SQLE tg mice and facilitates the development of NASH fibrosis in tg mice fed HFHC diet. SQLE inhibitor terbinafine protects against NASH formation and may serve as a potential therapeutic target for patients with NASH.
Disclosure: Nothing to disclose

P0647 EVALUATION OF CIRCULATING HORMONES IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE AS POTENTIAL BIOMARKERS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of hepatic dysfunction ranging from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH), which may potentially progress to liver cirrhosis and hepatocellular carcinoma. Liver biopsy remains the gold standard method to distinguish steatosis from NASH and to identify the extent of liver injury and fibrosis despite its invasive nature with potential serious complications.
Aims and Methods: We aimed to evaluate the performance of circulating levels of hormones relevant for the pathogenesis of NAFLD/NASH as potential biomarkers. Serum levels of adiponectin, leptin and insulin-like growth factor-I (IGF-I) were evaluated in a cohort of morbidly obese patients with a clinical and biopsy-proven diagnosis of steatosis (n = 26) or NASH (n = 13), using enzyme-linked immunosorbent assays (ELISA) recently developed and produced by Mediagnost. Hormone levels were correlated with fasting serum glucose and insulin, hepatic transaminases, gamma-glutamyltransferase (*GGT*), direct bilirubin, free fatty acids, triglycerides, apoliprotein A1, cytokeratin 18, high-density lipoprotein (HDL) and low-density lipoprotein cholesterol, and total cholesterol. Serum of liver disease-free individuals was also analyzed (n = 7–13).
Results: Leptin levels were significantly augmented in steatosis and NASH patients, compared with healthy controls ($p < 0.005$). The area under the receiver-operating characteristic (AUROC) related to NAFLD *versus* healthy controls was 0.88 (95% CI = 0.77–0.98; $p < 0.0001$). In turn, IGF-I concentrations were significantly diminished in steatosis and NASH patients, compared with controls ($p < 0.05$), showing an AUROC of 0.81 (95% CI = 0.68–0.94; $p < 0,05$). Finally, adiponectin levels were significantly decreased in NASH patients compared with steatosis ($p < 0.05$) or healthy individuals ($p < 0,01$), and the AUROC was 0.79 (95% CI = 0.62–0.96; $p < 0.01$). Circulating concentrations of adiponectin were negatively correlated with serum levels of glucose, insulin, GGT, alanine aminotransferase and bilirubin in the cohort of NAFLD patients (at least, $p < 0.05$).
Conclusion: Overall, these parameters are potentially valuable tools for non-invasive stratification of patients with NAFLD. Particularly, adiponectin might discriminate the presence of NASH in morbidly obese patients. Future studies should validate these biomarkers in independent larger cohorts, as well as the impact of confounding factors such as obesity.
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Disclosure: Nothing to disclose

P0648 HIGH PREVALENCE OF DYSLIPIDEMIA BUT INSUFFICIENT STATIN USE IN PATIENTS WITH NON-CIRRHOTIC AND CIRRHOTIC LIVER DISEASE

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Introduction: Dyslipidemia increases cardiovascular risk in the general population. Chronic liver disease (CLD) affects lipoprotein synthesis, but prevalence/relevance of dyslipidemia in CLD is controversial. Interestingly, statins and fibrates may have hepatoprotective effects. Therefore, we investigated lipid profiles in patients with non-cirrhotic and cirrhotic CLD of different etiologies, as well as the utilization of statins in these patients.
Aims and Methods: Patients with alcoholic liver disease (ALD; n = 121), hepatitis C (HCV, n = 1438), hepatitis B (HBV, n = 384), NAFLD (n = 532), cholestatic liver disease (n = 119), or autoimmune hepatitis (AIH, n = 114) were included. Liver stiffness values ≥15kPa defined cirrhosis. Dyslipidemia was diagnosed by either (i) total cholesterol > 200mg/dL, (ii) LDL > 130mg/dL or (iii) triglycerides > 200mg/dL.
Results: Across all etiologies, total cholesterol levels was lower in patients with cirrhosis as compared to non-cirrhotic patients. Similarly, LDL levels were lower in cirrhotic HCV, HBV, NAFLD and AIH. HDL decreased in HCV and NAFLD cirrhosis. Triglyceride levels did not differ between non-cirrhotic and cirrhotic patients. Comorbidities (arterial hypertension, NIDDM and IDDM) were more prevalent in patients with cirrhosis, while in general, the prevalence of dyslipidemia was lower in cirrhotic than non-cirrhotic patients (33.9% vs. 22.4%, $p < 0.001$). Lipid lowering therapy was underutilized in patients with liver disease as 27.9% did not receive indicated therapy (29.9% in patients without and 20.0% in patients with cirrhosis, respectively).
Conclusion: Dyslipidemia and cardiovascular comorbidities are common in patients with CLD. Progression to cirrhosis affects total cholesterol and HDL/LDL levels. Lipid-lowering therapy is highly underutilized in patients with CLD.
Disclosure: Nothing to disclose

P0649 COMPARISON BETWEEN M AND XL PROBES OF TRANSIENT ELASTOGRAPHY FOR THE ASSESSMENT OF HEPATIC STEATOSIS WITH CONTROLLED ATTENUATION PARAMETER (CAP)

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Introduction: Controlled attenuation parameter (CAP) is a new method for the non-invasive diagnosis of hepatic steatosis (HS) acquired by transient elastography. The aims of this study were to assess the concordance of HS measurements with the M and XL probes of Fibroscan® as well as to determine the concordance of classification of the grade of steatosis using the cut-off values determined by de Lédinghen et al [1].
Aims and Methods: In a cross-sectional prospective study, transient elastometry acquisitions were performed using the M probe then the XL probe. The inter-observer concordance for CAP measurements was assessed using the intraclass correlation coefficient and the concordance of the steatosis grade classification was characterized using the κ index. Cutoffs were (M and XL probes respectively) 246/242 for the presence of HS and 285/286 dB/m for the presence of severe HS.
Results: A total of 136 patients were included. Women accounted for 51.5%. Fifty (36.8%) patients were hepatitis C virus (HCV) monoinfected, 46 (33.8%) were hepatitis B virus (HBV) monoinfected, 17 (12.5%) had NAFLD, 5 (3.7%) were HIV/HCV coinfected and 2 were HBV/HCV coinfected (1.5%).
Thirty one percent of our patients were obese (BMI $\geq$ 30kg/m^2) and 32.6% were overweight (BMI $\geq$ 25 kg/m^2). The mean CAP value using the M probe was significantly higher than the mean CAP value using the XL probe (255.5 dB/m vs 245.4 dB/m, p = 0.007). The corresponding median liver stiffness measurements were 6.5kPA and 5.9 kPA respectively. The overall intraclass correlation coefficient for the single measures was 0.738 (95% confidence interval: 0.645–0.808).
Hepatic steatosis was present in 51.9% and 55.6% of patients with the M and XL probes respectively. Severe HS was noted in 28.9% and 25.2% of patients with the M and XL probes respectively. The κ indexes for the concordance of classification for the presence of significant HS and severe HS were 0.581 and 0.605, respectively.
The rates of CAP examinations with IQR > 50 using the M probe was 7.4% whereas it reached 46.7% using the XL probe.
Conclusion: Single CAP values with the M and XL probes are well correlated however the use of cutoff values leads to a suboptimal concordance of grade classification. The rate of examinations with an IQR > 50 is much higher using the XL probe.
Disclosure: Nothing to disclose

Reference

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P0651 NEUTROPHIL-TO-LYMPHOCYTE RATIO: AN ACCURATE METHOD FOR PREDICTING INFECTION IN CIRRHOSIS

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Introduction: Patients with cirrhosis have increased susceptibility to bacterial infections. It is critical, but frequently challenging, to diagnose an early bacterial infection in cirrhotic patients. The neutrophil-to-lymphocyte ratio (NLR) reflects systemic inflammation. It is an emerging biomarker that replicates cirrhosis' imbalanced immune response.
Aims and Methods: We aimed to determine the correlation between NLR values and infection
Retrospective, unicenter study, including patients with cirrhosis, admitted to the hospital at first decompensation, during 6 years. NLR was calculated at admission. Applying logistic regression models and testing for discriminative power, we correlated NLR with the outcome infection.
Results: We included 139 patients. The main cirrhotic etiology was alcoholic, 118 (84.9%). The major admission cause was inaugural ascites, 80 (57.6%). Infection affected 43 (30.9%) patients, 18 (12.9%) were community infections and 26 (18.7%) were hospital-acquired infections.
Higher NLR values were associated with significant increase in infection risk (p = 0.005), for each unit increase in NLR the odds of infection increased 1.15 times. Stratifying by admission cause, this association persisted on GI bleeding (OR 1.22, p = 0.012) and encephalopathy (OR 1.22, p = 0.022). We report similar Odds on community infections. On the hospital-acquired infection group, only the GI bleeding subgroup was significant (OR 1.15, p = 0.049). NLR has an acceptable discriminative power to predict infection (AUC 0.618, p = 0.027). Adjusting for admission cause, we obtained a better discriminative power on encephalopathy (AUC 0.754, p = 0.010).
On the community infections subgroup, we account the cut-off point 3.6, for better acknowledging infection risk (< = 3.6: Community infection risk 1.8%; > 3.6: Community infection risk 20.2%).
Conclusion: NLR is a simple and clinically forward approach to attest the individual infection risk on cirrhotic patients. We report the NLR cutoff 3.6 as the optimal for infection prediction.
Disclosure: Nothing to disclose

P0652 HOSPITAL READMISSION RATES IN HEPATIC CIRRHOSIS: WHICH PATIENTS PRESENT HIGHER RISK?

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Introduction: Patients with hepatic cirrhosis (HC) are at high risk of hospital readmission (HR).
Aims and Methods: We aimed to determine the HR rate at 30 and 90 days after index hospitalization (IH) for decompensation, as well as the reasons and possible predictors.
Retrospective and unicentric study involving patients with HC who were hospitalized within 9 years.
Results: Included 177 patients, 85.3% with alcoholic HC.
At IH, 73.4% of the patients presented with ascites, 47.5% with variceal bleeding, 22.6% hepatic encephalopathy (HE), 7.9% hepatocellular carcinoma and 1.1% hepatorenal syndrome (HRS). Regarding intra-hospital complications, 11.9% had Spontaneous Bacterial Peritonitis (SBP), 20.9% acute kidney injury (AKI) and 20.3% other types of infections (respiratory, urinary, cutaneous).
The HR rate at 30 and 90 days was 40.1% and 28.2% respectively.
In the univariate analysis we found that patients with HE (60% vs 34.3%, p = 0.004), SBP (66.7 %% vs 36.5%, p = 0.008) and AKI (56.8% vs 35.7%; p = 0.02) were more frequently readmitted at 30 days. Patients with HE (45% vs 23.4%, p = 0.007) and AKI (43.2 vs 24.3%; p = 0.023) in IH were more frequently readmitted at 90 days.
In the multivariate analysis, the presence of HE (OR 2.485 CI 95% 1.166–5.298;p = 0.018) and SBP (OR 3.599 IC95% 1.333–9.721; p = 0.012) were predictors of HR at 30 days.
In the multivariate analysis HE was the only predictor for HR at 90 days (OR2.345 ± 95% 1.097–5.014; p = 0.028)
Conclusion: In a population of cirrhotic patients, a high rate of hospital readmission of 40.1% and 28.2% was observed at 30 and 90 days respectively. HE was a common predictor of readmission at 30 and 90 days.
Disclosure: Nothing to disclose

P0653 CEREBRAL VASCULAR RESISTANCE IS INCREASED IN CIRRHOTIC PATIENTS WITH MINIMAL HEPATIC ENCEPHALOPATHY AND REMAINS UNCHANGED AFTER MEDICAL TREATMENT

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Introduction: In cirrhotic patients, cerebral vascular resistance indices (resistivity index, RI and pulsatility index, PI) are good indicators of cerebral hemodynamic abnormalities and are closely correlated with the severity of cirrhosis, hepatic encephalopathy (HE) and ascites. However there are still poor data about cerebral vascular indices and minimal HE (MHE).
Aims and Methods: The aim of this study was to correlate cerebral arteries resistance indices with the presence of MHE and to evaluate their modification after treatment with rifaximin.
38 consecutive cirrhotic patients were enrolled in this study. Exclusion criteria were overt HE (West Haven $\geq$ 1), age < 18 years, active alcohol consumption, sepsis, cerebrovascular diseases, cerebral neoplasms, cardiac diseases, peripheral vascular diseases, treatment with rifaximin in the previous 30 days. Patients presenting signs of MHE at the psychometric evaluation (TMT-A, TMT-B and DST) received rifaximin 1200 mg daily for 10 days. All patients underwent TCD for the measurement of RI and PI of the mean cerebral artery (MCA) and of posterior cerebral artery (PCA) at baseline and within 2 weeks after rifaximin treatment. Median value of the right and left side arteries have been used for the analysis. Intra-abdominal vessels (renal arteries, mesenteric artery, portal vein) flow parameters were also assessed, and the Child-Pugh score was calculated.
Results: Among the patients enrolled in the study 17 had MHE (44.7%). MCA-PI, PCA-PI and RI were significantly increased in patients with MHE compared to those without (MCA-PI 1.04 vs 1.05, p = 0.05; PCA-PI 1.12 vs 0.9, p = 0.02; PCA-RI 0.64 vs 0.56, p = 0.01) while MCA-RI showed a trend towards the increase (0.65 vs 0.61, p = 0.07). No significant difference was found in the intra-abdominal vessels flow parameters between the two groups. Furthermore, cerebral arteries resistance indices were not associated with the Child-Pugh score. After treatment with rifaximin, TMT-A and B and DST showed a significant

improvement (p = 0.05, p = 0.03 and p = 0.003 respectively). Only PCA-RI was ameliorated after rifaximin treatment (p = 0.024).
Conclusion: MHE is associated with increased cerebral vascular resistance in cirrhotic patients, which remains substantially unchanged after medical therapy.
Disclosure: Nothing to disclose

P0654 ACUTE OCCLUSION OF EXPANDED POLYTETRAFLUOROETHYLENE-COVERED TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT: INCIDENCE, CLINICAL OUTCOMES, AND PROGNOSTIC FACTORS

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Introduction: The expanded polytetrafluoroethylene (ePTFE)-covered stent has been widely used in the transjugular intrahepatic portosystemic shunt (TIPS) procedure. The purpose of this study was to evaluate the incidence, clinical outcomes, and prognostic factors of acute TIPS occlusion (ATO) in TIPS recipients using ePTFE-covered stents.
Aims and Methods: A retrospective study, including 222 TIPSs created with ePTFE-covered stents between June 2015 and June 2017 was performed. Medical records were reviewed to identify demographics, underlying liver disease, and TIPS procedure data, and the influence of these variables on ATO was assessed by multivariate logistic regression analysis.
Results: TIPS technical success was achieved in 219 patients (98.6%). Two patients were excluded due to missing data, leaving 217 patients for final analysis. ATO occurred in nine patients (4.1%). In all series, parameters that were significantly different between patients with and without ATO were platelets levels, previous splenectomy, portal vein thrombosis, portal cavernoma, shortage of stent in the hepatic vein, stricture on the shunt, and residual thrombosis below the shunt. On multivariable logistic regression, stricture on the stent (hazard ratio = 36.09; 95% confidence interval [CI]: 2.93–443.96; p = .005), and previous splenectomy (hazard ratio = 22.99; 95% CI: 1.29–408.39; p = .033) were demonstrated as independent, significant risk factors for ATO.
Conclusion: ATO is not uncommon in the era of ePTFE-covered stents. The stricture on the shunt and previous splenectomy are vital prognostic factors for ATO in TIPS recipients.
Disclosure: Nothing to disclose

P0655 NEUTROPHIL TO LYMPHOCYTE RATIO AS PREDICTOR OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME AND MORTALITY IN PATIENTS WITH DECOMPENSATED LIVER CIRRHOSIS

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Introduction: Fatal infections with signs of systemic inflammatory response syndrome (SIRS) are often seen in patients with decompensated liver cirrhosis. SIRS in these patients is associated with progressive organ dysfunction. Simple prognostic factors to predict mortality in such patients are needed.
Aims and Methods: The aim of the study was to to evaluate the role of the neutrophil-to-lymphocyte ratio (NLR) to predict SIRS and mortality in patients with decompensated liver cirrhosis during hospitalization.
In this retrospective observational cohort study were enrolled 36 patients with decompensated liver cirrhosis between January 2009 and December 2016. The primary end points of the study were survival during hospitalization and presence of SIRS. NLR along with Child-Pugh score, MELD score, leukocyte, lymphocyte and neutrophil counts were assessed for the prediction of mortality and SIRS.
Results: A strong correlation was found between mortality and the following parameters: the level of neutrophils (r = 0.720; p < 0.001), lymphocytes (r = −0.760; p < 0.001), NLR (r = 0.749; p < 0.001), presence of SIRS with proven infection (r = 0.750; p < 0.001) and MELD (r = 0.795; p < 0.001). The median NLRs were 2.4 (IQR: 1.9–3.9) and 21.6 (IQR: 9.3–30.6) in surviving and non-surviving patients, respectively (p < 0.001). Multivariable analysis showed that a low lymphocyte count was an independent risk factor for mortality (OR: 0.68 [95% CI 0.517–0.895]; p = 0.006). The AUC values were 0.958 ± 0.028 (p < 0.0001) for NLR and 0.816 ± 0.087 (p < 0.0003) for lymphocyte count. The sensitivity and specificity of the NLR > 4.033 were 100% (95% CI 73.5–100) and 79.17% (95% CI 57.8–92.9), respectively, with 70.6% (95% CI 52.2–84.0) positive and 100% negative predictive values. The sensitivity and specificity of the lymphocyte count ≤ 0.9 were 83.3% (95% CI 51.6–97.9) and 75% (95% CI 53.3–90.2), respectively, with 62.5% (95% CI 44.4–77.7) positive and 90% (95% CI 71.3–97.0) negative predictive values.
Multifactorial analysis of SIRS with proven infection showed that NLR was an independent risk factor for its development (OR: 1.21 [95% CI 1.046–1.41]; p = 0.011). The AUC value was 0.865 ± 0.085 (p < 0.0001). The sensitivity and specificity of the NLR > 4.869 were 83.3% (95% CI 51.6–97.9) and 83.3% (95% CI 57.8–92.9), respectively, with 71.4% (95% CI 49.7–86.4) positive and 90.9% (95% CI 73.6–97.3) negative predictive values.
A subanalysis of 22 patients with Child-Pugh C cirrhosis also demonstrated that lymphocyte count was an independent risk factor for the development of SIRS with proven infection (OR: 0.76 [95% CI 0.609–0.955]; p = 0.018), as well as for mortality (OR: 0.69 [95% CI 0.503–0.957]; p = 0.026). The AUC value was 0.758 ± 0.115 (p < 0.025), with a cut-off value ≤0.8 and 70% (95% CI 34.8–93.3) of sensitivity and 83.3% of specificity (95% CI 51.6–97.9), PPV - 77.8% (95% CI 48.1–93.0), NPV - 76.9 (95% CI 55.6–89.9) for SIRS outcome. In mortality analysis, the lymphocyte AUC was 0.864 ± 0.09 (p < 0.0001), with a cut-off value ≤1.3 and 90% (95% CI 58.7–99.8) of sensitivity and 81.8 % of specificity (95% CI 48.2–97.7), PPV - 83.3% (95% CI 58.5–94.7), NPV - 90 (95% CI 57.6–98.3).
Conclusion: According to these results NLR and lymphocyte count can be regarded as independent prognostic factors for the development of SIRS with proven infection and for mortality during hospitalization in patients with decompensated liver cirrhosis. Nevertheless, further research is essential to confirm these findings.
Disclosure: Nothing to disclose

P0656 HEPATIC OSTEODYSTROPHY - IS THERE CLINICAL RELEVANCE?

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Introduction: Hepatic osteodystrophy, including osteoporosis, is an abnormal bone metabolism related with chronic liver disease. Osteoporosis is associated with an increased risk of bone fractures, with a significant impact on morbidity, quality of life and mortality. Several factors may contribute to reduced bone mineral density (BMD) in liver cirrhosis, such as malnutrition, cholestasis, alcohol and tobacco abuse and low vitamin D levels.
Aims and Methods: We aimed to assess the prevalence of osteopenia and osteoporosis in patients with liver cirrhosis.
We conducted a prospective study between September/2017 and March/2018 including patients with liver cirrhosis. BMD was determined by dual energy X-ray absorptiometry at L1-L4 and femoral neck. As defined by the World Health Organization criteria, osteopenia was present when a t-score lied between −1 and −2.5 standard deviations (SD), and osteoporosis when a t-score was ≤−2.5 SD.
Results: 60 patients were included (87% male, mean age of 63±9 years; 91.7% alcoholic etiology; Child-Pugh A-65%, B-28.3%, C-6.7%).
53.5% had history of falls and 21.7% prior fragility fracture (mainly long bones). Osteopenia was diagnosed in 73% and osteoporosis in 22% of cases. Femoral neck was more frequently affected.
Patients with osteopenia or osteoporosis had lower weight and body mass index (p < 0.05) and higher Child-Pugh score (p < 0.01).
There was a correlation between osteoporosis and prior fragility fracture (p = 0.015, R = 0.313), esophageal varices (p = 0.04; R = 0.278), concomitant chronic pancreatitis (p = 0.002; R = 0.389) and proton-pump inhibitors (p = 0,037, R = 0.27). There was also a correlation between low vitamin D levels and the t-score at the femoral neck (p = 0.025; R = 0.296).
Conclusion: This study demonstrates a high prevalence of metabolic bone disease in patients with chronic liver disease. The prevalence of prior bone fracture is also concerning.
Osteoporosis and bone fractures have a harmful effect on quality of life and are associated with increased morbidity and mortality. BMD measurement is clinically relevant in patients with liver cirrhosis, allowing the detection of bone disorders and the institution of prophylactic measures to optimize bone health.
Disclosure: Nothing to disclose

P0657 ROYAL FREE HOSPITAL CIRRHOSIS GLOMERULAR FILTRATION RATE (RFHC-GFR): APPLICATION AND IMPLICATIONS FOR LIVER CIRRHOSIS IN CLINICAL PRACTICE

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Introduction: Both serum creatinine and current creatinine-based equations for GFR estimation have been proven to be inaccurate in cirrhotic patients. A more accurate formula has been proposed[1] - the RFHC-GFR that warrants further validation.
Aims and Methods: To compare different creatine-based equations for GFR estimation in liver cirrhosis. We also aimed to compare the conventional and corrected Model For End Stage Liver Disease (MELD-Na) as predictors of 12-month mortality.
Clinical and laboratory data of 123 consecutive outpatients with cirrhosis between January and December of 2016 were retrospectively analysed. Patients with acute kidney failure, extra-hepatic neoplasms and history of kidney or liver transplantation were excluded. GFR rates were calculated using RFHC, Modification of Diet Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. A 'corrected creatinine value' was obtained through backward application of MDRD equation using RFHC-GFR values. ''Corrected MELD-Na'' was then calculated.

Results: Of the 123 patients included in the study 78.9% were male and the mean age was 58.23 (±8.95) years. 86.2% had alcohol-related liver disease, 22.8 % had significant comorbidities and 8.9% had hepatocellular carcinoma. The percentage of patients in the Child-Pugh Score A, B and C was 53.7%, 35.8% and 10.6% respectively. Median MELD score was 13 (±12). There was a statistically significant difference in GFR depending on which formulae was used ($p < .001$). RFH-GFR was significantly lower when compared to CKD-EPI or MDRD ($p < .001$). When RFHC-GFR was used a significantly larger proportion of patients were considered to have moderate-to-severe GFR reduction than with CKD-EPI or MDRD (59.3% vs. 9.8% and 10.6%, respectively $p < .001$). The median value of 'corrected MELD-Na' was 2 points higher than conventional MELD-Na ($p < .001$) and had a higher AUC (0.788 vs. 0.775 $p = 0.56$) for 12-month mortality prediction.
Conclusion: Lower unrecognised GFR can potentially increase the risk of adverse outcomes such as renal toxicity and more importantly increase conventional calculated MELD-Na scores which could alter liver transplant priority.
Disclosure: Nothing to disclose

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P0658 DANAPAROID SODIUM AND ANTITHROMBIN III FOR PORTAL VEIN THROMBOSIS: EXPERIENCE OF A SINGLE JAPANESE HOSPITAL

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Introduction: Anticoagulant therapy or thrombolytic therapy is often administered for portal vein thrombosis (PVT). However, starting these therapies is usually hesitated, especially in the patients with decompensated liver cirrhosis with bleeding tendencies. Danaparoid sodium, a heparinoid glycosaminoglycuronan with highly selective anti-Xa activity, and antithrombin III (ATIII) have been reported to be treatment choices for PVT in Japan, instead of conventional anticoagulants. In this study, we investigated its efficacy for PVT in our hospital.
Aims and Methods: Twenty-three consecutive patients treated for PVT from 2012 to 2017 in our hospital were included in this study. Treatment choices, efficacy, and complications were retrospectively studied. Efficacy is defined as the disappearance or decreased volume of PVT in the follow-up image studies.
Results: Twenty-three patients, aged from 44 to 82 years, included 12 males and 11 females. Thirteen cases (57%) were of liver cirrhosis, three of acute pancreatitis, two of acute cholangitis, two of sepsis, and 3 cases of indeterminate origin. Nine patients (39%) were treated by warfarin, 8 patients (35%) were treated by ATIII combined with danaparoid sodium or heparin, 4 patients (17%) were treated by ATIII only, and 2 patients (9%) were treated by direct oral anticoagulants. PVT disappeared or decreased in volume in 17 cases (74%). Complete obstruction of portal vein was noticed in 3 of 6 ineffective cases. In 12 cases with ATIII administration, ten cases (83%) showed effective PVT control without complications including any bleeding events. PVT was aggravated in 3 cases (13%) after initial therapy. In four cirrhotic patients that anticoagulant therapies were continued for prevention of PVT recurrence, two cases ceased anticoagulation due to bleeding events.
Conclusion: Various treatment choices had comparable effects for PVT. Ineffectiveness was frequently encountered in cases of complete portal vein obstruction, despite of prompt treatment administration. Timely treatment strategy modification should be considered in those cases. Moreover, it is important to evaluate the need of maintenance anticoagulation since PVT recurs frequently, along with the risk of complications such as bleeding.
Disclosure: Nothing to disclose

P0659 RESULTS OF LIVER CIRRHOSIS REGISTRY IN IRAN: EPIDEMIOLOGY, UNDERLYING CAUSES AND COMPLICATIONS

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Introduction: Liver cirrhosis is characterized by chronic hepatic parenchymal damage, hepatocyte loss, fibrosis formation causing progressive hepatic dysfunction and hepatic failure. Liver cirrhosis causes significant morbidity and mortality and accounts for 2% of all annual death worldwide. The epidemiology of liver cirrhosis is variable in different geographical areas of the world.
Aims and Methods: This study is the first registered data on epidemiology of liver cirrhosis in Iran focusing on underlying liver diseases and complications. This registry has been established at Gasteroeterohepatology Research Center, Shiraz, Iran. The registry has been started from March 2015. All patients with confirmed liver cirrhosis by biopsy and/or transient elastography plus clinical clues were included. Patients with liver cirrhosis that had been admitted in hospitals due to various complications of cirrhosis were also included. Data of patients were recorded in a web-based software designed and produced based on data gathering forms and questionnaires of the registry. Demographic data, laboratory data, anthropometric indices, drug history, social history including alcohol consumption, cigarette and water pipe smoking, opium consumption, co-morbid diseases were recorded. Complications of liver cirrhosis including hepatocellular carcinoma (HCC), esophageal or gastric varices, spontaneous bacterial peritonitis (SBP), ascites, hepatorenal syndrome, portal vein thrombosis (PVT) and hepatic encephalopathy were recorded.
Results: 3287 patients were included up to 30th March 2018. 2144 patients (65.2%) were male and 1143 patients (34.8%) were female. Mean age of patients were 46.50 ± 21.28 years. Main underlying causes of liver cirrhosis in our study population were outlined in Table. Hepatitis B virus (HBV) induced liver cirrhosis was the most common cause of liver cirrhosis that was diagnosed in 664 patients (20.20%). The second and third most common etiologies of liver cirrhosis were cryptogenic liver cirrhosis and hepatitis C virus (HCV) induced liver cirrhosis that were diagnosed in 619 patients (18.83%) and 443 patients (13.47%) respectively. The highest prevalence in patients with cryptogenic cirrhosis, HBV and HCV induced cirrhosis and autoimmune hepatitis (AIH) was observed between 50–60 years. The highest prevalence of non-alcoholic steatohepatitis (NASH) was seen between 60–70 years. Ascites was detected in 1639 patients (50%) and esophageal varices in 1118 patients (36%). 969 patients had at least one episode of hepatic encephalopathy and 382 patients had at least one episode of SBP. Variceal bleeding was occurred in 636 patients and hepatorenal syndrome (HRS) in 254 patients. PVT was diagnosed in 360 patients and HCC in 293 patients. Ascites, esophageal varices and hepatic encephalopathy were the most common complications in all etiologies of liver cirrhosis.
Conclusion: Viral hepatitis is still a major cause of liver cirrhosis in Iranian population. There is also a significant male predominance among patients with liver cirrhosis secondary to HBV and HCV. Cryptogenic cirrhosis and autoimmune liver diseases including AIH and primary sclerosing cholangitis (PSC) are other main etiologies of liver cirrhosis.

	HBV	Cryptogenic	HCV	AIH	PSC	Alcoholic	NASH
Frequency	664	619	443	427	154	83	54
Percent (%)	20.20	18.83	13.47	12.9	4.68	2.52	1.64
Male/female (%)	81/19	59/41	79/20.5	50.5/49.5	64/33	98/2	61/39

[Frequencies and proportions of major causes of liver cirrhosis in the registry]
Disclosure: Nothing to disclose

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P0660 SPONTANEOUS BACTERIAL PERITONITIS: ARE WE FOLLOWING GUIDELINES?

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Introduction: Spontaneous bacterial peritonitis (SBP) is the most common serious infection in patients with cirrhosis, occurring in 25% of those who develop ascites. It is associated with significant morbidity and mortality rates of 20–40%.[1]
British Society of Gastroenterology (BSG) and National Institute of Clinical Excellence (NICE) guidelines recommend long-term prophylaxis (LTP) with Ciprofloxacin or Norfloxacin in patients with cirrhosis who have low ascitic fluid protein concentration (< 15g/L) with or without prior episode of SBP (primary LTP) or who have had an episode of spontaneous bacterial peritonitis (secondary LTP)[1,2].
Aims and Methods: We carried out a retrospective observational study using our electronic system for admissions with a diagnosis of ascites and cirrhosis across the East Kent Hospitals NHS Foundation Trust from April 2014 to April 2017. Ascitic fluid analysis results were reviewed against discharge summaries to audit whether LTP was started according to national guidelines.
Results: 337 cases of ascites with cirrhosis were identified (93 female: 244 male) with a median age of 58 (range 30–92 years).
61 out of 337 cases had a current or previous diagnosis of SBP. 5 out of 61 died during their admission. 10 out of 61 were discharged on secondary LTP and 46 patients were discharged without LTP.
11 out of 337 cases had low ascitic fluid protein with no current or previous episodes of SBP. None of these patients were discharged with primary LTP.
Conclusion: East Kent Trusts followed national guidelines in starting secondary LTP for SBP in 18% (10 out of possible 56) of cases and 0% of cases requiring primary LTP from April 2014 to April 2017. This low adherence rate may reflect lack of clinician awareness of guidelines for prescribing LTP for SBP in patients with ascites. There may also be a relation to local microbiology guidelines not following BSG or NICE guidelines on initiation of primary or secondary LTP for SBP. This study serves as a reminder to clinicians to carefully consider LTP in patients with ascites secondary to cirrhosis on each admission. We also recommend that trusts review local microbiology guidelines to ensure it adheres to national guidelines.
Disclosure: Nothing to disclose

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P0661 STAGE 1 OF ACUTE KIDNEY INJURY IN CIRRHOSIS - THE SUBCLASS REALLY MATTERS!

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Introduction: Recent studies propose a subclassification of stage 1 of acute kidney injury (AKI) in patients with cirrhosis, according to the serum creatinine value (sCr) at the time of diagnosis.[1,2,3]

Aims and Methods: The aim was to evaluate the association of subclassification stage 1 of AKI in patients with cirrhosis with the presence of acute-on-chronic liver failure (ACLF), progression of AKI and 30-day mortality.

A retrospective assessment of patients with cirrhosis admitted for acute decompensation with AKI stage 1 was performed. AKI stages were determined based on sCr at the time of hospital admission and according to criteria defined by the International Ascites Club. Stage 1 was subclassified in 1A if sCr < 1.5 mg / dL and 1B if sCr ≥ 1.5 mg / dL.

Results: Ninety patients were included, 45 in stage 1A 45 (50%) and 45 (50%) in stage 1B.

The mean differences between sCr at diagnosis and baseline were higher at stage 1B compared to 1A, 0.7 ± 0.23 vs 0.43 ± 0.11, $p < 0.001$.

Progression of AKI occurred more frequently in patients with stage 1B (40%) compared to patients 1A (4.4%), $p < 0.001$. Hepatorenal syndrome occurred more frequently in stage 1B than in 1A, 20% vs 2.2%, $p = 0.007$.

ACLF was more frequent in patients with stage 1B (42.2%) compared to patients with stage 1A (4.4%), $p < 0.001$.

There was a higher mortality at 30 days in 1B patients compared to patients with 1A, 40% vs 8.9%, $p = 0.001$.

Conclusion: Stage 1B patients are at higher risk for progression of AKI, higher mortality, and more frequently present ACLF, thus requiring more attention in identifying, monitoring and treating them early.

Disclosure: Nothing to disclose

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P0662 THE POLYMORPHIC VARIANT OF SERPINB3 (SCCA-PD) IS ASSOCIATED WITH THE SEVERITY OF PORTAL HYPERTENSION AND COMPLICATIONS ONSET IN PATIENTS WITH ADVANCED LIVER DISEASE

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Introduction: Hepatic fibrosis and portal hypertension are major determinants of clinical outcome in advanced chronic liver disease. Liver fibrosis is driven by persistent activation of hepatic stellate cells, with TGF-β being the key fibrogenic cytokine. SerpinB3 (or SCCA1) has been reported to activate hepatic stellate cells and SerpinB3 transfected cells up-regulate TGF-β1 production, an effect shown to rely on the integrity of the reactive site loop of this serpin. The polymorphic variant SCCA-PD presents a substitution in the reactive center loop of the protein (Gly351Ala), determining an improved anti-protease activity of this isoform.

Aims and Methods: To assess the effect of SCCA-PD polymorphic variant on TGF-β1 expression by using *in vitro* models and to disclose the clinical characteristics and the outcome in a cohort of cirrhotic patients carrying or not this polymorphic variant.

TGF-β1 transcripts and protein levels were determined in HepG2 and in Huh7 cells transfected with either wild-type SerpinB3 (SCCA-WT) or with SCCA-PD polymorphic variant. Cells transfected with the plasmid alone were used as control. TGF-β1 expression was also evaluated in the human stellate cell line LX2 in response to recombinant SCCA-WT or SCCA-PD proteins. In addition, SCCA polymorphism was assessed in 59 cirrhotic patients (72.9% male; mean age±SD: 53.9 ± 9.1 years), prospectively followed up at our outpatient Clinic for a median period of 114 months (range 60–120). The results were analyzed in relation to clinical data, hemodynamic features at baseline and the onset of new complications during follow up.

Results: Transfected cell lines showed increased TGF-β1 expression, compared to controls and this finding was more prominent in cells transfected with SCCA-PD, both at transcript and protein levels (SCCA-WT vs SCCA-PD, mRNA: $p = 0.027$, protein: $p = 0.009$). Accordingly, the addition of recombinant SCCA-PD to human LX2 cells induced higher TGF-β1 production, compared to SCCA-WT protein ($p < 0.01$). SCCA-PD polymorphism was detected in 27% of the enrolled patients that at baseline, despite they had similar age than patients carrying SCCA-WT (52±8 vs 54±9 years), presented signs of more advanced portal hypertension, including portal vein dilation (portal vein >14 mm: 50% vs. 34%), marked splenomegaly (spleen >16 cm: 62.5% vs. 25%, $p = 0.008$), and varices at higher risk of bleeding (F2-F3: 33% vs. 15%). In addition, patients carrying SCCA-PD variant presented a significantly higher MELD score (14 vs. 11 $p = 0.01$) and during a 5 years follow-up they developed a higher number of cirrhosis complications (40% vs. 11.6%, $p = 0.016$). In the multivariate Cox regression analysis, SCCA-PD (OR $= 3.78$, $p = 0.026$) and MELD score (OR:1.16; $p = 0.016$) were identified as independent predictors of cirrhosis complications development.

Conclusion: The polymorphic variant SCCA-PD is able to increase TGF-β production *in vitro* more efficiently than the corresponding wild type protein. Patients with advanced liver disease carrying the SCCA-PD polymorphism present signs of more severe portal hypertension and develop more frequently cirrhosis complications during follow up, supporting a role of this polymorphic variant in liver disease progression.

Disclosure: Nothing to disclose

P0663 LONGITUDINAL MONITORING OF LIVER FIBROSIS STATUS BY TRANSIENT ELASTOGRAPHY IN CHRONIC HEPATITIS B PATIENTS DURING LONG-TERM ENTECAVIR TREATMENT

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Introduction: There has been a marked increase in studies revealing that oral antiviral treatment can suppress the replication of hepatitis B virus (HBV) and induce the regression of liver fibrosis, in which the degree of liver fibrosis is of great significance. In addition to liver biopsy, the gold standard, liver stiffness measurement (LSM) by non-invasive transient elastography has shown its outstanding value in monitoring the progression and regression of fibrosis and chronic hepatitis B (CHB)-related complications. In this study, we aim to evaluate the prognosis performance of LSM in predicting the subsequent regression of liver fibrosis in patients receiving long-term entecavir (ETV) treatment.

Aims and Methods: The study was designed to explore the correlation between improvement in longitudinal liver stiffness and fibrosis regression during long-term antiviral therapy in CHB patients. We prospectively recruited a total of 120 consecutive adult patients with CHB, which received oral antiviral therapy with ETV after enrollment. Five-five CHB patients were enrolled in the non-cirrhosis group and 65 CHB patients were enrolled in the cirrhosis group. In study, liver stiffness was serially performed by Fibroscan apparatus (Echosens pavis, France) every 26 weeks. At baseline and week 78 of ETV therapy, paired liver biopsies were performed for every patients. The liver tissue was obtained by ultrasonography-guided percutaneous biopsy (Bard@ Magnum@16G;USA). Serum fibrosis markers, Fibrosis-4 (FIB-4) and aspartate aminotransferase (AST) to platelet ratio index (APRI) scores were assessed at baseline and every 26weeks. Continuous variables were summaried as mean ± standard deviation or median and interquartlie range (IQR) and categorical variable as frequency and percentage. Analyses of unpaired data were evaluated by the Mann-Whitney U-test, Chi-squared test and Fish's exact test. Statistical analyses were performed using SPSS software version 22.0 (SPSS INC Chicago, USA)

Results: Compared with non-cirrhosis group, gamma-glutamyltransferase, international normalized ratio (INR), APRI, FIB-4 and LSM were significantly higher in cirrhosis group at baseline. Marked decreases were found sequentially at time point of week 26, week 52 and week 78 during antiviral treatment. The serum levels of ALT, AST and INR gradually decreased after antiviral therapy. While albumin and cholinesterase levels were significantly increased after initiating ETV treatment. The serological fibrosis scores (APRI and FIB-4) also declined gradually during the antiviral treatment. Dynamic changes of LSM and serum biomarkers also show the association of LSM improvement with fibrosis regression at 78 weeks after ETV treatment. Moreover, percentage decline of 78-week liver stiffness was moderately predictive of fibrosis regression (AUROC $= 0.694$, $p < 0.001$). while the optimal cut-off values were different between non-cirrhosis and cirrhosis patients (38% vs. 45%). Fibrosis regression could be predicted with a high positive predictive value (96%) in non-cirrhosis patients and could be excluded with a high negative predictive value (94%) in cirrhosis patients.

Conclusion: Serial liver stiffness measurement could be applied for longitudinal monitoring of fibrosis status in CHB patients. Continuous decline of liver stiffness after effective antiviral treatment could partially reflect fibrosis regression at an optimal cut-off value.

Disclosure: Nothing to disclose

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P0664 RESOLUTION OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION AFTER SUSTAINED VIROLOGIC RESPONSE TO INTERFERON-FREE REGIMENS PREVENTS HEPATIC DECOMPENSATION

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Introduction: Sustained virologic response (SVR) to interferon (IFN)-free therapies ameliorates portal hypertension (1–4). However, the impact of the hemodynamic response on hepatic decompensation has yet to be investigated in this setting.

Aims and Methods: Seventy-seven patients with portal hypertension (HVPG ≥6mmHg) who underwent hepatic venous pressure gradient (HVPG) and liver stiffness (LS) measurement before (baseline [BL]) and after (follow-up [FU]) IFN-free therapy were retrospectively studied.

(Further) hepatic decompensation was defined by variceal (re-)bleeding, incident ascites/worsening of ascites (requirement of paracentesis), or incident hepatic encephalopathy (HE)/worsening of HE (admission for grade 3/4 HE).

Results: Patient characteristics at BL: Child-Pugh A: 81%, B: 19%; MELD: 8 (interquartile range [IQR]: 2) points; HVPG: 13 (IQR: 8) mmHg.

In the subgroup of patients with a BL-HVPG of 6–9mmHg (n = 22), no patient progressed to clinically significant portal hypertension (CSPH; HVPG ≥10mmHg). Among patients with BL-CSPH, a HVPG-decrease ≥10% was observed in 65% (36/55), while 24% (13/55) had a FU-HVPG < 10mmHg (i.e., resolved CSPH).

During a median FU of 24.9 (IQR: 15.1) months after the end of HCV treatment, 10 patients developed (further) hepatic decompensation, with variceal bleeding (n = 1), ascites (n = 4), or HE (n = 5) being the first events. Two patients underwent liver transplantation (both had further decompensation) and one patient died (non-liver-related).

In patients with BL-CSPH, a HVPG-decrease ≥10% tended to decrease the risk of (further) hepatic decompensation at 2 years (10% vs. 27%, p = 0.072). Overall, the absence of FU-CSPH was fully protective of the development of (further) hepatic decompensation (0% vs. 21%, overall p = 0.002). This was confirmed in the subgroup of patients with BL-CSPH (p = 0.004).

The area under the receiver operating characteristic curve (AUROC) of FU-LS for diagnosing FU-CSPH/predicting (further) hepatic decompensation was 0.923/0.887. None of the patients with FU-LS values < 12kPa or < 18.9kPa had FU-CSPH or (further) hepatic decompensation, respectively.

Conclusion: The resolution of CSPH after SVR to IFN-free regimens is associated with a negligible risk of (further) hepatic decompensation, while a HVPG-decrease ≥10% is not fully protective. Moreover, FU-LS seems to provide prognostic information.

Disclosure: M.M. has served as a speaker and/or consultant for AbbVie, Bristol-Myers Squibb, Gilead, Janssen, and W. L. Gore & Associates.

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P0665 NUTRITIONAL PARAMETERS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS, THEIR INFLUENCE IN EARLY READMISSION AND 1-YEAR MORTALITY

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Introduction: The prevalence of malnutrition among patients with cirrhosis is particularly concerning due to its association with mortality and inherent complications. Multiple studies described a rate of protein-calorie malnutrition around 50–100% in patients with decompensated cirrhosis, and at least 20% with compensated cirrhosis. Early hospital readmissions (within the next 30 days after discharge) among patients with decompensated cirrhosis predict a poor outcome and increase the 1-year mortality. We consider that early re-hospitalization could be predictable and therefore, potentially preventable. This study aims to recognize an association between the nutritional status of the patients with decompensated cirrhosis and early readmissions.

Aims and Methods: This is a prospective study performed in a tertiary referral hospital of Spain. This study included 136 patients admitted to the Hepatology Unit with decompensated cirrhosis. Before the discharge, we collected clinical and laboratory data from the medical chart. We evaluated the following nutritional parameters: weight, height, body mass index (BMI), albumin at income, brachial perimeter, tricipital skinfold, and scapular skinfold. We also calculated the "dry weight" known as the weight adjusted to the ascites grade (subtracting from the total weight: 2.2 kg. in grade I, 6 kg. in grade II, and 14 kg. in grade III). The follow up was performed 30 days, 6 months and 1 year after the discharge, via telephone or in the clinic if the dates matched with the visits.

Results: The median of BMI in patients with early readmission was 26.0 kg/m^2 (p = 0.01). Nutritional parameters with statistic significance in the univariate analysis related with early readmission were: BMI < 18.5 (0.0 vs 10.8%; p = 0.001) BMI 25–29 (47.5% vs 21.6%; p = 0.02), Dry BMI < 18.5 (0.0 vs13.5%; p < 0.01), brachial perimeter in mm. (270 vs 250 mm; p = 0.03) and albumin (32 vs 29 g/L; p = 0.02). The early readmission rate was 27.2%. The 1-year overall mortality was increased in those patients who had early readmission (56.8% vs 20.2%). In the multivariate model two nutritional parameters showed association with early readmission: Dry BMI < 18.5 (HR 4.23, 95% CI: 1.14–15.74; p = 0.03) and albumin as a protector factor (HR 0.89, 95% CI: 0.82–0.96; p = 0.004). None of the nutritional factors presented an association with 1-year mortality.

Conclusion: Dry BMI < 18.5 and albumin are the nutritional parameters that influence in 30-day readmission. Therefore, nutritional status should be a target of preventive actions of early readmission. As these variables are also related to progression of liver failure, more studies with advanced nutritional measurements are needed in this population.

Disclosure: Nothing to disclose

P0666 SEROLOGICAL INDICES OF LIVER FIBROSIS IN THE COURSE OF ALCOHOLIC LIVER CIRRHOSIS - A PILOT STUDY

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Introduction: Liver biopsy has been described as a gold standard in the assessment of the severity of liver fibrosis so far. However, due to its limitations, it is crucial to look for noninvasive laboratory parameters, which make it possible to monitor liver stiffness.

Aims and Methods: The aim of our investigation was to determine the usefulness of selected serological indices in the assessment of liver fibrosis in the course of alcoholic liver cirrhosis (ALC). We enrolled 55 participants in the survey and among them 22 patients with ALC in research group together with 33 persons in control group. The diagnosis of ALC was based on commonly known criteria. We measured concentration of direct indicators of liver fibrosis in serum of all participants: platelet-derived growth factor AB (PDGF-AB), transforming growth factor α (TGF-α), N-terminal propeptide of type III collagen (PIIINP), procollagen I carboxyterminal propeptide (PICP) and laminin. Several indirect parameters of liver fibrosis were obtained too: aspartate aminotransferase (AST) to alanine aminotransferase ratio (AAR), AST to platelet (PLT) ratio index (APRI), fibrosis-4 (FIB-4) score and red cell volume distribution width (RDW) to PLT ratio (RPR). To evaluate a clinical outcome of patients, we assessed Model for End-Stage Liver Disease (MELD) score and neutrophil to lymphocyte ratio (NLR). Finally, we also measured PLT indices: mean PLT volume (MPV), PLT distribution width (PDW) and plateletcrit (PCT). We looked for any correlations between assessed parameters in patients with ALC, too.

Results:

	ALC patients (n = 22)	Controls (n = 33)	p value
PLT (10^9/L)	***135.14 ± 83.62***	***275.3 ± 73.15***	p < 0.01
RDW (%)	17.12 ± 2.26	17.98 ± 23.73	p < 0.01
RPR	0.22 ± 0.19	0.06 ± 0.07	p < 0.01
MPV (fl)	9.9 ± 1.73	8.72 ± 0.91	p = 0.01
PCT (%)	0.14 ± 0.08	0.28 ± 0.12	p < 0.01
PDW (%)	59.98 ± 6.74	53.02 ± 6.83	p = 0.027
NLR	11.38 ± 11.89	2.62 ± 1.49	p < 0.01
AAR	2.79 ± 2.35	1.27 ± 0.46	p < 0.01
APRI	4.81 ± 7.12	0.29 ± 0.13	p < 0.01
FIB-4	6.04 ± 6.14	1.01 ± 0.48	p < 0.01
MELD	15.41 ± 7.44	–	–

(continued)

Continued

	ALC patients (n = 22)	Controls (n = 33)	p value
PICP (ng/mL)	93.51 ± 29.44	78.64 ± 37.15	p = 0.037
PIIINP (ng/mL)	7.81 ± 3.47	8.87 ± 3.48	p > 0.05
PDGF-AB (pg/mL)	8518.49 ± 5427.92	17241.85 ± 10041.99	p < 0.01
TGF-α (pg/mL)	38.23 ± 9.94	38.04 ± 15.26	p > 0.05
LAMININ (ng/mL)	1331.53 ± 941.16	717.57 ± 299.74	p < 0.01

[The results of performed tests in examined patients presented as mean ± SD. A value of p < 0.05 was considered statistically significant.]

Obtained results are presented in Table 1. Significantly lower concentration of PDGF-AB and higher concentrations of laminin and PICP were found in ALC patients. Subsequently, we observed significantly higher values of AAR, APRI, FIB-4, RPR, NLR, MPV and PDW in research group. PCT value was significantly lower and correlated negatively with APRI, FIB-4 and RPR ($p < 0.01$). Furthermore, APRI correlated positively with both FIB-4 and RPR ($p < 0.01$). Another positive correlation was observed between between NLR and AAR ($p < 0.01$). Finally, we observed a negative correlation between PIIINP and TGF-α ($p = 0.038$).

Conclusion: Our survey indicates that noninvasive parameters embracing liver, PLT and red blood cells indices might be useful in the assessment of liver fibrosis in the course of ALC. Additionally, higher concentrations of laminin and PICP and lower values of PDGF-AB seem to accompany ALC.

Disclosure: Nothing to disclose

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P0667 HEPATITIS B VIRUS (HBV) IN PATIENTS WITH CHRONIC HEPATITIS C (HCV) TREATED WITH DIRECT ANTIVIRAL AGENTS (DAA) IN THE SOUTHERN REGION OF MADRID

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Introduction: Current guidelines recommend screening HVB in patients with chronic HCV before starting DAA therapy since HBV reactivation cases under treatment have been reported.. The objectives of our study were: 1) To know the screening rates of HBV in our community; 2) To assess the prevalence of HBV / HCV coinfection in HCV patients starting DAA therapy in our population, and 3) To determine the incidence of HBV reactivation in treated patients and its clinical relevance.

Aims and Methods: We retrospectively evaluated 1337 patients with HCV treated with DAA in 2 general hospitals in the southern region of Madrid from January 2015 to June 2017. We investigated HBV screening rates, the prevalence of HBV / HCV coinfection, and the incidence of virological reactivation by HBV (viral load elevation > 1 log), and biochemical reactivation.

Results: Ninety five (7.1%) out of the 1337 treated HCV patients did not have done HBV serology before treatment; 293 (21.9%) had negative HBsAg and HBcAg 584 (43.6%) had vaccination pattern; 9 (0.7%) were HBSAg positive and 356 (28.6%) had antiHBc and/or antiHBc antibodies as sign of past HVB infection.

Two hundred and twenty five (61%) out of 365 HCV patients with HBV or past HBV infection were male, with a mean age of 59 years (range: 20–85), 357 (98%) of Caucasian race, 118 (51.5%) genotype 1b, 164 (44.9%) were F4 and 252 (69%) had been previously treated with IFN. DAA regimens were Sofosbuvir / Ledipasvir (n = 155; 42.4%), Paritaprevir / Ombistasvir / Dasabuvir (n = 111; 30.4%) and other combinations (n = 99, 27.2%). SVR was obtained in 298 (99%) out of the 301 patients who could be evaluated.

Among HBsAg-positive patients, 5 out of 9 were receiving nucleos(t)ide analogs (NUCs) before starting DAA therapy. Two out of 4 patients without HBV treatment (50%) developed HBV virological reactivation but not biochemical flare. Reactivation occurred early at week 4 in the first patient and achieved virological response after 4 weeks of tenofovir; and in the second patient, reactivation was detected at week 4 of follow-up, with spontaneous decrease in viral load to baseline.

All of the 356 with HBV past infection pattern (100%) maintained normal transaminases at the end of treatment and during follow-up. Although HBV DNA was not available a biochemical reactivation can be excluded.

Conclusion: In our community, there is a high rate of HBV screening in patients with HCV prior to DAA therapy. The prevalence of HBV infection (positive HBsAg) in chronic HCV patients in the southern region of Madrid is low. HBV reactivation in HCV/HBV coinfected patients receiving AAD is frequent, but without clinical relevance.

Disclosure: Nothing to disclose

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P0669 ASSOCIATION BETWEEN LOW VITAMIN D SERUM CONCENTRATION WITH HIGH LEVELS OF HEPATITIS B VIRUS REPLICATION IN CHRONIC HEPATITIS B PATIENTS FROM ALGERIA

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Introduction: Vitamin D is an important immune modulator that plays an emerging role in inflammatory and metabolic liver diseases, including infection with hepatitis C virus (HCV), wich has been intensively studied. However, studies on the potential interaction between vitamin D level and chronic hepatitis B are still limited.

Aims and Methods: This study aimed to explore whether any association existed between serum vitamin D level and clinical determinants in patients with chronic hepatitis B infection. Therefore, we quantified 25(OH)D3 serum levels in a cohort of 187 treatment naıve patients with chronic hepatitis B virus (HBV) infection and tested for their association with clinical parameters of CHB.

Results: Mean 25-hydroxyvitamin D value was 21.90ng/ml. The percentage of patients with different concentration of 25-hydroxyvitamin D (adequate ≥20ng/ml, insufficiency10–20ng/ml, deficiency < 10ng/ml) were 29.5%, 43.2% and 27.3%, respectively. In both uni- and multivariate analyses, HBV DNA viral load (log10 IU/mL) was a strong predictor of low $25(OH)D_3$ serum levels (P50.0008 and P50.000038, respectively) and vice versa. Mean $25(OH)D_3$ serum concentrations in patients with HBV DNA < 2,000 versus 2,000 IU/mL were 18 versus 12 ng/mL, respectively ($p < 0.00001$). In addition, hepatitisB early antigen (HBeAg)-positive patients had lower $25(OH)D_3$ serum levels thanHBeAg-negative patients (P50.0013). 25-hydroxyvitamin D serum level is not associated with viral load or fibrosis stage in chronic hepatitis B patients. Finally, $25(OH)D_3$ and HBV DNA serum levels showed inverse seasonal fluctuations.

Conclusion: We demonstrate a significant association between low $25(OH)D_3$ serum levels and high levels of HBV replication in chronically infected patients. Future studies to evaluate a therapeutic value of vitamin D and its analogs in HBV infection may be justified.

Disclosure: Nothing to disclose

Reference

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P0670 EFFICACY OF ANTI CHRONIC B HEPATITIS VACCINATION IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction: Hepatitis B virus (HBV) is a public health problem in the world and in Tunisia. Hemodialysis (HD) patients are at high risk of infection and vaccination against HBV remains the best prevention option for these patients. However, the immune deficiency of chronic renal failure (CRF) patients leads to a low seroconversion rate after vaccination and a faster decrease in antibody levels compared to healthy subjects.

Aims and Methods: To evaluate the efficacy of the vaccine protocol in chronic renal failure patients at the hemodialysis stage and to identify the factors that may influence the immune response.

This was a descriptive and cross-sectional retrospective study conducted in six hemodialysis centers in the southern suburbs of Tunis, in patients who had received an accelerated vaccination against hepatitis B virus., in single dose and deltoid intramuscular protocol by a recombinant vaccine of 2nd generation without pre-S2. The endpoint is the titer of anti-HBs antibodies. The response was described as non response, low response and good response for an anti-HBs antibody titer of less than 10 IU / L, between 10 and 100 IU / L and greater than 100 IU / L, respectively. Age, sex, diabetes, high blood pressure and the notion of active smoking were tested according to an analytical scheme in univariate and multivariate studies. The Chi-square test was used. A threshold of 5% was considered significant.

Results: In total, 61 patients were included in our study. The mean age of patients was 56.9 ± 17.3 years with a sex ratio of 1. The notion of active smoking was found in 47.5% (n = 29) of patients. Comorbidity was noted in all patients of

which 70.5% (n = 43) were diabetic and 72.1% (n = 44) were hypertensive. C-Viral serology was positive in only one patient and HIV serology was negative in all cases. Vaccine seroprotection was obtained in 54% of patients after a primary vaccination. The patients were low responders in 33.3% (n = 11) of cases and good responders in 66.7% (n = 22) of patients. In univariate and multivariate studies, the predictors of non-response and low response to the B virus vaccine were advanced age, female gender, active smoking, and the presence of diabetes.
Conclusion: In our series, anti-viral B vaccination in hemodialysis patients is less effective compared to literature data. Smoking control and a review of the legislation governing the modalities of vaccination for hemodialysis may improve immunization coverage.
Disclosure: Nothing to disclose

P0671 COMPARISON BETWEEN TWO POPULATION-BASED SEROSURVEYS, SIXTEEN YEARS AFTER THE IMPLEMENTATION OF UNIVERSAL HEPATITIS B VACCINATION IN A HEPATITIS DELTA ENDEMIC AREA IN GREECE

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Introduction: The prevalence of hepatitis B virus (HBV) and hepatitis delta virus (HDV) infections has declined significantly in Greece, particularly after the introduction of universal HBV vaccination (1997). A rural area in Greece (Archangelos, Rhodes) was reported to be highly endemic for HBV/HDV during the 1980s, with 10.5% of the local population testing positive for hepatitis B surface antigen (HBsAg) and 27.3% of the HBsAg carriers testing positive for anti-HDV.
Aims and Methods: To compare between two population-based HBV/HDV serosurveys with a 16-year interval (1997–2013) in a highly-endemic area in Greece. Two population-based cross-sectional serosurveys were performed among the population aged 1–75 years in the same sample area (Archangelos, Rhodes, Greece), in 1997 (n = 1938; M/F = 900/1038, children: 29.5%, immigrants: 0%) and 2013 (n = 1076; M/F = 505/571, children: 21%, immigrants: 17.4%), respectively. From each individual, a blood sample was obtained and tested for HBsAg; all HBsAg-positive individuals were tested for anti-HDV. The demographic and ethnic origin data were recorded.compare between two population-based HBV/HDV serosurveys with a 16-year interval (1997–2013) in a highly-endemic area in Greece.
Results: In the 1997 serosurvey, 223/1938 (11.5%) subjects were positive to HBsAg and among them 56/223 (25.1%) were positive to anti-HDV. In children, 5/571 (0.9%) were HBsAg-positive, with no anti-HDV positivity. In the 2013 serosurvey, 35/1076 (3.76%) were HBsAg-positive and among them 7/35 (20%) were positive to anti-HDV. All children were HBsAg-negative. The seroprevalence of HBsAg was significantly higher among immigrants compared to native Greeks [12/187 (6.4%) vs 23/889 (2.6%) respectively, p = 0.01], although no significant difference was found concerning the prevalence of anti-HDV [2/12 (16.7%) vs 5/23 (21.7%) respectively, p = ns). The HBV-infected and HBV/HDV-coinfected immigrants were younger as compared to the respective native Greek population [HBV-infected: mean 51 vs 59.6 years respectively, p = 0.07; HBV/HDV-coinfected: 43.5 vs 60 years respectively, p = 0.04].
Conclusion: In a high endemic area, implementation of universal vaccination has led to a dramatic decline in the seroprevalence of HBV. However, a consistent reservoir of HDV remains, likely sustained by two different pools of infected individuals: a residual ageing domestic pool, and a newer one composed by younger patients migrating from countries where HBV/HDV remains endemic. Our findings deserve further investigation by phylogenetic analyses.
Disclosure: Nothing to disclose

P0672 THE USE OF THE PATIENT SAFETY FORM APPLICATION IN PATIENTS RECEIVING IMMUNOSUPPRESSIVE THERAPY CAN IMPROVE THE LOW RATES OF HEPATIS B VIRUS SCREENING AND ANTIVIRAL PROPHYLAXIS IN REAL LIFE

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Introduction: Hepatitis B virüs(HBV) prophylaxis in patient receiving immunosuppressive therapy can effectively prevent reactivation (1). However the rate of HBV screening and starting HBV prophylaxis is low in daily practice (1). While starting the biological agents treatments, use the patient safety form is mandatory in Turkey but there is no mandatory for other immunosuppressive treatments.
Aims and Methods: The aim of this study was to determine how much screening and rates of antiviral prophylaxis in patients receiving immunosuppressive therapy in daily practice and to evaluate the relationship between the patient safety form and rate of HBV screening and antiviral prophylaxis. This is a retrospective study. Patients who received biological agents (group 1; including anti-tumour necrosis factor-α and other monoclonal antibodies, use of the patient safety form mandatory)and cytotoxic chemotherapy, rituximab, long-term high-dose steroids (group 2: use of the patient safety form not mandatory) in Medical University of Mustafa Kemal were included in the study. HbsAg and Anti-HbcIg tests performed during the period up to 1 year before treatment of immunosuppressive agent were accepted as screening. Methylprednisolone or equivalent steroid of its use for at least 4 weeks and at least 20 mg /day were considered to be as long-term high-dose. HbsAg and/or HbcIg positivity was defined as a riskly patients for HBV reactivation.
Results: A total of 1302 patients were included in the study. The immunosuppressive treatment distributions of the patients were as follows; 648 cytotoxic chemotherapy (356 combined with steroids), 325 long-term high-dose steroids, 218 biological agents, 111 rituximab. Six hundred and fifty two (50.1%) of the patients had screened for HbsAg and/or anti-HBcIg. HbsAg positivity was found in 6.6% (43/652) of patients and HbsAg negative and anti-HBcIg positivity in 29.7% (113/380) of patients. The rates of HBsAg and/or anti-HBcIg screening were 94% (205/218) in group 1 and 42.7% (447/1084) in group 2. There was a statistically significant difference group 1 compared to the group 2 ($p < 0.001$). The rates of HBsAg and/or anti-HBcIg screening according to the immunosuppressive treatment were as follows;in patients receiving cytotoxic chemotherapy was 53% (348/648), in rituximab patients was 51% (57/111) and in patients with long-term high-dose steroid treatments was 13% (42/325). There was a statistically significant difference in the patients receiving biological agent treatment compared to other treatment groups (biological agent vs cytotoxic chemotherapy $p < 0.05$, biological agent vs rituximab $p < 0.05$, biological agent vs long-term high-dose steroid $p < 0.001$). Rates for risky patients for HBV reactivation were found in 23.4% (48/205) in group 1 and 23.9(108/447) in group 2 ($p > 0.05$). Rates antiviral prophylaxis were 98% (47/48) in group 1 and 49.1% (53/108) in group 2. There was a statistically significant difference group 1 compared to the group 2 ($p < 0.001$).
Conclusion: The screening rates are very low in patients receiving cytotoxic chemotherapy, rituximab and long-term high-dose steroids and it was found that only half of risky patients received antiviral treatment. Interestingly, almost all of the patients using the biological agent had screened and starting HBV prophylaxis. We suggested that the patient safety form, which is mandatory in patients receiving biologic therapy, is effective at this end. We also believe that the use of the patient safety form application in patients receiving immunosuppressive therapy can improve the low rates of HBV screening and antiviral prophylaxis in real life
Disclosure: Nothing to disclose

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P0673 REACTIVATION OF HEPATITIS B VIRUS INFECTION DURING TREATMENT OF HEPATITIS C WITH DIRECT-ACTING ANTIVIRALS

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Introduction: Reactivation of hepatitis B virus (HBV) can occur during treatment of hepatitis C with direct-acting antivirals (DDAs). It has been almost exclusively described in the cases of positive AgHbs and in no case of positive antiHBs. The risk in cases of isolated anti-HBc positive (anti-HBcPI) is minimal and its surveillance is not well defined.
Aims and Methods: The aim of this study was to investigate the risk of reactivation of HBV during treatment with DDAs in anti-HBcPI patients.
A prospective study was conducted in a cohort of 329 chronic hepatitis C patients treated with DDAs from February 2015 to March 2017. Virological reassessment of HBV infection was performed in the 12 and 24 week posttreatment period. Definitions of HBV reactivation: DNA detectable HBV with or without elevated transaminases and increased HBV DNA > = 1 log10 in cases of positive DNA initially.
Results: At baseline, HBV infection was identified in 125 patients (77% men, 53 years ± 8.1 years): 2 positive AgHBs (one with treatment criteria who started) and 123 with past infection (negative AgHBs and positive AcHBc with or without positive AcHBs - 55 and 68, respectively).
Fibrosis stage: F0 / F1 (n = 47); F2 / F3 (n = 31); F4 (n = 47). The 68 AntiHBcPI patients had undetectable DNA. Viral load follow up was achieved in 29 patients (mean follow-up time of 87.8 weeks). The sustained virologic response (SVR12) was 92% (115/125): 3 relapses, 4 deaths and 3 lost to follow-up. All cases of SVR12 maintained normal transaminases at follow up. There was no biochemical or virological reactivation in cases of antiHBcPI.
Conclusion: In this cohort, past HBV infection with HBcPI was prevalent (21%). However, none of these patients had biochemical or virological reactivation at short-term follow-up. The frequency of surveillance of these patients remains to be defined.
Disclosure: Nothing to disclose

P0674 ROLE OF BIOLOGICAL NON-INVASIVE TESTS IN PREDICTING FIBROSIS IN CHRONIC HEPATITIS B

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Introduction: The evaluation of fibrosis has been based on liver biopsy. The use of non-invasive tests is more and more common, despite they are still not recommended in hepatitis B due to lack of data.

Aims and Methods: The aim of this study was to compare the results of some biological non-invasive tests with those of liver biopsy in chronic hepatitis B (CHB).

We investigated all the CHB patients admitted in our department in the period between January 2009 and December 2015. Only patients who underwent a liver biopsy were enrolled. The following scores were calculated: ratio aspartate aminotransferase (AST)/alanine aminotransferase (RAA), APRI, FIB-4 and Pohl's score. The results of these scores and liver biopsy were compared.

A significant fibrosis (SF) was defined by a fibrosis score $\geq$ F2 and an advanced fibrosis (AF) by a fibrosis score $\geq$ F3 on liver biopsy.

Results: Eighty eight patients were included in our study. Their mean age was 38.5 years [18–63] and the sex ratio was 3.4 (68M/20F). HBeAg was positive in 28.4% of cases. Mean serum HBV DNA level was estimated to 6.3 Log 6 UI/ml [20 - 1.7 Log 8]. The mean levels of AST and ALT were 1.6 times ULN [0.5 - 36.6] and 1.9 times ULN [0.4 - 40] each. Mean Platelet count was 196×10^9/L [66–397]. On liver biopsy, 29.5% of patients had a SF and 11.4% had an AF. The mean values of RAA, APRI and FIB-4 were respectively estimated to 0.99 [0.38 - 1.89], 0.8 [0.15 - 18.48] and 1.36 [0 - 7.1]. Pohl's score was positive in 9.1% of cases.

SF was correlated to APRI and FIB-4 scores with AUC calculated to 0.766 and 0.668 each, and inversely correlated to platelet count with an AUC estimated to 0.692. This correlation wasn't found with RAA (AUC = 0.457).

AF was also correlated to APRI and FIB-4 scores with AUC respectively estimated to 0.854 and 0.821, and inversely correlated to platelet count with an AUC of 0.756, however, this correlation was not significative with RAA (AUC = 0.482).

In addition, Pohl's score was comparable to AF ($p = 0.014$) but not to SF ($p = 0.18$).

Conclusion: In our study, APRI, FIB-4 and Pohl's scores in addition to platelet count were useful in predicting advanced fibrosis. These simple tests could in some cases be sufficient, without need to a liver biopsy.

Disclosure: Nothing to disclose

P0675 SERO-PREVALENCE OF DELTA HEPATITIS ANTIBODIES, LIVER FUNCTION TEST PROFILE AND SEVERITY OF LIVER DISEASE AMONG INDIVIDUALS WITH CHRONIC HEPATITIS B INFECTION SEEN IN A TERTIARY HOSPITAL IN ABUJA, NIGERIA

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Introduction: Hepatitis D virus (HDV) is a defective RNA virus that requires the helper function of hepatitis B virus (HBV) to be infectious. About 5% of the 350 million HBV carriers worldwide are estimated to have HDV infection. There is paucity of studies in Nigeria on the contribution of HDV to the burden of HBV infection.

Aims and Methods: The study aimed at determining the prevalence rate of delta hepatitis antibodies (IgM and IgG anti-HDV) among subjects with chronic hepatitis B (CHB) infection. The other objectives were to compare the liver function test (LFT) profile and disease severity, using the Child-Turcotte-Pugh (CTP) score, among the anti-HDV positive and anti-HDV negative subjects.

The study was a cross-sectional study of 180 consecutive chronic hepatitis B infected individuals presenting to the Gastroenterology Unit of U.A.T.H. The IgM and IgG anti-HDV were assayed using ELISA test kits manufactured by Creative Diagnostics, N.Y, U.S.A. LFT profiles were done using test kits manufactured by Randox Laboratories Ltd, U.K. Severity of liver disease was assessed using the CTP score.

Results: There were 180 subjects comprising of 150 (83.3%) subjects with uncomplicated CHB infection and 30 (16.7%) subjects with complicated CHB infection (14 liver cirrhosis and 16 hepatocellular carcinoma). Thirty-four (18.9%) of all the participants were positive for anti-HDV. This comprised of 16 (8.9%) participants who were positive for IgM anti-HDV and 24 (13.3%) were positive for IgG anti-HDV. Six (3.3%) were positive for both IgM and IgG anti-HDV. The prevalence rate of IgG anti-HDV+ve was significantly higher among the subjects with complicated CHB (26.7%) than those with uncomplicated CHB (10.7%) ($p = 0.019$). The mean serum ALT, AST, albumin levels and INR in all the anti-HDV positive subjects were 16.5 $\pm$ 13.8 IU/L, 26.3 $\pm$ 32.6 IU/L, 38.9 $\pm$ 7.6 g/L, and 1.2 $\pm$ 0.2 respectively. On the other hand, the mean values for the same parameters in all the anti-HDV negative subjects were 10.8 $\pm$ 9.5 IU/L, 13.4 $\pm$ 11.2 IU/L, 41.4 $\pm$ 6.0 g/L and 1.1 $\pm$ 0.2 respectively ($p < 0.05$). Among the patients with complicated CHB, only the mean serum AST was significantly higher in those who were anti-HDV positive (63.6 $\pm$ 46.5 IU/L) compared to those who were anti-HDV negative (27.3 $\pm$ 20.8 IU/L) ($p = 0.006$). The LFT parameters were, however, not significantly different in the patients with uncomplicated CHB irrespective of their anti-HDV sero-status. The mean CTP scores in the anti-HDV positive and anti-HDV negative subjects were 6.1 $\pm$ 2.1 and 5.5 $\pm$ 1.2 respectively ($p = 0.025$). However, within the different diagnostic groups, the CTP scores were not significantly different in the anti-HDV positive compared to the anti-HDV negative subjects.

Conclusion: The sero-prevalence rate of anti-HDV in this study is higher than previously reported in Nigeria. HDV may contribute to the progression of liver disease in chronic hepatitis B infected individuals. Screening for HDV should be part of the routine evaluation for all individuals with CHB in Nigeria

Disclosure: Nothing to disclose

P0676 DIFFUSION-WEIGHTED MR IMAGING AND MICRO-RNA IN DIAGNOSIS AND STAGING OF HEPATIC FIBROSIS IN CHRONIC HEPATITIS C

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Introduction: Non-invasive tests for the evaluation of the severity of chronic liver diseases seem to be an alternative option designed to replace liver biopsy. These new non-invasive methods are including radiological techniques or biochemical markers like Diffusion weighted MRI and microRNAs.

Aims and Methods: To assess diffusion-weighted MR imaging (DWI) and microRNAs (miR) (200b, 21 and 29b) in diagnosis and staging of hepatic fibrosis in patients with chronic hepatitis C. Comparative cross-sectional study was conducted upon 208 patients and 82 age and sex-matched controls underwent DWI of the abdomen, miR and liver biopsy. The pathological score was classified according to METAVIR scoring system. The ADC and miR were calculated and correlated with pathological scoring.

Results: The ADC value was decreased significantly from controls (F0), patients with early fibrosis (F1 and F2) and those with late fibrosis (F3 and F4), (median 1.92, 1.53 and $1.25 \times 10^{-3} mm^2/s$) respectively ($p = 0.001$). The cutoff ADC value used to differentiate patients from controls was (1.83×10^{-3} mm^2/s) with area under curve (AUC) of 0.992. Combined ADC and miR-200b revealed highest AUC (0.995) for differentiating patients from controls with accuracy (96.9%). The cutoff ADC to differentiate early fibrosis from late fibrosis was $1.54 \times 10^{-3} mm^2/s$ with AUC of 0.866. Combined ADC and miR-200b revealed best AUC (0.925) for differentiating early fibrosis from late fibrosis with accuracy (80.2%). The ADC correlated with miR-200b ($r = -0.61$, $p = 0.001$), miR-21 ($r = -0.62$, $p = 0.001$) and miR-29b ($r = 0.52$, $p = 0.001$).

Conclusion: Combined ADC and miR (200b, 21 and 29b) offer an alternative surrogate noninvasive diagnostic tool for diagnosis and staging of hepatic fibrosis in CHC patients.

Disclosure: Nothing to disclose

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P0677 IMPROVEMENT OF LIVER STIFFNESS, INDIRECT PARAMETERS OF PORTAL HYPERTENSION IN CHRONIC HEPATITIS C VIRUS PATIENTS ONE YEAR AFTER SUSTAINED VIROLOGICAL RESPONSE TO DIRECT ACTING ANTIVIRALS

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Introduction: The outcome of patients with chronic hepatitis C virus infection (HCV) and advanced, compensated liver disease who have obtained a sustained virological response (SVR) to treatment with direct-acting antivirals (DAAs) has not yet been completely depicted. In particular, previous studies included heterogeneous patients populations, or patients with advanced, decompensated liver disease.

Aims and Methods: In this prospective study, our aim was to assess the clinical and instrumental outcome of patients with advanced, compensated chronic HCV-related liver disease who had obtained a SVR to DAAs treatment, and who had at least 1-year follow-up following the end of treatment. We included 52 patients with cirrhosis (n = 27) and a METAVIR fibrosis stage F3 (n = 25) who

were followed-up for a median of 60 weeks (95%CI, 52–68 weeks) following the end of successful DAAs treatment. Clinical work-up, liver transient elastography, and measurement of the spleen bi-polar diameter were carried out before treatment and at the end of follow-up. The transient elastography results compatible with the presence (*i.e.*, ≥21.0 kPa) or absence (*i.e.*, < 13.6 kPa) of clinically significant portal hypertension were obtained from the current literature.
Results: We observed that liver stiffness decreased ($p < 0.0001$) from a median baseline of 15.2kPa (12.0–20.0kPa) to 9.3kPa (7.5–12.0kPa) at follow-up. Overall, absolute liver stiffness values decreased in 45 patients (86.6%), were unmodified in 2 patients (3.8%), and increased in 5 patients (9.6%). At the end of follow-up liver stiffness values were compatible with a METAVIR stage F4 in 17 patients (32.6%), F3 in 8 patients (15.4%), F2 in 7 patients (13.5%), F1 in 13 patients (25.0%), and F0 in 7 patients (13.5%). Moreover, we observed that a liver stiffness value suggestive of the presence (*i.e.*, ≥21.0kPa) of clinically significant portal hypertension was found in 13 patients (25.0%) at baseline and in 7 patients (13.5%) at follow-up ($p = 0.037$). Platelet count significantly increased [143×10^9/L (117–176×10^9/L) to 153×10^9/L (139–186×10^9/L), $p = 0.003$], while spleen bi-polar diameter significantly decreased [120mm (112–123mm) to 110mm (102–116mm), $p = 0.0009$] from baseline to the end of follow-up.
Conclusion: In patients advanced, compensated chronic liver disease, liver stiffness significantly improves in the long-term after SVR, and this improvement is accompanied by an amelioration of indirect indices of portal hypertension.
Disclosure: Nothing to disclose

P0678 A REPORT OF EFFICACY AND SAFETY OF THERAPY WITH OMBITASVIR, PARITAPREVIR/ R+DASABUVIR+RIBAVIRIN IN 5853 PATIENTS WITH LIVER CIRRHOSIS

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Introduction: We previously reported a very high rate of HCV- SVR in a large cohort of 2070 patients: 96.6% in intention-to-treat and 2.9% rate of serious adverse events (SAE) leading to discontinuation of therapy (1).
Aims and Methods: The aim of this study is to report the incidence and the predictive factors of SAE in a large cohort of 5853 subjects with liver cirrhosis treated with ombitasvir, paritaprevir/ r+dasabuvir+ribavirin (OBV/PTV/r + DSV). In Romania, through a nationwide government-funded programme in 2015–2016, 5853 patients with virus C liver cirrhosis received fully reimbursed DAA therapy with OBV/PTV/r+DSV+RBV for 12 weeks, all with genotype 1b. The only key inclusion criteria was advanced fibrosis (Metavir stage F4) confirmed by Fibromax testing (or liver biopsy/Fibroscan). Efficacy was assessed by the percentage of patients achieving SVR 12 weeks post-treatment (SVR12). Only SAE leading to discontinuation of therapy were reported. Ordinal and scale variables with non-normal distribution were summarized as median (min, max), and compared by Mann-Whitney U test, while categorical variables were summarized as number (%) and compared by Fisher exact test.
Results: 55 patients were lost to follow-up. 65 stopped the treatment because of hepatic decompensation (1.1%), 38 patients stopped because of other adverse events. This cohort was 51% females, mean age 60 years (25÷82), 67% pretreated, 70% associated NASH, 67% with severe necro-inflammation (severity score 3-Fibromax), 37% with co-morbidities, 10.4% with Child Pugh A6, 0.5% B7. The median MELD score was 8.09 (6 ÷ 22). SVR by intention to treat was reported in 5654/5853 (96.6%), 41/5853 failed to respond. Liver decompensation was statistically associated in multivariate analysis with platelets < 10^5/mm^3 ($p = 0.03$), increased total bilirubin ($p < 0.001$), prolonged INR ($p = 0.02$), albumin < 3.5g/dl ($p = 0.03$). Other SAE were the following: pancreatitis (9), bacterial or viral infections (8), cardiovascular events (7) (probably unrelated to DAA therapy), psychiatric events (7), alergic reactions (4), severe anemia (3). The main predictors for these other SAE in multivariate analysis were: advanced age ($p < 0.001$), female sex ($p < 0.001$), presence of comorbidities ($p = 0.01$). Mortality was 71% for cardiovascular SAE (probably unrelated to DAA therapy), 32% for hepatic decompensations and 25% for infections.
Conclusion: OBV/PTV/r+DSV+RBV proved to be highly efficient in our population of cirrhotics with a 96.6% SVR in ITT. Safety of this DAA therapy in our difficult to treat- patients was very good, as long as SAE leading to therapy discontinuation were reported in 103/5853 (1.8%), most of them liver decompensation (1.1%), related to hepatic dysfunction, and lower platelet count.
Disclosure: Nothing to disclose

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P0679 FROM ALFA-INTERFERON TO DAAS: IMPACT ON HOSPITALIZATION RATE FOR HCV LIVER-RELATED DISEASES FROM 2000 TO 2016 IN NORTH EST ITALY

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Introduction: Hepatitis C virus (HCV) epidemiological data in Italy is changing due to the decline of iatrogenic etiology and the persistence of infection in populations at risk. To analyse the trend of hospitalization for liver HCV-related disease in Veneto Region in order to report the impact of HCV treatment with different therapeutic schedule over the time period.
Aims and Methods: This is a retrospective cohort study based on Veneto Region anonymous computerised database of hospital discharges between 2000 and 2017. All Veneto residents discharge records with principal diagnosis of hepatitis (cod. ICD9-CM: 070.41, 070.44, 070.51, 070.54, 070.70, 070.71, 571.5, 571.9) were included in the study. The Standardised Hospitalisation Ratio (SHR) per five-year age group (ref. pop. Veneto 2008) was calculated and expressed per 100 000 population.
Results: In the period considered 37046 hospital admissions diagnosed with HCV have been recorded. Approximately half of patients were males (56%). Despite their lower age (56.2±7.2 vs. 65.2±8.3), they had the greatest ospitalisation rate (49.4 vs. 36.3; OR: 1.36; 95% CI: 1.33–1.39; $p < 0.001$).
The analysis of the hospitalisation trend shows a 14% increase in the average age of patients (from 57.3±9.5 to 65.9±9.9) and a substantial decrease in hospital admissions (X^2 per trend: 9315,644; $p < 0.001$). Between 2000 and 2017, there has been a 78% decline in hospital admissions (i.e. from 78.9 to 17.3). with a comparable decrease in both genders/sexes (ratio M:F 1.5) and in the last year considered (2017) SHR were respectively 20.3 and 14.3 It can be observed that the introduction of new therapies has been followed by several reductions in SHR, all with statistically significant values. The decline of hospitalization rate from 2000–2005 (73.6) to 2006–2012 (73.6 to 35.5; OR: 0.48; 95% CI: 0.47–0.49; $p < 0.05$) reflects the efficacy of Interferon standard and the subsequent improvement of the cure through the use of Peg Interferon plus Ribavirin. Then with new therapies SHR felt from 21.3 of triple therapy 2013–2014 (OR: 0.29; 95% CI:0.28–0.30; $p < 0.05$) to 18 of DAAS 2015–2017 (OR: 0.24; 95% CI: 0.24–0.26; $p < 0.05$).
Conclusion: HCV liver-related disease as cause of hospital admission is in progressive and constant decline. The slope of the curve representing the decline of hospitalization rate is significantly related to the treatment schedules available in each period and care setting.
Disclosure: Nothing to disclose

P0680 HIGH EFFICACY OF THE CURRENTLY RECOMMENDED REGIMENS OF 2 DIRECT ACTING ANTIVIRALS (DAAS)±RIBAVIRIN (R) IN HCV GENOTYPE 4 (GT4) PATIENTS (PTS) WITH ADVANCED FIBROSIS OR CIRRHOSIS IN HERACLIS REAL-WORLD COHORT

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Introduction: GT 4 accounts for 20% of hepatitis C virus (HCV) infections in Greece. Pts with GT4 are underrepresented in phase 3 clinical trials. Results from real-world cohorts from regions with increased prevalence would add important knowledge to the management of these pts.

Aims and Methods: We analyzed the efficacy of regimens with different combinations of DAAs in HCV GT4 pts from a large cohort of 14 Greek centers. All GT4 pts who received DAAs in the HERACLIS cohort were included. All pts fulfilled the national criteria for DAA reimbursement [F4 naive, F3-F4 retreated, decompensated cirrhosis (decomp-Ci), OLT, severe extrahepatic manifestation] were analyzed in this cohort. SOF+SMV±R, SOF+DCV±R, SOF/LDV±R, 3D±R (2D+R for GT4), SOF/VEL±R & EBR/GZR±R considered as currently recommended regimens according to the international and local guidelines. The primary efficacy endpoint was SVR12; predictors of response to treatment were assessed.

Results: 259 pts with GT4 from a total 1309 HCV pts (19.8%) were included (males 58%, age 55±10 yrs, PDU 28%; F0-F2 3%, F3 20%, F4 66%, decomp-Ci 10.4%, treatment experienced 63%, DAA failures 7.3%). The DAA regimens employed were Peg-IFN + RBV (PR) + SMV in 4 (1.5%), PR+SOF in 14 (5.4%), SOF+R in 2 (0.8%), SOF+SMV±R in 33 (12.7%), SOF+DCV±R in 15 (5.8%), LDV/SOF±R in 42 (16.3%), 2D+R in 139 (53.7%), SOF/VEL+R in 3 (1.2%), EBR/GZR±R in 7 (2.7%). Treatment duration was 12 weeks for all combinations except for PR+SMV and another 6 pts (24 weeks; 2 SOF+R, 2 LDV/SOF+R, 2 2D+R). SVR12 rates for the first 189 pts who completed post-treatment follow-up was 100% for PR+SMV, 64% for PR+SOF, 100% for SOF+R, 90% for SOF+SMV±R, 93% for SOF+DCV±R, 89% for LDV/SOF±R and 97% for 2D+R and 100% for EBR/GZR. SVR12 was 100% for F0-F2, 97.4% for F3, 92.6%, for F4, and 82.6% for decomp-Ci ($p = 0.153$). Pts without than with SVR had higher BMI [(28.5 vs 26.2 kg/m^2); $p = 0.01$]], lower PLT ($p = 0.018$), or albumin ($p = 0.061$), and more frequently albumin < 3.5g/dl [41.7% vs 15.3% ($p = 0.032$)], PLT $< 100 \times 10^9$/L (33.3% vs 14.1%; $p = 0.063$), decomp-Ci (26.7% vs 10.1%, $p = 0.072$) and use of non-recommended regimens [33.3% vs 7.9%; $p = 0.006$]. SVR rates in pts with decomp-Ci treated with currently recommended DAAS was 81% (17/21). Logistic regression analysis showed that lower SVR rate was independently associated only with the use of non-currently recommended regimens (OR: 0.2163, 95% CI:0.033–0.81; $p = 0.027$).

Conclusion: The currently recommended combinations of two DAA +R for 12 weeks has excellent efficacy in HCVGT4 pts with F3 fibrosis and compensated cirrhosis, achieving SVR rates 95%–100%. Further treatment optimization seems to be required in GT4 pts with decomp-Ci.

Disclosure: Nothing to disclose

P0681 IMMEDIATE DIRECT-ACTING ANTIVIRAL THERAPY (DAA) OF RECURRENT HCV INFECTION AFTER LIVER TRANSPLANTATION IMPROVES POST-TRANSPLANT SURVIVAL: SINGLE-CENTRE EXPERIENCE (2014-2017)

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Introduction: HCV infecton represents the most common indication for liver transplantation (OLT) in Western world. Recurrence of HCV in the liver graft negatively influences survival. The use of Direct-acting antivirals (DAA) substantially improved treatment efficacy. The aim of the study was to assess DAA efficacy in OLT recipients who were treated between 7/2014 and 5/2017 and analyze DAA treatment impact on post-transplant survival.

Aims and Methods: We retrospectively analyzed 195 (14.2% of 1373 total OLT) patients who underwent OLT between 7/1995 and 5/2017 for HCV infection, 127 males and 68 females, average age 54.7 ± 8.2 years. 97% of patients were infected with genotype 1b. In Czech Republic, DAA became available in 5/2014 (DAA era, N = 43). Until that time, patients were treated with peginterferon-α and ribavirin (PEG-α/RBV) (pre-DAA era, N = 152). Treatment efficacy (sustained virological response, SVR) in individual groups was assessed by Fisher's exact test, patient survival 3 years post-transplant by log-rank test.

Results: In the DAA era, we treated 64 patients with biopsy-proven recurrent HCV infection. The choice of DAA was determined by DAA availability at the respective time: 2 patients were treated with sofosbuvir (SOF)/RBV combination, 11 patients with SOF/daclatasvir, 12 patients with SOF/simeprevir, 26 with SOF/ledipasvir and 13 with paritaprevir/ritonavir/ombitasvir/dasabuvir. DAA were administered at an average of 100 months post-transplant as a *salvage therapy* to 38 patients with graft cirrhosis in whom previous PEG-α/RBV treatment had failed, or as an *immediate therapy* in 26 patients at an average time of 6 months after OLT. SVR was achieved in 97.4% and in 88.5% patients in the salvage and immediate treatment groups, respectively (P = NS). In the DAA era patients, only 1 died. This translated into significantly better 3-year survival, when compared to a historical cohort of 152 patients with HCV graft recurrence from pre-DAA era (97% vs. 78%, $p < 0.001$). After DAA introduction, none of the patients died of fibrosing cholestatic hepatitis and none underwent re-OLT owing to chronic HCV graft failure, as compared to pre-DAA era patients out of whom 6.7% died of fibrosing cholestatic hepatitis and 5.7% required re-OLT.

Conclusion: The introduction of DAA in the treatment of post-transplant HCV recurrence achieved excellent SVR rates and significantly increased post-transplant survival in patients with HCV recurrence in the liver graft.

Disclosure: Nothing to disclose

P0682 EFFICACY AND SAFETY OF DASABUVIR, OMBITASVIR, PARITAPREVIR AND RITONAVIR TREATMENT IN ROMANIAN PATIENTS WITH HEPATITIS C, WITH MULTIPLE CO-MORBID CONDITIONS AND ADVANCE FIBROSIS

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Introduction: The prevalence of hepatitis C in Romania is estimated to 3.2%, over the European reported average data [1], [2]. The peculiarity of Romanian epidemic is the predominance of genotype 1b (99%) [1]. Interferon-free antiviral treatment with Dasabuvir, Ombitasvir, Paritaprevir and Ritonavir (DOPR) is available in our clinic since 2017, according to a national protocol.

Aims and Methods: We assessed the results of DOPR in the end of the treatment (EOT).

This prospective study included patients with Hepatitis C, treated with DOPR for 12 weeks, in the Infectious Disease Clinic Galati, Romania. The eligibility criteria were limited to advanced fibrosis (FibroMax F3/F4; Child-Pugh score ≤6). The demographic data, Hepatitis C Virus - Ribonucleic Acid (HCV-RNA), co-morbidities and the rate of EOT were statistical analyzed.

Results: Demographic characteristics of 103 eligible patients are the old age (median age: 61±10.8 y.o) and predominance of female gender (62%). The baseline data are: HCV-RNA average 2026243±2741998 IU/ml, F3/F4 ratio 0.98, Alanine Aminotransferase (ALT) 98,1 ± 63.0 IU/l, Aspartate Aminotransferase (AST) 81.6 ± 52.7 IU/l, total bilirubin 0.8 ± 0.3 mg/dl, serum albumine 4.2 ± 0.3 mg/dl, prothrombin concentration 80.8 ± 17.2%, Alpha Fetoprotein 11.3 ± 15 IU/ml, degree of esophageal varices 0: 79.6% patients, 1: 15.5% patients, 2: 3.8% patients, 3: 0.9% patients. As minimum one co-morbidity was counted in 61% patients, most frequent hypertension (26%), diabetes (18%), depression (10.6%), oncologic history (8%), ischemic cardiopathy (5.8%), hepatitis B co-infection (4.8%). The rate of the complete 12 weeks treatment was 97%. All patients achieved viral suppression (HCV-RNA < 15 IU/ml) in EOT and had normal transaminases. The interruption of DOPR was decided for 3 patients, due to adverse events (nausea, vomiting, renal failure, acute pancreatitis, increase over 5 times the initial transaminases), but these events were not serious and there were not any deaths. The follow-up on 24 weeks is available to 35% patients, all of them with sustain virologic response.

Conclusion: The antiviral regimen with Dasabuvir, Ombitasvir, Paritaprevir and Ritonavir was 100% effective after 12 weeks for the patients with hepatitis C who completed the therapy. Very good tolerability and safety was proved in difficult to treat patients, including old age, advance fibrosis and multiple co-morbid conditions.

Disclosure: Nothing to disclose

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P0683 HEPATITIS C SCREENING PROGRAMME IN MILITARY MEDICAL ACADEMY, SOFIA, BULGARIA - SINGLE-CENTRE EXPERIENCE

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Introduction: The prevalence of hepatitis C infection (HCV) in Bulgaria is estimated to be 1.28% in multicenter study in 2010, but no national representative study on HCV prevalence in general population exists so far.
Aims and Methods: The aim of this study is retrospectively to analyze HCV screening programme in Military Medical Academy (MMA), for the period January 2014 – December 2016.
HCV screening programme of the MMA consists of: risk-based screening for all clinics in in- and out-patient settings; voluntary screening offered to everyone admitted in surgery clinics/entering emergency department; obligatory screening for all blood donations; obligatory screening for all candidates for military service. Serological anti HCV Ab tests (III/IV generation) were used. For the period January 2014 – December 2016 29,600 patients, 22,717 males/ 6,883 females, age between 18–87 years old, were screened.
Results: The prevalence of HCV in 29,600 screened patients was 0.65% (n-194). In the Group of blood donors (n-17,394) the HCV prevalence was 0.59% (n-104), but in first-time blood donors (n-6,700)–0.35% (n-27). In the Group of in/out-patients (n- 9,050) the HCV prevalence was 0.92% (n-84) and in Group of candidates for military service (n-3,156)–0.19% (n-6). There was no gender difference in the HCV prevalence (0.68% in males and 0.55% in females). The most frequently affected age group was 31–40 years old (32.6%). Linkage to care was achieved in 82.5% (84/104) of HCV-infected blood donors and in 61% (61/100) of in/out patients and candidates for military service. Viremic prevalence was found to be 73% (106/145) and out of them 68% (72/106) initiated antiviral treatment.
Conclusion: Screening for HCV in hospital setting is feasible options for the countries where no national screening programme exists and provide excellent opportunity for linkage to care.
Disclosure: Nothing to disclose

P0684 PROCALCITONIN AS EARLY PREDICTOR OF ACUTE LIVER INJURY IN ACETAMINOPHEN POISONING – A PROSPECTIVE COHORT STUDY IN 116 PATIENTS

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Introduction: Acetaminophen is one of the most commonly prescribed drugs and the leading cause of poisoning and acute liver injury (ALI) in developed countries. For more than four decades, prediction of the risk of liver toxicity has been based on the Rumack-Matthew nomogram, which has helped determine when N-acetylcysteine (NAC) is indicated as preventive antidote. However, this nomogram is not validated 1) after repeated acetaminophen exposure; 2) if time to presentation is unknown or > 24 hours; and 3) as a predictive measure of liver injury in vulnerable patients, despite NAC administration. Consequently, there is a current need for predictive biomarkers in addition to the nomogram to better identify acetaminophen-poisoned patients with increased risk of ALI despite NAC therapy. Since the liver has been considered as potential source of sepsis-related procalcitonin (PCT) production, we aimed to assess the diagnostic value of plasma PCT, commonly used in the intensive care unit (ICU) to identify bacterial infections, in patients likely to develop acetaminophen-induced ALI.
Aims and Methods: All consecutive acetaminophen-poisoned patients admitted in our ICU and requiring NAC treatment were prospectively included between January 2011 and December 2017. The primary outcome was the occurrence of ALI defined as a peak of alanine aminotransferase (ALT) >100 IU/L. Liver function tests, PCT and acetaminophen levels were measured on admission. Data was reported as median (interquartile range) or absolute value (percentage) as required. Multivariate analysis based on a Cox proportional-hazard regression model was used to identify parameters associated with ALI. The corresponding hazard ratios and 95%-confidence intervals (CI) were determined.
Results: 116 patients were included [age: 32 (21–53)], with a median ingestion of 16 g (9–30) of acetaminophen. Multidrug ingestion was noted in 77% of the patients. The Rumack-Matthew nomogram could not be used in 47% of the cases. ALI occurred in 36 patients (31%) despite NAC treatment provided after a median 6-hour (4–12) delay. In these patients, plasma PCT concentrations were significantly increased as compared to patients without ALI (23.13 vs 0.08 ng/mL $p < 0.001$). The increase in PCT preceded the increase in ALT by 33 hours (10–74). Multivariate analysis showed that PCT levels > 1ng/mL was significantly associated with ALI [hazard ratio: 4.72 (95% CI, 1.76–12.66); $p = 0.002$], independent from the dose of ingested acetaminophen, the delay of NAC administration and the presence of suspected community-acquired infection (Table 1). PCT levels predicted ALI with a sensitivity, specificity, and area under the ROC curve of 0.94, 0.83 and 0.88 (95% CI, 0.81–0.95), respectively.
Conclusion: Our results suggest that plasma PCT is predictive of acetaminophen-induced ALI. PCT is a potential useful biomarker for the early identification of 1) high-risk ALI patients whom may benefit from closer monitoring and should be referred to a specialized liver ICU and 2) lower-risk ALI patients requiring abbreviated NAC regimens and early discharge safely. Our findings require further validation in larger studies.
Disclosure: Nothing to disclose

P0685 POST-TRANSPLANT *DE NOVO* MALIGNANCIES: IS HCC AN ADDITIONAL RISK FACTOR?

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Introduction: Patients with hepatocellular carcinoma (HCC) are at higher risk for second primary malignancies compared with the corresponding general population. Such risk could be even higher after liver transplantation (LT), due to chronic immunosuppression. It has been consistently demonstrated that patients transplanted for alcoholic liver disease and primary biliary cholangitis are at higher risk for the development of post-LT *de novo* neoplasms (DNN). However, evidence on the additional risk that pre-LT HCC could confer to transplanted patients are lacking. As HCC has become the leading indication for LT, it is important to investigate whether such patients deserve more intensive post-LT DNN screening compared to other transplanted patients.
Aims and Methods: A cohort study was conducted using data collected among 9 Italian centers between 1985–2014. Patients were excluded if: ≤18 years old, follow-up shorter than 30 days after LT, cancer diagnosis within 30 days after LT. Person-years (PYs) at risk for DNN were computed from 30 days post-LT to the date of death, date of cancer diagnosis or end of follow-up, whichever came first. Hazard ratios (HR) of DNN development (excluding non-melanoma skin cancers) and 95% confidence intervals (95% CI) for patients transplanted for HCC (HCC-patients) compared to those undergoing LT without any pre-transplant neoplastic history (non-HCC patients), were estimated using Cox proportional hazards models, irrespectively from liver disease etiology. All models were adjusted for sex, age at transplant, and calendar year at transplant.
Results: A total of 2,801 patients were followed up for 18,021 PYs of observation [median follow-up: 5.3 years (IQR 2.4–9.9)] during which 194 (6.9%) developed 206 DNNs. Out of 991 HCC-patients (median age at LT 57 years, 86% males) 64 (6.4%) developed 66 DNNs, while out of 1810 non-HCC patients (median age at LT 51 years, 69% males) 130 (7.2%) developed 140 DNNs. No significant association with the risk of all DNN emerged for HCC-patients as compared to non-HCC (HR = 1.18, 95% CI 0.85–1.64), after median follow-ups of 3.6 (IQR 1.9–6.7) and 6.2 years (IQR 2.7–11.1), respectively ($p < 0.01$). However, there was a significant difference in occurrence timings: median time from LT to first DNN diagnosis was 2.5 years (IQR 1.5–4.3) for HCC-patients and 4.3 years (IQR:1.8–7.9) for non-HCC ($p < 0.01$). In the analysis by specific tumor types (Table 1), a significant increased risk emerged for bladder cancer only (HR = 8.66, 95% CI 1–74).
Conclusion: In our cohort, patients transplanted for HCC were not at higher risk for DNN than other transplanted patients. Nonetheless, DNN seemed to occur earlier in HCC-patients, probably due to their higher susceptibility to carcinogens and shared risk factors with primary cancer, leading to a possibly accelerated carcinogenic process. Pre-LT liver neoplastic history could therefore represent an additional risk factor for early DNN occurrence and should be taken into account for surveillance-individualization, to improve early detection and management. Further investigations in wider cohorts with different patients' characteristics are necessary to confirm these results.
Disclosure: Nothing to disclose

P0686 ASSOCIATION OF TOLL-LIKE RECEPTOR -2 GENETIC POLYMORPHISM AND ITS SERUM LEVEL WITH INFECTION IN RECIPIENTS AFTER LIVING DONOR LIVER TRANSPLANTATION :A SINGLE CENTRE STUDY

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Introduction: Innate immune defenses against infection are altered after liver transplantation (LT) and may increase the risk of infection after transplantation. Toll like receptors (TLRs) are a large section of pathogen associated molecular patterns recognition (PAMP) receptors of the innate immunity. These receptors help stimulation of downstream signaling pathways in reaction to many antigens, mainly to Gram +ve and Gram-ve bacteria, all related to release of cytokines and enhancement of the inflammation. One of the most important elements of these innate defenses is Toll like receptors (TLRs) particularly TLR2.

Aims and Methods: The aim of this work is to assess Association of Toll-Like Receptor -2 single nucleotide genetic polymorphism and its serum level with infection in Recipients after living donor liver transplantation.

Out of 125 subjects enrolled in our work, 109 subjects completed this cohort case control prospective study. Subjects were classified into two groups: 66 patients who undergone LDLT and 43 healthy donors as a control group. Serum TLR2 protein was measured using 3rd generation ELISA technique in the serum of the recipient's pre and post transplantation and as well as in the serum of the donors before transplantation. In addition, single-nucleotide polymorphisms (SNPs) of 3 snips of Toll-like Receptor-2 (TLR2) gene (rs3804099 +597, rs5743708 +75, rs121917864 +677) were studied where the allelic genotyping of each DNA sample was performed using real-time PCR reaction.

Results: post liver transplantation developed in 84.8% of the recepients where 55.36% infected with single organisms while 54.69% with mixed infections. Serum TLR2 was significantly higher in recipients post transplant period when compared with recipients and donor in pre transplant period ($p < 0.001$). Conversely, no significant difference was detected in post transplant serum TLR2 of recipients on comparing non infected group with infected groups (gram positive, gram negative and fungal infections) regarding blood, urine and sputum cultures ($p = 0.9$, $p = 0.097$ and $p = 0.36$) respectively. On the other hand, serum TLR2 in recipients post LDLT is significantly higher in cases showing CMV infection when compared with those without CMV infection ($p=0.02$). As Regard the analysis of SNPs of TLR2 it was found that T allelle of rs3804099, G allele of rs5743708 and the C allele of rs121917864 were significantly higher in non infected group when compared to both non infected (OR: 0.1471, 0.148 and 0.1838 respectively, $p < 0.05$) and control groups (0.1238,0.2044 and 0.2528 respectively $p < 0.001$) but no significant association was found with type of infections $p > 0.05$.

Conclusion: The current study showed that serum level of TLR2 was increased in the recipients after post LDLT in comparison to pretransplant level but no significant association with the type of infection except CMV infection. In addition **T allelle of rs3804099, G allele of rs5743708** and the C allele of **rs121917864 are protective alleles against the development of infection but no significant association with the type of infection.**

Disclosure: Nothing to disclose

P0687 PROTECTIVE EFFECT OF APELIN PRECONDITIONING IN A RAT MODEL OF HEPATIC ISCHEMIA REPERFUSION INJURY; POSSIBLE INTERACTION BETWEEN APELIN/APJ SYSTEM, ANGIOTENSIN II/ANGIOTENSIN I RECEPTOR (ANG II/AT1R) SYSTEM AND ENDOTHELIAL NITRIC OXIDE SYNTHASE (ENOS)

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Introduction: Hepatic ischemic reperfusion (I/R) injury, a major cause of liver damage, occurs in multiple clinical settings. It is responsible for nearly one third of delayed graft function cases in liver transplantation. Recently, a number of peptides have been developed to attenuate hepatic I/R injury in several animal models. However, novel potential protective agents are still needed, hoping for promising results for alleviating hepatic I/R injury with the potential to increase the number of livers suitable for liver transplantation.

Apelin, a small regulatory peptide, is the endogenous ligand of the G protein coupled receptor APJ. It has various isoforms, among which Apelin-13 is the most active isoform. The apelin-APJ axis is widely expressed in hepatic parenchymal, Kupffer, stellate and endothelial cells.

Recently, exogenously administered apelin was shown to protect against I/R injury in different organs including the heart and the brain. However, the protective mechanism of apelin on hepatic I/R injury is not yet clear.

Aims and Methods: We aimed to evaluate the effect of apelin-13 preconditioning on hepatic I/R injury and its effect on hepatic expression of Angiotensin-1 receptor (AT1R), endothelial Nitric Oxide Synthase (eNOS) and hepatic tissue level of apelin in an attempt to clarify the possible interaction between apelinergic, Renin-Angiotensin System (RAS) systems and eNOS.

60 male albino rats were randomly assigned to one of the following 4 groups (15 rats each); Control sham-operated (group I), ischemia reperfusion (group II), Apelin-treated I/R (group III) and Apelin + L-NAME-treated I/R (group IV). Apelin-13 and L-NAME (N-nitro-L-arginine methyl ester) were administered intraperitoneally at dose of 2 μg/kg/day, 3 days prior to surgical hepatic I/R procedure and10mg/kg/day, 2 weeks prior to the surgical procedure, respectively. Ischemia was induced for 30 minutes. After 2 hours of reperfusion, serum samples were collected for measurement of serum ALT and AST. Hepatic tissue specimens were harvested for biochemical (MDA; Malondialdehyde, apelin, gene expression of CASP-3; Caspase-3, eNOS and AT1R) and histopathological analyses.

Results: Compared to I/R group, apelin pretreatment provided marked hepatic protection with significant reduction in the serum levels of ALT and AST, hepatic MDA (oxidative stress marker), hepatic expression of CASP-3 (apoptosis marker) and AT1R, while hepatic apelin level and hepatic eNOS expression were significantly increased in group III. Moreover, apelin preconditioning reduced the hepatic histological damage induced by the I/R injury. Hepatic apelin level was positively correlated with hepatic expression of eNOS, while it was negatively correlated with serum liver enzymes, hepatic MDA, hepatic expression of CASP-3 and AT1R.

Co-adminstration of L-NAME with apelin in group IV partially reversed the hepatoprotective effect of apelin.

Conclusion: Exogenous apelin-13 preconditioning exerts protective effect against hepatic I/R injury, probably by modulating the oxidant stress together with its antiapoptotic effect. Several signaling pathways may be involved including suppression of hepatic AT1R expression and elevation of hepatic apelin levels. The hepatic apelinergic system may be implicated in vasodilatory effects during hepatic I/R injury through increase the hepatic expression of eNOS which counteracts the pathologic effects of Ang II/AT1R system. These results clearly demonstrate a strong interaction between Apelin/APJ system, RAS and eNOS signaling pathways in hepatic I/R injury pathophysiology.

Disclosure: Nothing to disclose

P0688 CORRELATES OF MORTALITY IN PATIENTS ON WAITING LIST OF LIVER TRANSPLANTATION: A 4-YEAR PROSPECTIVE COHORT STUDY

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Introduction: Liver transplantation (LT) is the most effective treatment for end stage liver disease but due to demand-supply imbalance and prolonged waiting time, LT candidates may die before transplantation. This study aimed to detect prevalence and new predictors of mortality in LT candidates.

Aims and Methods: In this 4 years prospective cohort study, 544 LT adult candidates who referred to Shiraz LT center of Iran were followed on arrival and in 3 months intervals. A comprehensive check list including socioeconomic, nutrition, medical history, physical examination, laboratory and imaging data and death causes (in dead cases) was filled for each patient. Data analysis was performed in Nutritionist, SPSS and R software. Kaplan-Meier test was done and Cox proportional hazard (HRc) and LASSO Cox regression hazard (HRL) were measured.

Results: Mean age of patients was 46.7 ± 13.7 years while 336 (61.7%) were male. Till the end of study, 414 (76.1%) were alive and 130 (23.9%) dead, while 33.1%, 57.7% and 79.2% of deaths were occurred in the first 3, 6 and 12 months of waiting period. Hepatopulmonary syndrome ($HRC = 4.7$, $HRL = 1.8$), history of myocardial infarction (MI) ($HRC = 3.3$, $HRL = 1.6$) and low carbohydrate (CHO) diet ($HRC = 2.7$, $HRL = 1.5$) showed strong association with mortality of patients. In addition to the MELD score, CA 125, high PMN count, weight loss, high level of ALT, positive HBV markers, high MCV of RBCs, ascites, edema of gall bladder wall, high level of BUN and psychological problems showed significant association with death in LT candidates.

Conclusion: About one-fourth of patients die while they are waiting for LT. Therefore to achieve a better outcome besides MELD score, HPS, MI, malnutrition and psychological status of patients should also be considered and managed at the beginning and during the waiting time for LT.

Disclosure: Nothing to disclose

P0689 METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION: LONG-TERM FOLLOW UP IN A PROSPECTIVE COHORT

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Introduction: Metabolic syndrome (MS) is a common condition among liver transplanted patients, resulting in an increased mortality and morbidity in the long term after liver transplantation (LT).

Aims and Methods: This prospective study assessed the short and mid-term prevalence of MS and metabolic complications after LT. Patients who underwent LT at the Padova Liver Transplant Centre between April 2013 and August 2015 and regularly followed-up at Multivisceral Transplant Unit were prospectively included. Paediatric patients, multiorgan transplantation or re-transplantation and patients who had MS before LT were excluded. For each patient general and metabolic variables were collected at time of LT and at 3, 6, 12 and 24 months after LT. MS was evaluated according to the modified NCEP-ATP III criteria.

Results: Twenty-eight patients were included in the study (78% male, mean age 54.2 ± 8.1 years). The most common indication to LT was HCV cirrhosis (42.9%), 25% of the patients presented HCC and the mean MELD at transplantation was 23 ± 8.7. Prevalence of MS at 3, 6, 12 and 24 months after LT was 35.7%, 28.6%, 42.9% and 39.3% respectively ($p = 0.003$). After LT a significant increase in diabetes mellitus (46.4% vs. 17.9%, $p = 0.02$) and hypertension (25% vs. 7.1%, $p = 0.07$), as well as in total cholesterol (mean values 171.7 ± 46.7 vs. 94.6 ± 41.1, $p < 0.001$) and triglyceride levels (135.6 ± 62.2 vs. 95.4 ± 73.9, $p = 0.01$). The higher prevalence of MS, diabetes mellitus, and hypertension was observed at 12 months after LT, whereas cholesterol and triglyceride levels did not show significant differences overtime. Considering body weight, the proportion of obese patients progressively increased overtime, moving from 4% at 6 months to 23% at 24 months.

Conclusion: Occurrence of MS is an early phenomenon after LT, affecting nearly half of patients at 12 months post-LT. Diabetes, hypertension and increased in body weight are the main responsible factors for developing post-LT MS. A strict metabolic and weight control is necessary, starting early after LT period.

Disclosure: Nothing to disclose

P0690 GENDER DISPARITY IN DONOR-RECIPIENT IN LIVER TRANSPLANTATION AND GRAFT FAILURE

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Introduction: The influence of donor-recipient sex mismatches on graft failure after liver transplant (LT) is still controversial.

Aims and Methods: The aim of this study was to assess graft failure and to evaluate postoperative analitic outcomes after LT, regarding donor-recipient gender mismatch. This was a restrospective unicenter cohort study during one year (2016) including patients hospitalized in an intensive care unit (ICU) after LT.

Results: 136 patients were included (72.8% men, with a mean age of 54.09 ± 11.25 years). The main reason for LT in male patients was hepatocellular carcinoma (26.3%), followed by decompensated alcoholic cirrhosis (21.2%) and in female patients was acute fulminant hepatic failure due to drug toxicity (16.2%) and biliary cholangitis (8.1%).

Of the patients included, 42.6% ($n = 58$) had donor-recipient sex mismatches (13.2% male donor-female recipient and 29.4% female donor-male recipient).

The female sex was the prevalent sex donor organ in patients with donor-recipient sex mismatches ($p < 0.001$). The mean ICU stay was 4.7 days, with no difference between patients with donor-recipient sex mismatches and donor-recipient sex matches (4.91 vs 4.54, $p = 0.383$).

Patients with donor-recipient sex mismatches revealed lower values of ALT (1762 UI/L Vs 3075 UI/L $p = 0.022$), AST (1206 UI/L Vs 2040 UI/L, $p = 0.05$) and LDH (2304 UI/L Vs 4304 UI/L $p = 0.06$) than patients with donor-recipient sex matches in 48 hours postoperatively. There was no difference in the use of postoperative vasopressors among patients with donor-recipient sex mistmatches and matches ($p = 0.341$). 49 patients (36%) had graft failure, however there was not signficantly difference between graft failure and patients with donor-recipient sex mismatches and matches ($p = 0.262$).

Conclusion: There was no difference in graft failure in patients with donor-recipient sex mismatches and matches after LT. Although lower values of liver enzymes and LDH can point less hepatic injury at immediate postoperative outcome in patients with with donor-recipient sex mismatches.

Disclosure: Nothing to disclose

P0691 IMPACT OF ENTECAVIR IN REDUCING THE RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HEPATITIS B RELATED CIRRHOSIS

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Introduction: Chronic hepatitis B virus (HBV) infection is the most frequently identified cause of Hepatocellular carcinoma (HCC). The newer nucleos (t) ide analogues such as Entecavir (ETV) or Tenofovir have been shown to be effective in terms of virological response and improvement of liver function. However their impacts on the incidence of HCC are still not clear

Aims and Methods: The aims of this study were to investigate the incidence of HCC in patients with HBV-related cirrhosis and evaluate the effect of ETV in reducing this incidence. We performed a retrospective analysis of data from consecutive patients with HBV-related cirrhosis recruited from 2009 to 2016 and who were followed up for at least 12 months. The diagnosis of HCC was based on computed tomography scan and magnetic resonance imaging or liver biopsy. We evaluated the incidence of HCC among ETV treated patients and untreated patients.

Results: A total of 75 patients were included (78% male, age = 57 ± 12 years, follow up for 37 ± 24 months). Our patients were classed Child Pugh A, B, C in 29%, 49% and 22% of cases respectively. After a median of 19 months, 15 patients developed HCC (20%). The HCC was classed BCLC A, B, C and D in 20%, 33%, 7% and 40% of cases respectively. The treatment was curative in one patient (radiofrequency) and palliative in the 14 others cases (transarterial chemoembolization: 4 patients, Sorafenib : 1 patient, symptomatic treatment: 9 patients).

In the ETV group, HCC developed in 8 patients (21.1%). In the untreated group, HCC developed in 7 patients (18.9%). Log rank test did not reveal a statistically significant difference between the incidence of HCC in the ETV group and the untreated group ($p = 0.81$).

Conclusion: HCC still develop in patients with HBV-related cirrhosis treated with ETV. For this reason, patients under effective long term nucleos (t) ide analogues therapy should remain under surveillance for HCC.

Disclosure: Nothing to disclose

P0692 HEPATOCELLULAR CARCINOMA IN THE ELDERLY: CLINICAL CHARACTERISTICS, OUTCOMES AND TREATMENT EFFICACY, SAFETY IN OLDER THAN 75 YEARS

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Introduction: The number of elderly patients diagnosed with hepatocellular carcinoma (HCC) has been increasing because the increase in the longevity of the general population. But there is no proper management based on age stratification in elderly patients.

Aims and Methods: The aim of our study was to compare the clinical characteristics, outcomes and treatment efficacy and safety between oldest-old (aged more than 85 years), middle-old (aged between 80 and 85 years) and young-old (aged between 75 and 80 years) patients with HCC from January 2010 to December 2016. A total of 550 elderly patients whose data included demographics, comorbidity, etiology of liver disease, presence of cirrhosis, staging of HCC, treatment modality and treatment related adverse event were evaluated retrospectively. Also overall survival was assessed in enrolled patient.

Results: Fifty-one patients (oldest-old; median 87 years old), 153 patients (middle-old; median 82 years old) and 346 patients (young-old; median 77 years old) were diagnosed with HCC. Both oldest- and middle-old patients, compared to young-old patients, had significantly higher rate of hepatitis C-related disease (HCV antibody positivity 41.2% vs. 29.4% vs. 22.0%, p= 0.007) but had significantly lower rate of alcohol-related disease (11.8% vs. 19.0% vs. 30.3%, p=0.002). There were no significant difference in underlying sex, body mass index, presence of co-morbidity, hepatitis B-related disease and stage of HCC. The Child-Pugh class (CPT class A 88.9 vs. 84.1% vs. 83.6%, CPT class B 11.1% vs. 15.9% vs.15.0% and CPT class C 0.0% vs. 0.0% vs. 1.3%, respectively, $p = 0.912$) and Model for End Stage Liver Disease score (mean MELD score 8.89 ± 2.00 vs. 8.80 ± 2.78 vs. 9.19 ± 3.28, $p = 0.600$) were no significant difference between the patients with active treatment. The modified UICC staging (stage I 5.6% vs. 17.1% vs 18.6%, stage II 55.6% vs. 46.3% vs 47.3%, Stage III 22.2% vs. 24.4% vs 24.8%, Stage IV-A 11.1% vs. 6.1% vs. 4.9% and Stage IV-B 5.6% vs. 6.1% vs. 4.4%, respectively, $p = 0.826$) and Barcelona Clinic Liver Cancer staging (stage 0 5.6% vs. 9.8% vs.9.3%, stage A 16.7% vs. 17.1% vs. 22.1%, stage B 27.8% vs. 29.3% vs. 24.8%, stage C 50.0% vs. 43.9% vs. 41.2% and stage D 0.0% vs. 0.0% vs. 2.7%, respectively, $p = 0.878$) were no significant difference between the patients with active treatment. Furthermore, there were no difference between the age groups in treatment modality (Surgical resection 0.0% vs. 3.3% vs. 5.2%, $p = 0.442$; Radiofrequency ablation 2.0% vs. 8.5% vs. 11.0%, $p = 0.484$; Transcatheter arterial chemoembolization 21.6% vs. 34.6% vs. 41.6%, $p = 0.959$; Best supportive care 62.7% vs. 40.5% vs. 29.2%, $p < 0.001$), adverse event related treatment (p=0.731) and disease-free survival days (356.4 ± 321.3 days vs. 284.7 ± 459.5 days vs.

354.2 ± 561.1 days, p=0.299). Multivariate analysis showed that performance status, MELD score, modified UICC staging, presence of portal vein thrombosis and ruptured HCC are risk factors for mortality.
Conclusion: Clinician should make an active treatment in elderly patients with HCC not a age but performance status, liver function and disease status of cancer.
Disclosure: Nothing to disclose

P0694 IS THERE STILL A ROLE FOR ALPHA-FETOPROTEIN IN HEPATOCELLULAR CARCINOMA SCREENING?

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Introduction: Alpha-fetoprotein (AFP) is the most tested biomarker in hepatocellular carcinoma (HCC), and sustained elevated levels are a well-known risk factor. Only a suboptimal yield for screening purposes has been yet been described. Recently published guidelines on HCC treatment from AASLD, take in consideration the use of AFP for HCC surveillance.
Aims and Methods: The aim of this study was to evaluate the role of AFP in HCC screening by comparing two groups with different surveillance strategies. Incidence of HCC in each group was determined and correlated with early stage detection, curative therapeutic options and long-term survival.
In a retrospective study, 110 cirrhotic patients were included over a 12 year follow-up period, in a single center. Cirrhosis was defined on basis of clinical, biochemical and radiologic investigation. All patients underwent HCC screening each 6 months by US alone in one group and US plus AFP in the other.
Results: A hundred and ten patients were included (70.9% males). Surveillance strategy relied in US plus AFP in 46 cases (41.8%), and US alone in 59 cases (53.6%). Five patients had imagological evidence of suspected lesions in the first evaluation and were not included in any of the groups. The median age was 62,2 years (SD ± 12.4) and mean follow-up period was 4.6 years (SD ± 3.3). Most common etiologies of cirrhosis were alcohol (49.1%) and hepatitis C (27.3%). Of 110 patients 17 (15.4%) developed HCC, yet only 12 (10.9%) had a HCC diagnosis in surveillance setting. The mean period for HCC diagnosis was 3.7years (SD ± 2.8).
In the US plus AFP group, 8 patients (18.2%) were diagnosed with HCC. In 5 cases US findings were abnormal and AFP levels were normal while 2 patients had elevated AFP and abdominal US without suspicious lesions. Five patients (62.5%) had an intermediate stage (B) according to the Barcelona-Clinic Liver Cancer (BCLC) system, and were treated with transarterial chemoembolization (TACE).
Considering the group screened solely by US, 4 patients (6.9%) had HCC. In this group only 1 patient, with early stage (A) HCC was eligible for radiofrequency ablation (RFA).
Three-year survival rate was equal in both groups (25%). Overall mortality was higher (75%) in the US group when compared to the US plus AFP group (62.5%).
Conclusion: AFP should be considered in HCC surveillance once it allows diagnosis in patients with otherwise normal radiologic investigation.
Disclosure: Nothing to disclose

P0695 CANCER-ASSOCIATED FIBROBLASTS PROMOTE THE CANCER STEM CELL PLASTICITY OF CD24+ LIVER STEM CELLS VIA PARACRINE SIGNALLING

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Introduction: Cancer stem cells (CSCs) contribute to treatment resistance and tumor relapse in hepatocellular carcinoma (HCC). Cancer-associated fibroblasts (CAFs) have been reported to support tumor progress. However, the mechanisms by which CAFs contribute to stemness maintenance remain largely unknown. Here, we hypothesized that HGF and IL6 secreted by CAFs promote the stemness properties of $CD24^+$ HCC cells through the activation of STAT3 signaling.
Aims and Methods: CD24+ cells were isolated from HCC cell lines, and their stemness characteristics were demonstrated in vitro and in vivo (Xenograft tumors in NOD/SCID mice). CAFs isolated from fresh HCC samples were co-cultured with CD24+ HCC cells, and CSC functions were measured. HGF/c-Met, IL6/IL6R and STAT3 pathways were detected and then manipulated with pharmacologic and genetic approaches in CD24+ HCC cells with ot without CAF-CM. Finally, the expression of CD24, alpha-smooth muscle actin (α-SMA) and phospho-STAT3 in tissues from HCC patients were examined by immunohistochemistry.
Results: We found that the expression of CD24 was high in HCC tissues, and positively correlated with the poor prognosis and α-SMA expression in CAFs. Meanwhile, CD24+ cells isolated from HCC cell lines exhibited higher self-renewal, chemotherapy resistance, invasion and migration abilities in culture, and formed more xenograft tumors in mice than CD24- cells. Moreover, CAF-derived HGF and IL6 enhanced the stemness properties of CD24+ HCC cells via promoting STAT3 Tyr705 phosphorylation. Both the neutralizing antibodies of cytokines and blockade of HGF/c-Met or IL6/IL6R signaling significantly abolished the effect of CAFs on stemness properties, which compromised the activation of STAT3 pathway in CD24+ HCC cells. While knockdown of STAT3 in CD24+ HCC cells notably attenuated CAF-induced stemness characteristics of CD24+ HCC cells. Furthermore, in HCC patients, higher expression of phospho-STAT3 were also demonstrated to be positively correlated with poor clinical outcomes.
Conclusion: These findings suggested that HGF and IL6 secreted by CAFs promoted the stemness properties of $CD24^+$ HCC cells through the activation of STAT3 signaling.
References: This work was supported by grants from the National Natural Science Foundation of China (81172063 and 81372352).
Disclosure: Nothing to disclose

P0696 LIVER STIFFNESS AS A PREDICTOR OF HEPATOCELLULAR CARCINOMA BEHAVIOR IN PATIENTS WITH HEPATITIS C-RELATED LIVER CIRRHOSIS

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Introduction: Hepatocellular carcinoma (HCC) is a leading cause of death in cirrhotic patients. For improvement of patient outcome, early detection and treatment of HCC are mandatory, so strategies for screening, risk stratification and prognostication of HCC are important.
Aims and Methods: To explore the role liver stiffness measurment (LSM) inside HCC lesion, in peritumoral tissue and in cirrhotic non-malignant liver tissues in the prediction of HCC clinical behavior. We included 121 naïve patients with hepatitis C related HCC. Liver profile as well as serum alfa-fetoprotein (AFP) were done. The aspartate aminotransferase (AST) /platelet ratio (APRI) score was calculated. HCC evaluation (number of lesions, maximum diameter, tumor capsule, vascular invasion, and extrahepatic spread) was done based on the triphasic CT. HCC staging was done (TNM, OKUDA, CLIP and BCLC staging). LSM was measured (by acoustic radiation force impulse (ARFI) apparatus) inside the tumor mass, within 1 cm around the tumor and at the non-malignant cirrhotic liver tissue [expressed as meter/second (m/s)]. Patients were assigned to appropriate treatment according to the BCLC stage. Tumor recurrence-free interval was calculated from last CT evidence of HCC ablation to 1st CT evidence of recurrence.
Results: Patients were divided into 2 groups (early HCC including BCLC stage A and B [n = 54]; and late HCC including BCLC stage C and D [n = 67]). The mean value of LSM inside the tumor was 1.49 ± 0.79 (IQR = 0.91–2.02) m/sec, in the peritumoral area was 2.49 ± 1.07 (IQR = 1.38–3.39) m/sec, and in non-malignant cirrhotic tissue was 2.65 ± 0.63 (IQR = 2.35–2.95) m/sec. The mean value of LSM inside the tumor and in the peri-tumoral tissue were significantly lower in the late HCC group compared to the early HCC group (1.16 ± 0.53 m/s vs. 1.91 ± 0.87 m/s, $p < 0.001$ and 1.99 ± 0.87 m/s vs. 3.12 ± 0.98 m/s, $p < 0.001$ respectively) while there was no statistical difference between the two groups as regards LSM in the cirrhotic non-malignant tissue. The mean values of LSM inside the tumour as well as in the peri-tumoral tissue showed strong negative correlation with serum AFP, tumor number and diameter, portal vein invasion, CLIP, TNM, and BCLC stages ($p < 0.001$) and OKUDA stage ($p < 0.05$), and direct significant correlation with presence of tumour capsule and recurrence-free interval ($p < 0.001$). The mean value of LSM in the cirrhotic non-malignant tissue showed strong negative correlation only with the presence of vascular invasion ($p = 0.004$), and recurrence-free interval ($p = 0.001$). At a cut-off values of 1.25 m/s, LSM inside the tumour has sensitivity and specificity of 77.8% and 71.6% (AUC = 0.759; 95% CI = 0.67–0.85) in differentiating early from late HCC. On univariate analysis, platelet count, AST, Child-Pugh class, AFP, LSM inside the tumor, and LSM in the peri-tumoral tissue ($p < 0.05$) could predict early HCC. However, in multivariate analysis, AFP was the only predictor (OR = 1.07, $R^2 = 0.968$, $p = 0.044$). In addition, multivariate analysis showed that APRI score, AFP, LSM inside the tumor and peritumoral tissue, tumor number and diameter, and BCLC stage were independent predictors for the recurrence-free interval ($p < 0.001$).
Conclusion: Liver stiffness measurement inside the tumor and peritumoral tissue in patients with HCV related HCC is suggested as a potential non-invasive marker for prediction of HCC clinical behavior as well as recurrence-free interval following locoregional treatments. A cut-off value of 1.25 m/s of LSM inside the tumor could differentiate early from late HCC with 77.8% sensitivity and 71.6% specificity.
Disclosure: Nothing to disclose

P0697 CAPECITABINE IN ADVANCED HEPATOCELLULAR CARCINOMA: A MULTICENTER EXPERIENCE

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Introduction: Sorafenib is so far the only approved systemic therapy for advanced Hepatocellular Carcinoma (HCC) in patients with preserved liver function. More recently, Regorafenib (RESORCE trial) succeeded in improving survival in second-line treatment in patients progressing under Sorafenib. Despite this, the new systemic drug does not satisfy the needs of patients intolerant to Sorafenib. Recent data suggested the efficacy and tolerability of Capecitabine in the treatment of advanced HCC.
Aims and Methods: The aim of our study was to retrospectively evaluate efficacy and safety of Capecitabine in a cohort of patients with advanced HCC, also in relation to the different therapeutic schemes previously administered.
In this multi-centre retrospective study we analysed 143 Capecitabine-treated patients, 111 treated with Metronomic Scheme (MS, 1000 mg/day administered continuously) and 32 treated with Non-Metronomic Scheme (NMS, 2000 mg/day administered for 14 days followed by 7 days of interval). The tolerability and the efficacy of the treatment, evaluated in terms of Overall Survival (OS) and Progression Free Survival (PFS), were determined.
Results: Considering the entire cohort, hepatic cirrhosis was present in 112 patients (78%); 89 patients (62%) were Child-Pugh A, 130 (91%) were BCLC C, 56 (39%) patients had PVT e 74 (52%) patients had metastasis. NMS patients had significantly better Child-Pugh score, a better ECOG-PS, smaller nodules and less frequently PVT (all $p < 0.05$). Capecitabine was administered in I/II/III line in 43 (30%), 75 (52%) and 25 (18%) patients, respectively. Median duration of treatment was 5.6 months. Median OS and PFS for MS+NMS patients were 6.9 months [95% CI 5.73–8.13] and 2.6 months [95% CI 2.17–3.09], respectively. Median OS was 10.5 months [95% CI 7.2–13.7] for NMS patients versus 5.7 months [95% CI 4.0–7.3] for MS patients ($p = 0.0005$). Median PFS was 2.5 months [95% CI 2.11–2.89] in MS patients versus 3.9 months [95% CI 2.22–5.51] in NMS patients ($p = 0.005$). The disease control rate was 28.3% (complete response in 1.5% and partial response in 5.1%); 71.7% of patients had disease progression. A correlation between OS and radiological response to treatment was demonstrated ($p = 0.0002$). Median OS was 4.7 months [CI 95% 3.60–5.74] in patients treated with BSC after Capecitabine discontinuation compared to a median OS of 13.8 months [CI 95% 6.95–20.65] in patients subsequently treated with additional chemotherapy. In patients forced to Sorafenib discontinuation for toxicity, OS was 8.4 months [CI 95% 5.95–10.79] versus 5 months [CI 95% 3.60–6.34] in patients in cancer progression ($p = 0.024$). The most common drug-related adverse events were thrombocytopenia (38%), anemia (34%), fatigue (22%), leukopenia (18%), with no substantial differences between MS and NMS; only in 13 patients (9%) side effects lead to treatment discontinuation. At the Cox multivariate analysis number of nodules, response to Capecitabine and therapy after Capecitabine discontinuation were identified as independent predictors of survival.
Conclusion: Capecitabine is an effective treatment for patients with advanced HCC, useful also in those intolerant to Sorafenib. Non-Metronomic Scheme seems to be more efficient in terms of OS than Metronomic Scheme, but conclusions cannot be drawn in consideration of the marked differences between the two groups. Capecitabine confirms in our study its safety profile in patients with advanced HCC.
Disclosure: Nothing to disclose

P0698 "TORONTO HCC RISK INDEX": USEFUL TO PREDICT HEPATOCELLULAR CARCINOMA IN ALL PATIENTS WITH CIRRHOSIS, REGARDLESS OF ETIOLOGY?

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Introduction: The actual guidelines for liver cirrhosis recommend hepatocellular carcinoma (HCC) screening with ultrasound every 6 months, regarding of the etiology of liver disease. Toronto HCC risk index" (THRI) is a recent score used to predict the risk ok HCC that was validated in the Canadian and Dutch population.
Aims and Methods: The aim of this study was to evaluate the THRI for prediction of HCC development in Portuguese population.
Methods: Retrospective study of patients with liver cirrhosis under HCC screening with ultrasound and alpha-phetoprotein every 6 months in a tertiary center.
Results: We included 269 patients with liver cirrhosis, 70.3% male, with mean age of 66.3 ± 13.3 years. The median time of follow up was 54.5 [32.3–85.0] months. The main causes of liver cirrhosis were alcohol (53.5%), HCV infection (13.4%) and NASH (10.8%). Sixty percent of the patients revealed alcohol consumption more than 30g/day, 58.7% were classified as Child A and the median MELD was 7[6–9]. During the period of follow-up were diagnosed 44 HCC (incidence of 16.4%).
According to THRI, 59.9% of the patients were classified as high risk group patients for development of HCC, 36.4% as intermediate group and 3.7% as low risk group of HCC.
In the high risk group, 21.1% developed HCC, in the intermediate group 9.2% developed HCC and in the low risk group 10% of the patients developed HCC. The groups created according to THRI presented a low correlation with the development of HCC ($r_s = 0.155$, $p = 0.155$).
The THRI score presented a low correlation with the development of HCC ($r_s = 0.231$, $p < 0.001$).
Conclusion: Although validated in the Canadian and Dutch population, Toronto HCC risk index
was not a good tool to predict the development of HCC in the Portuguese population. One reason for this could be the main etiologies of chronic liver disease in our population, namely alcoholic and non-alcoholic fatty liver disease, much different from the population where THRI was validated (the major causes were HCV infection and autoimmune liver diseases).
Disclosure: Nothing to disclose

P0699 COMBINED BLOOD INDICES AND MELD SCORE AS PROGNOSTIC PREDICTORS FOR EARLY RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER TRANS-ARTERIAL CHEMOEMBOLIZATION

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Introduction: The first-line treatment option for intermediate -stage Hepatocellular Carcinoma (HCC) was Transarterial chemoembolization (TACE). Inflammation has been proved to play an important role in tumor progression and invasion. Inflammation profile, such as lymphocyte-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), Monocyte Granulocyte Lymphocytic Ratio (MGLR) and Red blood cell distribution width (RDW) have been identified as prognostic biomarkers in multiple cancers.
Aims and Methods: We aimed to investigate these different blood indices and MELD score as prognostic predictors for early recurrence of hepatocellular carcinoma after TACE.
Methods: NLR, LMR, MGLR, RDW and PLR were calculated and values determined in 147 patients (111 male and 36 female). Sensitivity and specificity of different indices for HCC recurrence were estimated by receiver operator characteristic curve. Relation between best predictors and recurrence free time in TACE treatment of HCC cases were studied by Kaplan-Meier curve
Results: MGLR had the best diagnostic performance for detection of early recurrence of HCC after TACE at cut off value 2.75 with sensitivity 70.7%, specificity 59.2%. MELD score at cut off value 9.5 had the best diagnostic performance for detection of early recurrence of HCC after TACE with 80% sensitivity and 55.8% specificity; also risk estimates for HCC recurrence was 2.489 with 95% confidence interval (1.280–4.838).
Conclusion: This study concluded that higher both MGLR and MELD score were associated with increasing occurrence of HCC recurrence after TACE and could be used as novel, simple, low-cost, non-invasive prognostic tests for HCC patients.
Disclosure: Nothing to disclose

P0700 QUALITY OF SLEEP IN PATIENTS WITH LIVER TRANSPLANT: A MULTICENTER, PROSPECTIVE STUDY IN A COHORT FROM SOUTH ITALY

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Introduction: Patients with liver cirrhosis and liver transplant (LT) candidates show sleep disturbances that negatively impact their quality of life. Data about the quality of sleep after LT are scanty.
Aims and Methods: We aimed to evaluate the quality of sleep in a cohort of adult LT patients from Southern Italy.
Adult LT patients were recruited from two Liver Following Transplant Centers of Southern Italy (Salerno and Gragnano). We collected the following data: age, gender, marital status, cause of transplantation, presence of hepatocarcinoma at the time of transplantation, early liver rejection, time from transplantation, type of immunosuppression, and presence of comorbidities. Age- and gender-matched healthy controls (HC) were also enrolled. All participants completed the Pittsburgh Sleep Quality Index (PSQI), the Zung Self-rating Depression Scale and the State-Trait Anxiety Inventory (STAI).
Results: 129 LT patients (91 males, mean age 60.2 ± 9.8 years) and 51 HC (29 males, mean age 60.3 ± 8.6 years) were enrolled. The most common indications for LT were HCV-related cirrhosis (44.3%), HBV-related cirrhosis (35%),

alcoholic cirrhosis (3.9%). The mean time from LT was 11.5 ± 6.7 years. Forty/129 patients (31%) were on Tacrolimus, 21 (16.3%) on Everolimus, 13 (10.6%) on Cyclosporine, 12 (9.3%) on Mycophenolate-Mofetil. Other patients (43/129, 33.3%) were on a combined treatment.

Table 1 showed no significant differences between LT patients and HC in PSQI mean score and the prevalence of pathological sleep; however, LT patients had a significantly higher score in Zung than HC and a borderline significance for STAY 1.

The univariate analysis did not show any significant association between PSQI scores as dependent variable and gender, age, marital status, type of immunosuppressive therapy, indication for LT.

Tables 1 Mood disorders in LT patients compared to HC. Data were expressed as percentage (%) or mean (Standard Deviation).

Conclusion: More than half of LT patients had sleep disorders. Age, gender, type of immunosuppressive therapy, indication for LT did not relate to the presence of sleep disorders. The improved LT patients survival stresses the importance of characterizing psychosocial aspects, including anxiety, depression, and sleep quality after LT. New strategies focused on recognizing and treating alteration of the sleep pattern of LT patients are needed because a better sleep may promote a better quality of life.

	LT patients N = 129	Healthy Controls (HC) N = 51	p
PSQI mean (SD)	6.7 (3.9)	6.4 (3.6)	0.7
% pathological sleep (PSQI > 5)	69 (53.9)	27 (52.9)	0.9
STAI Y1	40.2 (13.0)	36.9 (8.9)	0.08
STAI Y2	38.6 (10.2)	36.4 (8.8)	0.2
ZUNG	38.7 (10.0)	33.7 (6.0)	0.002

[Table 1]

Disclosure: Nothing to disclose

P0701 TRANSLATING POLICY TO REAL WORLD IN RARE LIVER DISEASES REGISTRIES; A EUROPEAN PERSPECTIVE

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Introduction: A rare disease is defined by the European Health Commission (EHC) as a disorder found in less than 5/10,000 population. The importance of collaborations in the field of rare diseases where data is scarce and fragmented is well-known.

The OrphanXchange project was set up by Orphanet to promote collaborations between academia and industry. Moreover, the European Union Committee of Experts on Rare Diseases (EUCERD) encouraged the exchange of relevant experience, policies and practices in rare diseases among member states and promoted cooperation across Europe and beyond, including Japan. The committee identified multiple important challenges for successful registry utilisation; discrepancy in coverage with multiple fragmented registries for some conditions, complete lack of registries for other conditions and registries that were mainly academic rather than clinical.

A critical output of EUCERD was the provision of a basic framework for European data collection and registration in rare diseases across 6 domains:

- International Operability
- Sources Of Data,
- Collection Of Data,
- Good Practices,
- Use Of Data For Regulatory Purposes
- Sustainability.

There are approximately 20 rare liver diseases (RLD), meaning the hepatology community can be influential in informing and developing such registries.

Aims and Methods: Our aim was to identify how many of the defined non-cancer orphan conditions have an established registry in keeping with EHC's recommendations. A Pubmed and google scholar search using the MESH terms ''registries'', ''database management systems'', ''database'' and the non-MESH terms ''database$'', ''registry'', ''repository'' and ''repositories'' for English literature in humans was performed. The results were screened manually.

Results: Registries were identified for most RLD in many countries. The results are summarised in the table below. Slovenia, Slovakia, FYROM, Malta, Luxemburg, Lithuania, Estonia and Cyprus do not appear to have RLD registers.

Abbreviations: Alpha 1 antitrypsin deficiency (A1AD), autoimmune hepatitis (AIH), acute liver failure (ALF), biliary atresia (BA), Caroli's disease, hereditary haemorrhagic telangiectasia (HHT), IgG4 disease, primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), polycystic liver disease (PLD), porphyria, vascular liver disorders (VLD), Wilson disease (WD) and hepatitis D (HDV).

Conclusion: Despite concerted efforts of the European Union, there is variability in the number of registries for RLD. The EUROPLAN was set up to provide a framework and support EU countries in developing their national strategies. Currently, 24/28 member countries have rare disease strategies. Thus far, action plans could not be found on the EU portal for Estonia, Finland, Malta, Poland. Interestingly, despite whilst not demonstrating a national strategy for rare diseases, Poland and Finland currently have registries for RLD and surprisingly, countries with established national policies such as Lithuania, Luxemburg, Cyprus, Slovenia, Slovakia and FYROM do not.

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Abstract No: P0701

Name of Country	Number of registries identified	Diseases with registries
United Kingdon	13	A1AD, AIH, ALF, BA, Caroli's, HHT, IgG4, PBC, PLD, Porphyria, PSC, VLD, WD
Germany	13	A1AD, AIH, ALF, BA, Caroli's, HDV, HHT, PBC, PLD, Porphyria, PSC, VLD, WD
France	12	AIH, ALF, BA, Caroli's, HH, HHT, PBC, PLD, Porphyria, PSC, VLD, WD
Spain	8	A1AD, HDV, PBC, PLD, Porphyria, PSC, VLD, WD
Netherlands	8	A1AD, BA, PBC, PLD, Porphyria, PSC, VLD, WD
Italy	8	A1AD, BA, HDV, PBC, Porphyria, PSC, VLD, WD
Belgium	7	A1AD, BA, PBC, Porphyria, PSC, VLD, WD
Austria	6	A1AD, BA, HDV, PSC, VLD, WD
Switzerland	6	A1AD, BA, Porphyria, PSC, VLD, WD
Poland	5	BA, PBC, Porphyria, PSC, WD
Sweden	4	A1AD, Porphyria, PSC, VLD
Porugal	4	A1AD, BA, VLD, WD
Norway	4	Porphyria, PLD, PSC, WD
Greece	4	HDV, PBC, PSC, WD
Denmark	4	WD, BA, PSC, VLD
Romania, Ireland, Czech Republic, Finland	3	
Hungary	2	
Serbia, Iceland, Croatia, Bulgaria, Latvia	1	

[European registries for rare liver diseases (non-cancer) by country]

P0702 TRACK & TRACE: RESULTS FROM A RETRIEVAL STRATEGY TO IDENTIFY LOST TO FOLLOW-UP CHRONIC HEPATITIS C PATIENTS

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Introduction: There are an estimated 23,000 chronic Hepatitis C-infected patients in the Netherlands. An unknown proportion has been lost to follow-up and received no adequate treatment. The advent of direct antivirals offers the prospect of safe and efficacious therapy.

Aims and Methods: We designed this study to examine a retrieval strategy that identifies chronic HCV (cHCV) patients lost to follow-up (LTFU) and brings them back into care. We also mapped disease and patient characteristics of this cohort. Our diagnostic pipeline started with data analysis of patient records of a virology laboratory that serves 2 hospitals : a tertiary referral and liver-expert centre and a rehabilitation clinic. Records from patients with positive HCV antibodies, immunoblot and/or HCV quantitative RNA PCR measurements between 2003–2017 were identified and linked to personal data. Chart review was performed to assess possibility of loss to follow-up and to map phenotypical characteristics of the LTFU cohort. Identification data was checked with the governmental citizen administration to adjust for death or change of municipality.

Results: Of all tested patients (n = 45276), 372 had at least one positive HCV RNA. Prevalence in this cohort would be estimated at 0.22%, which is similar to the prevalence in the Netherlands. In 175/372 patients (47%) the last measured RNA was still positive. Of these cHCV patients, 4 were still in care and 72 deceased. A total of 81 cHCV patients (22%) is LTFU and could benefit from linkage to care. Demographics, probable mode of infection, treatment attempts and disease severity are depicted in table 1. In approximately 50% disease severity is unknown, with data on imaging or fibrosis severity missing.

Age at last contact (mean, SD)	45 (13)
Male gender (n, %)	66 (82%)
Non-Dutch resident (n, %)	44 (55%)
Deceased since last contact (n, %)	8 (10%)
Probable mode of infection:	
Blood transfusion / IV drug use / Other (MSM/tattoo/needle stik injury) / Unknown	25% / 48% / 7% / 21%
Known HIV/HBV co-infection	12 (15%) / 2 (3%)
Previously in care of hepatitis specialist (n, %)	53 (63%)
Previous treatment attempt (n, %)	19 (24%)
PEG-interferon + ribavirin (n, %)	11 (58%)
Genotype (% 1/2/3/4/unknown)	42% / 4% / 16% / 5% /33%
Viral load (IU/L, median, IQR)	8 × 106 (3 × 106-40 × 106)
Unknown viral load (n, %)	10 (12%)
ALT (U/L, median, IQR)	58 (37–88)
ALT elevated (>2× ULN, n, %)	30 (37%)
ALT Unknown (n, %)	5 (6%)
Signs of fibrosis/cirrhosis on imaging (n, %)	15 (19%)
No imaging present (n, %)	39 (48%)
Fibrosis stage (% with F0/F1/F2/F3/F4)	9% / 10% / 9% / 0 / 5%
No liver biopsy (n, %)	54 (67%)

[Table 1 Characteristics of LTFU cohort]

Conclusion: Identification of patients through analysis of archival laboratory results and chart review is feasible. Disease severity is unknown in a significant part of the LTFU population. These patients could be at risk for serious complications. Together with the high percentage of LTFU patients observed in this centre, this emphasizes the need for a nationwide retrieval project to bring this group back in care.

Disclosure: This investigator-initiated study was funded by an unrestricted grant from MSD.

P0703 TREND IN HOSPITALIZATION RATE FOR ALCOHOL HEPATITIS IN VENETO REGION (NORTHEAST ITALY)

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Introduction: WHO Europe 2014 database reports a declinein per capita pure alcohol consumption in Italy, with a reduction from 18.1 to 7.1 litres from 1970 up to date. Despite this, Italian Report on Alcohol 2016 showed an increase in drinking outside meals and a rise in alcohol consumption and binge drinking among young people (age ranges 18–24, 14–17), particularly in males.

Aims and Methods: To evaluate the trends of hospitality discharge for alcoholrelated diseases in the period 2000–2017 in Veneto Region in North Eastern Italy (4.8 million inhabitants). This is a retrospective cohort study based on Veneto Region anonymous computerised database of hospital discharges between 2000 and 2017. All Veneto residents discharge records with principal diagnosis of alcohol-related disease (cod. ICD9-CM: 571.0, 571.1, 571.2, 571.3) were included in the study. The principal diagnosis was chosen as it is considered the primary reason for hospital admission. Standardised Hospitalisation Ratio (SHR) per five-year age group (ref. pop. Veneto 2008) was calculated and expressed per 100 000 population.

Results: Over the period 2000–2017, 30.089 hospital admissions for alcohol-related diseases were recorded. Most part of subjects were males (74%), who held the higher hospitalisation rate (52 vs. 17.5; OR: 2.95; 95% CI: 2.88–3.09; $p < 0.05$). The longitudinal analysis of the hospitalisation trend shows a 7% increase on average age in both sexes (from 58.8 ± 9.2 to 62.4 ± 9.7) and a substantial decrease of 63.5% in SHR ($\chi 2$ trend: 4099,827). Noticeably, in the last year of observation the hospitalisation rate tends to 20.9, confirming the greater risk for the male population (32.7 vs. 9.1; OR: 3.79; 95% CI: 3.28–4.38; $p < 0.001$). Considering the age groups, emerges as the highest SHR can be found in the ranges 45–64 (67) and >65 (67.8), which in 2017 was respectively at 35.6 and 46. Finally, hospitalization for alcoholic liver disease in population 25–44 appears clearly more limited. However, in this age range a slightly rising trend has been recorded betweeen 2013 and 2017.

Conclusion: Italian epidemiology of alcohol consumption is changing. In Veneto Region, the reduction in alcohol intake over the last 30 years has lead to a marked reduction in hospital admissions for alcohol-related diseases. These data suggest that the changing style of alcohol consumption, especially in young people, may explain both the decrease in hospitalisation for alcoholic liver disease, and the upward SHR trend in 2013–2017. Thus, it will be likely to observe in the next years an increase in hospital admissions for alcohol-related diseases. New strategies in Public Health approach are needed to address the new styles of consumption, especially in young populations.

Disclosure: Nothing to disclose

P0704 DEFINING AND CHARACTERISING THE BLUEPRINT FOR THE DEVELOPMENT OF A SUCCESSFUL REGISTRY FOR RARE LIVER DISEASES

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Introduction: A rare disease (RD) is defined by the European Health Commission as a disorder occurring in < 5/10,000 population whereas the United States definition sets a numerical maximum of < 200,000 affected individuals in the country. RDs are now a clinical priority of the European Union (the Europlan project and Eurordis), Asia-Pacific, USA and the World Health Organisation (WHO). The European Union Committee of Experts on Rare Diseases (EUCERD) was set up with the purpose of encouraging the exchange of relevant experience, policies and practices in rare diseases among member states. One of the most important output activity of EUCERD is the provision of the basic governance and foundation in data collection and registration in RDs across 6 domains:

1. International operability
2. Sources of data
3. Collection of data
4. Good practices
5. Use of data for regulatory purposes
6. Sustainability

Despite this core framework, a comprehensive guideline of how to create an effective and contemporary registry for rare liver diseases does not exist, despite there being approximately 20 non-cancer rare hepatic conditions.

Aims and Methods: Initial pilot work to identify governance, technical and data issues led to successful development of local registries for rare liver diseases including IgG4-Related disease, Wilson disease and hepatocellular carcinoma. This was then used as a platform to successfully develop a novel regional primary biliary cholangitis (PBC) registry in the UK which provides data-linkage from primary to secondary care in conjunction with various stakeholders including

hepatologists, the RCGP (Royal college of General Practitioners, the NIHR (National Institute of Health and Research), patient groups, charities and industry partners.

Results: The design process of creating a registry can be primarily divided into three main phases (theoretical, technical and data collection) and spans across 9 domains. The blueprint for these is shown in the table below:

1 Aims, objectives and endpoints	What is the purpose of the registry?
2 Define study population	Define the disease ontology and case eligibility
3 Information, research and clinical governance	1. Safety & Wellbeing of patients and investigators 2. Competence and adequate qualifications 3. Scientific and Ethical Conduct. Peer-reviewed research proposal 4. Patient, service user and public Involvement 5. Integrity, quality and transparency 6. Protocol to clearly explain the design of the study 7. Legality 8. Benefits and Risks to patients should be identified and stated 9. Approval by regional ethics committee, confidentiality advisory group (if necessary) and ultimately by the health research authority 10. Information about the research to be made publically available 11. Accessible findings (positive or negative) 12. Respect autonomy of participants and afford respect and choice in relation to consent or refusal of consent. Develop robust opt-out mechanisms. 13. Insurance and Indemnity to cover liabilities 14. Respect for Privacy by practising strict information governance rules and ensuring safe keeping of data 15. Compliance
4 Sponsorship & Funding	
5 Identify stakeholders & set up collaborations	Seek locoregional, national and international collaborations
6 Registry design and data quality	1. Define data fields and set core/mandatory and desired components 2. Is there a need for patient-identifiable information? 3. Create pseudonymised record identifier for each patient recruited 4. Create various levels of access for users 5. Build in data validation checkpoints 6. Engage with patients, the public and relevant charities
7 Data entry	1. Enable remote access and data entry 2. User-friendly interface for quick data entry
8 Data processing	1. Data linkage to other repositories available 2. Develop a strategy for handling missing data 3. Presentation of outcomes in local, regional and international meetings
9 Ensure sustainability	1. Form a steering committee 2. Regular consultations with stakeholders including patients and the public 3. Long-term funding 4. Continental/international data feeding into bigger datasets

[Blueprint for the design of a comprehensive registry for rare liver diseases]

Conclusion: Overall, the development of a bespoke registry for rare liver diseases is complex and requires a wide array of skills and expertise including clinical, IT, cyber security and information governance. Our experience was that the key element is clearly defining both the study population and the purpose of the registry. This will provide a solid foundation for the design and utility of the database which can be then be expanded appropriately and sustainably. The efforts should be guided by a carefully-selected steering committee which should also promote the establishment of loco-regional, national and international collaborations.

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P0705 OBESITY STARTS WITH THE ACCUMULATION OF FAT IN THE SUBCUTANEOUS ADIPOSE TISSUE IN ASSOCIATION WITH NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Adiposity due to a positive energy balance starts with the accumulation of fat in the subcutaneous adipose tissue, with relatively less influence on insulin sensitivity, until the limit is expanded through adipose tissue dysfunction. The lipids then overflow and the accumulation of visceral and ectopic fat sets in, resulting in insulin resistance and related cardiometabolic problems. Several factors differentiate the subcutaneous and visceral adipose tissues, including adipokine and cytokine production, adipogenic potential, and the ability to store and mobilize lipids. It has been widely accepted that liver fat is a type of ectopic fat and that it is strongly associated with visceral obesity. However, there is not yet a unified view about the association between nonalcoholic fatty liver disease (NAFLD) and subcutaneous obesity.

Aims and Methods: NAFLD is recognized as a hepatic manifestation of metabolic syndrome because of the association with visceral obesity. However, the association between NAFLD and subcutaneous fat accumulation remains unclear. The study population included 3197 subjects who consumed < 20 g of alcohol per day. They were divided according to the quantiles of subcutaneous (SFA) or visceral (VFA) fat areas on CT. Fatty liver was diagnosed using ultrasonography (FL-US).

Results: The prevalence of FL-US increased across the SFA categories, even after adjusting for the VFA, in both men (S-Q1, 13.7; S-Q2, 37.8; S-Q3, 52.3; S-Q4, 75.4%, $p < 0.001$, Mantel-Haenzel test) and women (S-Q1, 8.4; S-Q2, 19.0; S-Q3, 33.6; S-Q4, 50.4%, $p < 0.001$). The risk of FL-US increased with SFA—independently of VFA—in men (Odds ratio [95% confidence interval]: S-Q1, 1; S-Q2, 2.21 [1.54–3.18]; S-Q3, 3.57 [2.48–5.13]; S-Q4, 6.67 [4.52–9.86]) and women (S-Q1, 1; S-Q2, 1.74 [1.07–2.84]; S-Q3, 3.03 [1.90–4.82]; S-Q4, 4.12 [2.60–6.54]). In addition, the prevalence of FL-US increased across the VFA categories, even after adjusting for the SFA in men (V-Q1, 13.2, V-Q2, 41.9; V-Q3, 54.9; V-Q4, 69.4%, $p < 0.001$) and women (V-Q1, 8.4; V-Q2, 19.0; V-Q3, 33.6; V-Q4, 50.4, $p < 0.001$). The risk of FL-US increased with the VFA, independently of the SFA, in men (V-Q1, 1; V-Q2, 2.21 [1.54–3.18]; V-Q3, 3.57 [2.48–5.13]; V-Q4, 6.67 [4.52–9.86]) and women (V-Q1, 1; V-Q2, 1.74 [1.07–2.84]; V-Q3, 3.03 [1.90–4.82]; V-Q4, 4.12 [2.60–6.54]). In addition, this significant association between FL-US and the SFA was already detected from the second SFA quantile. It is noteworthy that the mean BMI values of the subjects in the second quantile were 23.7 kg/m^2 in men and 22.6 kg/m^2 in women, as these values were close to the in normal body weight range according to the Japanese criteria (obesity $\geq$ 25 kg/m^2 in both men and women). On the other hand, the components of metabolic syndrome were independently associated with the VFA, but were less associated (or not associated) with the SFA.

Conclusion: NAFLD may be independently associated with both visceral and subcutaneous adiposity, which is a characteristic that distinguishes NAFLD from other components of metabolic syndrome.

Disclosure: Nothing to disclose

P0706 EUS-FNA FOR EXTRAHEPATIC CHOLANGIOCARCINOMA IS A SAFER TISSUE SAMPLING METHOD THAN ERCP

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is a common method for tissue sampling in patients with biliary strictures by bile aspiration cytology, biliary brush cytology and forceps biopsy. However, the sensitivities of bile aspiration cytology, brush cytology, and forceps biopsy for biliary strictures varies from 6 to 72%, and hence remains unsatisfactory. Furthermore, the incidence rates of post-ERCP adverse events, which were reported as 4.0–6.9%, including pancreatitis (2.6–3.5%), bleeding (0.3–1.3%), and perforation (0.1–0.6%), can't be ignored. Recent studies reported that endoscopic ultrasonography guided fine needle aspiration (EUS-FNA) is superior to ERCP related tissue sampling in evaluating suspected malignant biliary strictures. However, there have been few studies comparing the diagnostic utility of EUS-FNA and that of ERCP related tissue sampling only for extrahepatic cholangiocarcinoma (ECC).

Aims and Methods: The aim of this study was to evaluate the efficacy and safety of the EUS-FNA for the diagnosis of ECC compared with ERCP related tissue sampling.

The patients who were received EUS-FNA or ERCP related tissue sampling, to differentiate ECC from benign biliary disease, were enrolled retrospectively

between October 2011 and March 2017 at our hospital. We evaluated the diagnostic performance of EUS-FNA and that of ERCP related tissue sampling on the basis of the pathological evaluation. We also compared the adverse event of EUS-FNA and that of ERCP related tissue sampling. The diagnosis of ECC was based on the pathological diagnosis of bile aspiration cytology, transpapillary forceps biopsy, EUS-FNA or surgical specimen. In histological findings, malignancy or suspicion of malignancy was considered as positive in this study. Patients without a malignant disease had a final benign diagnosis based on clinical and radiological follow-up data after 12 months or more.
Results: Seventy three patients with biliary disease were enrolled. Patients included 49 men and 24 women: age range 42–88 years; mean age, 71.3 years. An ECC was present in 37 patients and a benign lesion was present in 36 patients. We performed EUS-FNA for 19 patients and ERCP for 54 patients. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for ERCP related tissue sampling were 76.0%, 100%, 100%, 82.9%, and 88.9%, and for EUS-FNA were 81.8%, 87.5%, 90.0%, 77.8%, and 84.2%, respectively. There were no significant differences in the statistic value of ERCP related tissue sampling and EUS-FNA. The adverse event frequency of ERCP related tissue sampling was 25.9% (pancreatitis: 14.8%, infection: 11.1%). No adverse events were associated with EUS-FNA in any of 19 patients. The adverse event frequency of EUS-FNA was significantly less than that of ERCP related tissue sampling ($p = 0.033$). No serious adverse events such as perforation or hemorrhages were observed. Tumor seeding was not seen in any patients during follow up.
Conclusion: The diagnostic ability of EUS-FNA for ECC is similar that of ERCP-related tissue sampling. EUS-FNA is a safer tissue sampling modality for the evaluation of biliary disease than ERCP.
Disclosure: Nothing to disclose

P0707 CLINICAL UTILITY OF NEWLY DEVELOPED MICROFLUIDIC DEVICE FOR DETECTING CIRCULATING TUMOR CELLS IN THE BLOOD OF PANCEATICO-BILIARY MALIGNANCIES

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Introduction: Development of optimal screening method is required to improve prognosis of pancreatico-biliary malignancies. Recently developed microfluidic device showed high diagnostic yield to detect circulating tumor cells (CTCs) in the blood of cancer patients.
Aims and Methods: We aimed to investigate the clinical utility of measuring CTCs in diagnosing pancreatic-biliary cancer.
Thirty-two cases were enrolled in this study (12 pancreatic cancer, 10 biliary cancer and 10 healthy volunteer controls).
Peripheral venous blood (2 or 8 ml) was collected and stored in a special blood collection tube which minimized degradation of blood cells until measurement. Using a microfluidic chip device and image analyzer, circulating blood cells were selected based on their size and immunocytochemistry staining pattern. CTC was negative for white blood cell marker CD45 and positive for either pan-cytokeratin or vimentin. Primary endpoint was the positive rate of CTCs in cancer patients and controls. We also investigated diagnostic yield of serum tumor markers (CEA $>$ 5.1 ng/ml and CA 19-9 $>$37.0 U/ml) distinguishing cancer and control in the same cohort.
Results: CTC was negative in all controls (specificity was 100%). In pancreatic cancer patients (6 men and 6 women with a median age of 56 year-old, cStage III/IV: 6/6), CTC was positive in 83% of patients. CA 19-9 had high sensitivity of 100% while sensitivity of CEA was only 33%. Diagnostic accuracy was 91% in CTC, 95% in CA 19-9 and 60% in CEA. In biliary cancer (5 men and 5 women with a median age of 67 year-old, cStage I-II/III-IV: 5/5), CTC was positive in all cancer patients. Sensitivity was 70% in CA19-9 and 20% in CEA. Diagnostic accuracy was 100% in CTC, 80% in CA19-9 and 60% in CEA.
Conclusion: Newly developed microfluidic device could diagnose pancreatico-biliary cancers by detecting circulating tumor cells.
Disclosure: Nothing to disclose

P0708 PERORAL CHOLANGIOSCOPY BY SPYGLASS DS VERSUS CHF-B260 FOR EVALUATION OF THE LATERAL SPREAD OF EXTRAHEPATIC CHOLANGIOCARCINOMA

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Introduction: A newly developed peroral cholangioscopy (POCS) system, SpyGlass DS (Boston Scientific Co., Marlborough, MA, USA) has high maneuverability, whereas its image quality appears relatively low in comparison to that of a traditional cholangioscope, CHF-B260 (Olympus Co., Tokyo, Japan).
Aims and Methods: The aim of this study was to evaluate acceptability of the accuracy of SpyGlass DS accompanied by simultaneous POCS-guided biopsy compared with that of CHF-B260 after fluoroscopy-guided biopsy to diagnose the lateral extent of extrahepatic cholangiocarcinoma.
Patients who underwent surgical resection after preoperative examinations to diagnose lateral extent were evaluated. Between January 2004 and September 2015, patients who underwent mapping biopsy under X-ray fluoroscopy (ERC) without POCS were included (CHF group, $n = 56$). POCS using CHF-B260 was performed only when ERC-guided mapping biopsy findings was questionable because of possible discrepancy between the mapping biopsy findings and other examinations, such as ERC, intraductal ultrasonography, EUS, CT, and MRI. Between October 2015 and March 2017, SpyGlass DS accompanied by POCS-guided mapping biopsy was used in all candidates for surgery (SpyDS group, $n = 14$). The accuracy of overall preoperative diagnosis of lateral cancer extent, which was defined based on all examinations, including POCS, and was compared with the final diagnosis confirmed using the resected specimen, was the main outcome. The accuracies of optical evaluation by POCS, which was retrospectively reviewed by authors, and accuracy of EUS-guided mapping biopsy were evaluated.
Results: Accuracy of the overall preoperative diagnosis of lateral cancer extent for both the liver side and the ampullary side were 93% and 100%, respectively, in the CHF group, and 85% and 100%, respectively, in the SpyDS group ($p = 0.34$ for the liver side; p, not available for the ampullary side). Sensitivity and specificity for liver-side estimation were 92% and 93%, respectively, for the CHF group, and 70% and 100%, respectively, for the SpyDS group ($p = 0.13$ for sensitivity; $p = 1.00$ for specificity). Both the sensitivity and specificity for ampullary-side estimation were all 100% for both groups.
Diagnostic accuracy of simple optical evaluation by using POCS for both the liver side and the ampullary side were 81% and 100%, respectively, for the CHF group, and 69% and 80%, respectively, for the SpyDS group ($p = 0.44$ for the liver side; $p = 0.26$ for the ampullary side). When comparing groups, the accuracy rates seemed lower for the SpyDS group, although statistical significance was not detected.
The accuracy of the ERC-guided mapping biopsy in the CHF group was 80% (44/51) for the liver side and 92% (12/13) for the ampullary side. The reasons why the tumor spread toward the liver side was misdiagnosed in seven patients was due to contamination in five patients (false positive), inappropriate biopsy site (i.e., unintended upstream bifurcation of which the tumor spread did not reach) in one patient (false negative), and impossibility of advancement of the biopsy forceps beyond the obstruction in one patient (specimen was not obtained).
Conclusion: The SpyGlass DS system was found to be acceptable for the diagnosis of lateral cancer extent when cholangioscopy-guided biopsy was applied, although the accuracy rates of simple optical evaluation seemed lower than those using the traditional cholangioscope. It could be a standard approach for determining resection lines in an era in which preoperative histological confirmation is increasingly demanded.
Disclosure: Nothing to disclose

P0709 RISK FACTORS FOR RECURRENT BILIARY OBSTRUCTION AFTER ENDOSCOPIC METALLIC STENT PLACEMENT IN PATIENTS WITH UNRESECTABLE MALIGNANT DISTAL BILIARY OBSTRUCTION

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Introduction: Recurrent biliary obstruction (RBO) is one of the most common complications after endoscopic metallic stent (MS) placement for unresectable malignant biliary obstruction. However, there have only been a few reports regarding its risk factors.
Aims and Methods: The aim of this study was to investigate the risk factors for RBO after endoscopic MS placement in unresectable distal malignant biliary obstruction. Between January 2005 and June 2017, 200 patients (mean age, 76 ± 11 yrs.; 117 males, 83 females) with unresectable malignant distal biliary obstruction who underwent endoscopic MS placement were included in this study. Patients with less than 90 days of follow-up were excluded from the study. Main outcome measurements were time to RBO and risk factors for RBO. RBO was defined as stent occlusion and stent migration. Time to RBO was analyzed by using the Kaplan-Meier method and risk factors for RBO were assessed by using log-rank test and Cox regression analysis.
Results: One hundred and seventeen patients had pancreatic cancer, 57 had bile duct cancer, 11 had gallbladder cancer 11 had lymph node metastases from other cancers, and 6 had ampullary cancer. The stents used were uncovered MS in 31 patients, partially covered MS in 66, and fully covered MS in 103. Cholangitis at the time of stenting was seen in 22% (43/200). The mean time to RBO was 583 days (median, 324 days). Non-RBO rate at 3, 6, and 12 months after MS placement was 90%, 71%, and 44%, respectively. Univariate analysis including 17 factors revealed that sex (male, $p = 0.088$), bile duct cancer ($p = 0.068$), MS except WallFlex (Boston Scientific, Co., Ltd., Natic, MA, USA) ($p = 0.023$), and cholangitis at the time of MS placement ($p = 0.001$) were risk factors for RBO. Multivariate analysis showed that cholangitis at the time of MS placement (HR 2.0, 95%CI 1.3–3.2, $p = 0.003$) and MS except WallFlex (HR 1.9, 95% CI 1.1–3.1, $p = 0.017$) as the significant risk factors for RBO.
Conclusion: Endoscopic MS placement for unresectable malignant distal biliary obstruction should be considered after improvement of cholangitis due to the high risk of RBO. WallFlex is recommended as a MS for unresectable malignant distal biliary obstruction.
Disclosure: Nothing to disclose

P0710 PREOPERATIVE BILIARY DRAINAGE USING PLASTIC STENTS VERSUS SELF-EXPANDABLE METAL STENTS FOR PERIAMPULLARY CANCER

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Introduction: Periampullary cancers frequently present as obstructive jaundice, which might lead to liver dysfunction, coagulation disorders, cholangitis, and immune system dysfunction. Preoperative drainage has become popular for patients with periampullary cancers suffering from acute cholangitis or intense pruritus, or receiving neoadjuvant chemotherapy or delayed surgery. If the stent dysfunction occurs during the preoperative period or neoadjuvant chemotherapy, surgery must be postponed or chemotherapy must be interrupted, so it is increasingly important to place self-expandable metal stents (SEMSs) that have a longer stent patency than plastic stents (PSs).

Aims and Methods: The aim of this study was to investigate the superiority of fully covered SEMSs over PSs as preoperative drainage for patients with resectable periampullary cancers and obstructive jaundice. We retrospectively reviewed 26 consecutive patients from September 2015 to February 2018 with resectable periampullary cancers who received preoperative biliary drainage with PSs or SEMSs (13 patients each). We excluded cases that received SEMS placement for repeated occlusion of PSs. Stent patency rates, time from endoscopic retrograde cholangiopancreatography (ERCP) to surgery, adverse events of stent placement, operating time, amount of bleeding during surgery, rate of negative resection margins (R0), and adverse events of surgery were compared between the PS and SEMS groups.

Results: In the PS group, the preoperative stents patency rates were significantly lower than in the SEMS group (54% vs. 100%, $p<0.05$). There were no significant differences between the PS and SEMS groups for median time from ERCP to surgery (33 vs. 35 days, $p=0.78$), median operating time (528 vs. 542 minutes, $p=0.77$), median amount of bleeding during surgery (644 vs. 660 ml, $p=0.69$), rate of R0 (15% vs. 0%, $p=0.54$), adverse events of stent placement (elevated serum pancreatic enzyme levels alone: 8% vs. 0%, $p=0.50$), or adverse events of surgery (pancreatic fistula: 15% vs. 15%, $p=1$; surgical site infection: 23% vs. 15%, $p=0.66$; or delayed gastric emptying: 0% vs. 8%, $p=0.50$).

Conclusion: Preoperative biliary drainage with SEMSs in patients with resectable periampullary cancers showed higher patency rate than that with PSs and a low complication rate similar to that with PSs.

Disclosure: Nothing to disclose

P0711 ASSOCIATION BETWEEN APPENDECTOMY AND RISK OF PRIMARY SCLEROSING CHOLANGITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Appendectomy is one of the most commonly performed surgeries worldwide. Recent epidemiologic studies have suggested that appendectomy could be a risk factor for primary sclerosing cholangitis (PSC) although the results were inconsistent.

Aims and Methods: This systematic review and meta-analysis was conducted to summarize all available evidence with the aim to better characterize the relationship between the two conditions. A comprehensive literature review was conducted using MEDLINE and EMBASE database through January 2018 to identify all studies that reported the risk of PSC among individuals who had appendectomy versus those with no history of appendectomy. Effect estimates from each study were extracted and combined together using the random-effect, generic inverse variance method of DerSimonian and Laird.

Results: A total of 6 case-control studies with 2,432 participants met the eligibility criteria and were included in the meta-analysis. The risk of PSC in individuals who had appendectomy was significantly higher than those with no history of appendectomy with the pooled odds ratio of 1.37 (95% CI, 1.15–1.63). The statistical heterogeneity was insignificant with an I^2 of 0%. Moreover, the funnel plot is relatively symmetric and does not suggest the presence of publication bias in favor of positive studies.

Conclusion: A significantly increased risk of PSC among individuals who had a history of appendectomy was found in this study.

Disclosure: Nothing to disclose

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P0712 SERVICE EVALUATION OF A DEDICATED PSC PROGRAMME: IDENTIFYING NEEDS AND BARRIERS TO TRANSITIONING TO A 21ST CENTURY APPROACH TO CARE

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Introduction: PSC is a rare auto-immune liver disease with significant impact on quality and quantity of life for patients. Modern health care delivery has the potential to change care for rare disease but before appropriate changes can be made to improve patient care, we must understand the healthcare burden and natural history of the disease.

Aims and Methods: We sought to evaluate our current service over a 10 year period, to identify patient and clinical themes of relevance to service redesign. We performed a retrospective service evaluation of all pre-transplant patients with PSC who were first seen at our centre between October 2005 and October 2015, to allow for a minimum of 12 months follow up data. Data was gathered on patient demographics, geographical location, referral source, symptom burden and clinical events.

Results: 484 patients were identified and their electronic records reviewed; 64% were male with a mean age of 44 years (range 16–84 years). 85% were Caucasian and 72% had large duct involvement, with 65% having co-existing inflammatory bowel disease. Median ALP at first clinic appointment 461 (range 48–5051) with median UKELD of 48 (range 40–66). Median distance travelled via road from the patient's home to our centre was 48 miles (range 2–380) with a median travel time by road of 80 minutes (range 9–500). In total we received referrals from 64 different centres; 88% of patients were from outside our local area; 20% were referred from another UK tertiary liver centre, 45% from secondary care services, and 19% via their GP. 28% were referred for diagnosis whereas 25% were referred for ongoing management, 20% for transplant assessment and 12% due to possible cholangiocarcinoma. The diagnosis of PSC was preceded by chronic symptoms in 23%, an acute hospital admission in 17% and incidentally on blood tests in 35%, often due to monitoring for pre-existing IBD. 85% of patient's experienced PSC-related symptoms at some point in their follow up; 36% described significant pruritus, 32% fatigue, 28% recurrent cholangitis and 16% right upper quadrant pain. During this period, median number of clinic appointments was 8 (range 1–74) with 38% of patients requiring at least one hospital admission; 11% required EUS and 7% underwent ERCP at our centre during their follow up. Overall, 39% have been assessed for transplantation, 85% of which were activated on our transplant list. Of the entire cohort there was a 21% mortality rate, with 23% undergoing transplantation and 3% were diagnosed with cholangiocarcinoma.

Conclusion: Parallel to the essential development of new treatments for PSC, is a need for clinicians to recognise the total burden PSC places on patients and to use such insights when considering a patient-centred service redesign relevant to 21st century healthcare. Given the large distances many PSC patients travel for vital specialist care, novel alternatives to conventional management, such as the use of telemedicine, should be considered.

Disclosure: Nothing to disclose

P0713 INVESTIGATING THE ACCEPTABILITY TO PATIENTS OF INTRODUCING A VIRTUAL CLINIC INTO TERTIARY HEPATOLOGY OUTPATIENT CARE: AN AUDIT OF PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Telemedicine is the use of telecommunication systems to deliver healthcare at a distance. It is potentially one way of improving access to healthcare as well as efficiency. However, the 2016 Cochrane review concluded that questions remain about the acceptability of this to patients (1). Patients with rare diseases face geographical hurdles to accessing disease specific care that may be improved by the introduction of telemedicine. Primary sclerosing cholangitis (PSC) is a rare auto-immune liver condition and University Hospitals Birmingham (UHB) is preparing to introduce a virtual clinic via video link, commencing first in the PSC clinic.
Aims and Methods: We aimed to investigate the patient burden of attending specialist care and the acceptance of the virtual clinic, in this patient group. We distributed anonymous questionnaires to all patients attending the weekly PSC clinic over a 5 week period. The questionnaire included questions on demographics, employment, travel to appointments, diagnosis and opinions on the introduction of the virtual clinic. Analysis was completed including Fisher's exact tests, with $p < 0.05$ deemed to be indicative of statistical significance.
Results: A total of 101 questionnaires were completed; a 66% return rate. 74% had a diagnosis of a rare auto-immune liver disease, 83% of which was PSC. 47% of all respondents had previously received a liver transplant. 79% of respondents stated that UHB was not their local hospital and 34% of patients travelled for over 2 hours for appointments. There was an overall mean travel cost of £28.72 per patient visit. Overall, 59% stated they would accept a virtual appointment however 22% would not and 13% were unsure. 84% stated they used a desktop computer, laptop or tablet at least weekly and this was associated with increased acceptance of the virtual clinic ($p = 0.001$). Travel time was not associated with acceptance. In the post-transplant group only, patients seen at 6 monthly intervals were more likely to accept a virtual appointment than those seen at 3 monthly intervals ($p = 0.04$).
Conclusion: This audit shows that despite time and financial burdens placed on many patients attending our specialist centre for their PSC care, patient acceptability of the virtual clinic is not universal. We are planning further research to more fully understand patient opinions about the use of virtual clinics, via a series of semi-structured interviews.
Disclosure: Nothing to disclose

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TUESDAY, OCTOBER 23, 2018 09:00–17:00

Paediatric: Liver, Biliary and Pancreas – Hall X1

P0714 ASSESSMENT OF RISK FACTORS OF POST-PARACENTESIS CIRCULATORY DYSFUNCTION WITH MULTIPLE LARGE VOLUME PARACENTESIS IN CHILDREN WITH CHRONIC LIVER DISEASE: PROSPECTIVE LONGITUDINAL STUDY

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Introduction: Ascites is a common complication of cirrhosis and is associated with poor prognosis. Post-paracentesis circulatory dysfunction (PPCD) is overall seen in one-third of cirrhotic children who undergo single-time large volume paracentesis (SLVP)[1]. It is not known whether PPCD occurs with multiple LVP (MLVP).
Aims and Methods: Our study aimed to analyse the safety, complications and effect of albumin infusion during MLVP on PPCD in children with severe ascites due to chronic liver disease. Enrolled children with severe ascites underwent single time or multiple LVP with albumin infusion. Plasma renin activity (PRA) assessed at baseline and day 6 of last performed LVP. Maximal PRA value in MLVP was noted. Delta PRA was defined as PRA difference from day 6 and baseline. Worsening PPCD was defined as ≥1.5 times increase of delta PRA of any 2 sessions of LVP in MLVP group. ''At-risk'' group was defined as any cirrhotic child with ≥2 worsening PPCD episodes. Their outcome at 3 months and maximal follow-up were noted. Poor outcome was defined as failure of definitive therapy, need for liver transplantation or mortality.
Results: Table 1 shows baseline characteristics of 37 children (SLVP, n = 17; MLVP, n = 20). 92% had high PRA at the onset. The overall incidence of PPCD was 43% (SLVP: 12%, MLVP: 70%; $p = 0.003$). Baseline pediatric end-stage liver disease (PELD) score >27 was associated with PPCD (sensitivity: 90%; specificity: 50%, $p = 0.01$) in MLVP group. Worsening PPCD (n = 28; 54%) and at-risk children (n = 9; 45%) were identified in 52 sessions of MLVP. In the MLVP group, PPCD occurred if cumulative ascitic fluid extraction volume was >585 mL/kg/week (sensitivity: 90%; specificity: 50%, $p = 0.01$), cumulative albumin infusion <4.2 g/kg/week (sensitivity: 93%; specificity: 55%, $p = 0.03$) and frequency of sessions were >2.3/week (sensitivity: 91%; specificity: 57%, $p = 0.02$). In those who developed PPCD, lowest volume of ascites extracted in SLVP and MLVP groups were 117 and 471 mL/kg/week respectively. MLVP patients (80%) were susceptible to asymptomatic, persistent hyponatremia (baseline vs. day 6 from first LVP, 131 ± 4 vs. 124 ± 4 mEq/L; $p = 0.001$), hemodynamic changes (25%), renal impairment (35%), recurrence of ascites (60%) and hospital readmission (70%). At risk patients had worsening of PELD scores (baseline: 25 ± 8 vs. follow-up 31 ± 6; $p = 0.01$) at 3 months. Poor outcome at maximal follow-up (18 ± 7.4 months) was seen in 35% (n = 1, SLVP; n = 12, MLVP) especially in the at-risk group (n = 8; 89%).
Conclusion: PPCD occurs in majority of those underlying multiple LVP. One third have poor outcome, more in the at-risk group. Risk factors of PPCD with multiple LVP are baseline PELD >27, cumulative extracted ascites >585 mL/kg/week, cumulative albumin infusion <4.2 g/kg/week and frequency of sessions >2.3/ week.

	Single time LVP group (n = 17)	Multiple LVP group (n = 20)	p value
Age (y), boys (n)	9.8 ± 4.4, 13	8.3 ± 5.1, 15	0.77, 0.81
Duration of ascites (months)	3.6 ± 5.3	7.1 ± 11.0	0.20
Weight Z-scores	−1.69 ± 2.21	−2.51 ± 1.84	0.26
Height Z-scores	−0.98 ± 1.75	−1.39 ± 1.32	0.46
PELD score	22 ± 6	28 ± 10	0.05
Volume of ascites extracted (mL/kg/week)‡	143 ± 77	506 ± 105	0.001
Ascitic fluid infection (n)	4	7	0.47
Baseline PRA (ng/mL/h)	27.5 ± 18.4	29.1 ± 20.7	0.65
D6 or Maximum cumulative value of PRA (ng/mL/h)	28.3 ± 21.2 (D6)	73.1 ± 19.8	0.01
Folds elevation from baseline*	1.1 ± 0.5	6.4 ± 5.3	0.02
Number of subjects with PPCD (n)	2	14	0.003

Note: values expressed as mean ± SD; LVP: large volume paracentesis PELD: pediatric end-stage liver disease, PRA: plasma renin activity, PPCD: post-paracentesis circulatory dysfunction. ‡Volume of ascites extracted (mL/kg) = Total volume (mL) ÷ Dry weight (kg); dry weight was calculated after completion of LVP. *Folds elevated = Day 6 PRA (SLVP) or maximum noted PRA after 6 of any LVP (MLVP) ÷Baseline PRA value. High PRA defined as PRA >2SD of normal. PPCD: PRA rise of >50% of baseline value on day 6 of paracentesis to a level 2 standard deviation (SD) above age-appropriate mean pediatric cut-off. Normal mean PRA (+ 2SD) are variable for different age groups, 0.5–1 y: 6.27 (14.49); 1-4 y: 4.47 (10.71); 5-10 y: 2.33 (4.79); 11-17y: 2.07 (6.11) ng/mL/h
[Table 1: Comparison of single time and multiple large volume paracentesis groups]

Disclosure: Nothing to disclose

Reference

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P0715 HEMODYNAMIC CHANGES IN THE VESSELS OF THE ABDOMINAL CAVITY IN THE POSTPRANDIAL PHASE IN HEALTHY CHILDREN

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Introduction: The postprandial test provides valuable information about the state of the digestive system. It is most often used to determine the function of the pancreas. Changes in the parameters of regional circulation of the abdominal cavity after eating are analyzed much less frequently. There are no standards of postprandial reaction of hemodynamic parameters in arteries and veins of the abdominal cavity in children. That fact complicates its evaluation in patients with gastroenterological pathology.
Aims and Methods: The aim of the work is to characterize the reaction of abdominal vessels to the food load in healthy children and to determine the reference values of postprandial changes in the regional blood flow.
44 healthy children aged 3 to 15 years were examined. Doppler study of hemodynamics in abdominal vessels was performed twice: on an empty stomach and 30 minutes after a standard breakfast. The parameters of blood flow in veins (inferior vena cava, portal vena) and arteries (abdominal aorta, ventral trunk, superior mesenteric, common hepatic and splenic) were evaluated. Vessel

diameters, resistance index (IR) and volumetric blood flow velocity (BFV) were determined.
Results: It was found that changes in hemodynamic parameters after eating in healthy children of different ages and sex has no statistically significant differences. The diameters of the abdominal aorta and the inferior vena cava after eating remain the same in most children (70.5% and 77.2%, respectively) or change slightly (within 10% of the initial values). 30 minutes after a standard breakfast dilation of the superior mesenteric artery (on average 22.4% of the initial values), the ventral trunk (22.6%), the common hepatic artery (17.7%), the splenic artery (24.4%) and the portal vein (34.2%) is recorded. The spleen vena in the postprandial phase is not expanding so much (7.1%). In the majority of cases (79.5%) the IR values do not change or reduce slightly. In all the examined vessels, an increase in the volume velocity of the blood flow is determined, which reflects the intensification of hemodynamics of the abdominal organs in the postprandial phase. In the superior mesenteric it averages 85% of the baseline, in the common hepatic artery – 38%, in the splenic artery – 56%, in the ventral trunk – 72%, in the portal vena – 161%, in the splenic vein – 15%. The minimum growth rates of BFV are observed in large vessels – abdominal aorta (5%) and in the inferior vena cava (13%).
Conclusion: In healthy children dilation of the ventral trunk, superior mesenteric, hepatic and splenic arteries, portal and splenic veins is registered in the postprandial phase. The transverse dimensions of the abdominal aorta and the inferior vena cava in most cases remain the same or change slightly. There is a significant increase in the volume rate of blood flow in all the vessels studied, which reflects the intensification of blood circulation in the abdominal cavity.
Disclosure: Nothing to disclose

P0716 THE NATURE OF THE HEMODYNAMIC CHANGES OF THE ABDOMINAL CAVITY IN CYSTIC FIBROSIS IN CHILDREN

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Introduction: Disorders of the hepatobiliary system are diagnosed in 80% of children with cystic fibrosis (CF), in 5–10% of cases multilobular cirrhosis of the liver is formed accompanied by portal hypertension syndrome.
Aims and Methods: The aim of the work was to determine the nature of hemodynamic changes in abdominal vessels in children with cystic fibrosis and their relationship with the degree of structural disorders of liver.
33 patients aged 3–17 years with severe CF were examined. According to the results of the standard ultrasound examination, 3 groups were identified: 1. Normal structure of liver (n = 15) 2. Moderate changes (n = 11) and 3. Significant changes (n = 7). Hemodynamics in the abdominal vessels was evaluated by dopplerography. To assess the adaptive reserve of the vascular system a postprandial sample was used, for which dopplerography was carried out twice: on an empty stomach and 30 minutes after a standard breakfast.
Results: It was found out that in the absence, as well as in the moderate severity of changes in liver parenchyma in patients with CF, the average value of the diameters of the abdominal cavity vessels corresponds to the indicators of healthy children. In the group of patients with significant violations of the structure of the organ, dilation of celiac trunk (on average by 25.5% compared to the normal range), superior mesenteric (23.4%), common hepatic (26.8%) and splenic (21.7%) arteries, portal (74.1%) and especially splenic (102.0%) vein was recorded. BFV in these patients increases significantly in the common hepatic artery (by 41.2%), portal (59.7%) and splenic (62.3%) veins. The IR rises in the ventral trunk and common hepatic artery to 0.75 ± 0.006 and 0.78 ± 0.02 against 0.71 ± 0.007 and 0.75 ± 0.006 in healthy children ($p < 0.05$). The postprandial test revealed a significant decrease in the growth of the diameter of the abdominal cavity arteries and veins after eating, which had already been determined in the group of patients with normal liver structure. In the group of patients with significant organ impairment postprandial response of abdominal vessels was practically absent. It is known that under normal conditions, eating causes a significant (in some cases, multiple) increase in the volume rate of blood flow in the abdominal arteries and veins. At CF there is a sharp decrease or absence of BFV growth in the postprandial phase. Doppler changes are observed in the group of children whose standard ultrasound examination results have not yet revealed structural disorders of the liver. This makes it possible to consider the change in Doppler indices (the degree of increase in vascular diameters and BFV in them) as the signs of early liver damage at CF.
Conclusion: Standard Doppler imaging of abdominal vessels in children with cystic fibrosis reveals changes in regional hemodynamics only in the presence of pronounced structural disorders of liver. This is manifested by dilation of abdominal vessels, increased arterial inflow and venous outflow in the vascular system of the liver, an increase in the resistance index in the ventral trunk and common hepatic artery. Postprandial test can detect a reduction of adaptive reserve of the abdominal cavity vascular system before structural changes in the liver are detected by ultrasound. This is manifested by the lack of adequate vasodilatation and increase in the volume of blood flow in arteries and veins after eating.
Disclosure: Nothing to disclose

P0717 PEDIATRIC SUB-ACUTE HEPATIC FAILURE IN DEVELOPING COUNTRIES: RISK FACTORS THAT DETERMINE OUTCOME

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Introduction: Sub-acute hepatic failure (SAHF) is a grey zone area of liver dysfunction which has a smouldering, variable course and is poorly understood. Though spontaneous recovery is known, case fatality is high. Pediatric experience of SAHF is poorly highlighted in literature.
Aims and Methods: We aimed to identify the high risk subset that determine poor outcome of SAHF in children. Children with SAHF (appearance of ascites ± encephalopathy occurring from 4th–24th week of onset of acute hepatitis with coagulopathy in the absence of pre-existing liver disease) were analysed. Poor outcome (PO: death or liver transplantation within 90 days) were compared with spontaneous recovery (SR: complete normalisation of liver functions in native liver) for risk factors. Pediatric End-stage Liver Disease (PELD) score and King's College Criteria (KCC) were applied as measures of outcome.
Results: SAHF (n = 60) constituted 15% of all liver failure (n = 351) referrals. Seven had cirrhosis on biopsy and were excluded. Etiological workup (n = 53) was hepatitis A (n = 19), co-infection hepatitis A and E (n = 7), hepatitis B (n = 6), hepatitis E (n = 1), cytomegalovirus (n = 1), autoimmune hepatitis type 2 (n = 1) and indeterminate etiology (n = 18). Table 1 compares SR (n = 14, 26%) with follow-up of 6 (1–24) months versus PO (n = 30, 57%).

Parameters	Poor outcome (n = 30)	Spontaneous recovery (n = 14)	P value
Age (years)	5.5 (2–16)	6 (3–15)	0.79
Male	22 (73%)	8 (57%)	0.31
Duration of illness (days)	52 (30–180)	50 (30–150)	0.33
Jaundice to ascites/ encephalopathy interval (days)	30 (22–150)	30 (22–120)	0.85
Prodrome	19 (63%)	13 (93%)	0.06
Ascites	28 (93%)	13 (93%)	1.0
Pallor	20 (67%)	5 (36%)	0.05
Edema	19 (63%)	7 (50%)	0.40
Total bilirubin (mg/dL)	19.4 (4.8–41.6)	22.5 (2.9–36)	0.29
Serum albumin (g/dL)	2.4 (1.6–3.5)	2.7 (2.1–3.9)	0.06

[Table 1: Baseline clinical and laboratory data of poor outcome versus spontaneous recovery groups]

Nine (17%) had improving trend but had follow-up duration < 30 days and were not analysed for outcome. Risk factors on univariate analysis between PO vs. SR were known viral etiology (8% vs. 43%, p = 0.03), international normalised ratio [5.5 (2.0–14.4) vs. 2.6 (1.6–5.1), p = 0.003], PELD score [40 (17–57) vs. 25 (13–39), p = 0.002], hepatic encephalopathy (77% vs. 36%, p = 0.02), bleeding manifestations (33% vs. 0, p = 0.02), systemic infections (83% vs. 43%, p = 0.01), ascitic fluid infection (27% vs. 0, p = 0.04), acute kidney injury (43% vs. 7%, p = 0.03), all significantly higher in PO group. On multivariate logistic regression analysis, indeterminate etiology (specificity 93%, positive predictive value 92%) and PELD score cut-off > 32 (AUC: 0.79, sensitivity 67%, specificity 79%) independently determined PO. King's college criteria (KCC) showed a sensitivity of 87%, specificity 36%, positive predictive value 74% and negative predictive value 56% for PO.
Conclusion: Hepatitis A is the most common cause of SAHF (49%). SAHF with indeterminate etiology, advanced or symptomatic coagulopathy, hepatic encephalopathy, infective focus and acute kidney injury determine poor outcome. PELD score with cut-off > 32, an independent risk factor has better specificity than KCC for poor outcome. A large proportion (43%) may escape liver transplantation.
Disclosure: Nothing to disclose

P0718 CONGENITAL DILATATION OF THE BILIARY TRACT: RADIOLOGICAL ASPECTS AND THERAPEUTIC MANAGEMENT

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Introduction: Congenital dilatation of the biliary tract (CDBT) is a rare and heterogeneous congenital malformation affecting the bile ducts in variable way. The aim of this study was to describe the various radiological aspects of this pathology and analyze its therapeutic management in our medical center.
Aims and Methods: From 2002 to 2017 all the patients with the diagnosis of congenital dilatation of the biliary tract were retrospectively enrolled. The diagnosis of CDBT was based on the imaging data (MRI and / or ERCP) and histology in operated patients. Biliary duct anomalies were classified according to Todani's classification. Therapeutic modalities whether surgical or endoscopic were identified for each patient.
Results: 32 patients were enrolled. The mean age was 46 years and the sex ratio was 1.1 [M / F = 17/15]. According to the Todani classification, patients were

classified as type I = 13 cases (40%), III = 4 cases (12.5%), IV = 4 cases (12.5%), V = 11 cases (34.4%). Therapeutic management was based on this radiological classification. Indeed, in the case of malformations type I, IVb : 6 patients were operated (resection of the choledochal cyst with hepaticojejunal anastomosis). One of them was secondary operated after a non-controlled cholangitis (after ERCP). In 7 other cases endoscopic sphincterotomy in ERCP was indicated according to the bad state of the patient's field or the good spontaneous evolution of symptoms and biology. Regarding the 4 cases of choledococele, endoscopic treatment (based on the ERCP with pre-cutting on the top of the choledococele) was recommended, only one patient was complicated of duodenal perforation leading to a surgical treatment. For the 11 cases of Caroli: 3 had congenital liver fibrosis indicating liver transplantation. This one was however not carried out for lack of availability. For the 8 other cases it was a left caroli disease: 5 patients were operated on (left lobectomy in 4 cases and biliodigestive anastomosis in 1 case). The remaining 3 patients were treated with ursodeoxycholic acid with endoscopic treatment in case of complications (acute cholangitis, lithiasis). No cases of degeneration were observed in our series.
Conclusion: Our study underlines the complexity of the therapeutic management of the congenital biliary tract dilatation. Surgery, whenever possible can prevent the risk of degeneration. However, endoscopic treatment has a fundamental place in case of impossibility of operating the patients or the occurrence of complications.
Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00
Pancreas II – Hall X1

P0719 ANTIBIOTICS IN ACUTE PANCREATITIS IN THE LAST YEARS – EXPERIENCE OF A TERTIARY REFERRAL CENTER

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Introduction: Antibiotic therapy in acute pancreatitis (AP) does not influence clinical course and mortality and it is not endorsed by current international guidelines [1]. Concerns regarding the increase in multidrug resistant bacteria has led to the implementation of measures to mitigate inappropriate antibiotic use in our center.
Aims and Methods: We aimed at comparing the patterns of antibiotic use and associated clinical outcomes over two different timelines. We included 200 patients with AP: 100 admitted between 2012 and 2017 (retrospective cohort, group A) and 100 patients admitted after 2017 (prospective cohort, group B). We defined inappropriate antibiotic therapy if: (1) no bacterial agent was isolated in microbiologic tests, (2) infected necrosis was not present, and (3) antibiotics were not due to documented extra-pancreatic infection. Statistical analysis was performed with SPSSv23; A p value < 0.05 was considered significant.
Results: No differences were found between demographics, etiology and severity of AP in both groups (table). In group A there was a significant higher use of antibiotics (52% vs 24%; $p < 0.001$) but no difference was found in mortality (5% vs 2%; $p = 0.200$). The prescribing of carbapenems was high in both groups (43.3% vs 50.0%; $p = 0.530$). In 2012 there was a significantly higher rate of extra-pancreatic nosocomial infections (7% vs 1%; $p = 0.030$). In group A nosocomial infections occurred in 71.4% of the cases of inappropriate antibiotic therapy; in multivariate analysis (including age, gender, etiology and severity) inappropriate antibiotic therapy was an independent predictor of nosocomial infection (OR 17.248 CI95% [2.1–144.0]; $p = 0.009$). In both groups, there was a significant association between severe AP and use of antibiotics (Group A: OR 8.251 CI95% [2.11–51.91]; $p = 0.004$; group B: OR 7.255 CI95% [2.32–22.67]; $p = 0.001$).
Conclusion: A significant decrease in inappropriate antibiotic therapy and nosocomial infections in AP was seen in our center. Higher use of antibiotics in the past was not associated with a decrease in mortality in AP. Inappropriate antibiotic therapy in AP was an independent predictor of nosocomial infection.

	2012	2017	p
Female gender (%)	60	51	0.200
Age (mean years)	63.06 [22–93]	63.12 [22–91]	0.467
Alcoholic AP (%)	21	27	0.321
Biliary AP (%)	39	42	0.666
Post-ERCP AP (%)	11	15	0.517
Idiopathic AP (%)	22	16	0.279
Other etiology AP (%)	7	4	0.352
Mild AP (%)	65	53	0.084
Moderate AP (%)	14	27	0.023
Severe AP (%)	21	20	0.861
Antibiotic therapy (%)	52	24	<0.001
Day of start of antibiotic therapy (mean)	1.52 [1–4]	2.19 [1–5]	0.370
Mortality rate (%)	2	5	0.248

[Table 1.]
Disclosure: Nothing to disclose

Reference

1. Tenner S, et al. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013. 108(9):1400–15;1416.

P0720 PREDICTIVE NATURE AND CLINICAL CHARACTERISTICS OF PAIN ON ADMISSION IN ACUTE PANCREATITIS

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Introduction: Pain is a very common symptom in acute pancreatitis (AP), therefore, understanding its characteristics and predictive role is important. Until now, the detailed characteristics have not been investigated. Here, we aimed to analyze the predictive role and clinical characteristics of pain on admission in AP.
Aims and Methods: The Hungarian Pancreatic Study Group (HPSG) has prospectively collected multicenter clinical data of 1435 adult patients between 2012 and 2017. The specific pain questionnaire contained data in four categories: intensity (visual analog scale, 1–10, mild (mildP):1–3, moderate (modP): 4–6, severe (sevP):7–10), duration of pain prior to admission (hours), localization (upper, middle, and lower abdomen), and type (sharp, dull, or cramping). These data were compared with parameters on admission and with the outcome of AP. Statistical analyses were performed accordingly.
Results: Most of the patients had severe abdominal pain (mildP: 5.23%, modP: 24.48%, sevP: 70.29%). The intensity of pain was directly associated with the severity of AP (mildP: 0% severe AP, modP: 2.81%, sevP: 4.50%; $p < 0.05$), mortality (mild:0% moderate: 1.98% severe: 1.76%; mildP vs modP and sevP: $p < 0.05$), local (mild:15.79% modP:28.09% sevP:25.25%; mildP vs modP and sevP: $p < 0.05$) and systemic complications (mildP:2.65% modP:9.55% sevP:7.83%; mildP vs modP and sevP: $p < 0.05$), higher white blood cell count, elevated lipase and amylase levels, but not with CRP level. The duration of pain was not associated with mortality and severity; however, it markedly influenced the laboratory parameters on admission. The level of amylase and lipase, the amount of RBC and hemoglobin, and pain intensity were decreasing, whereas the level of CRP and the amount of thrombocyte were increasing. Concerning the localization, most of the patients had upper abdominal and epigastric pain. However, localization was not associated with the above-mentioned parameters. Sharp pain was associated with higher mortality, severity, local, and systemic complications vs the other types of pain.
Conclusion: Higher intensity of pain is associated with worse clinical outcome; therefore, its role should be investigated in clinical trials. The duration of pain prior to admission strongly influence the laboratory parameters on admission, therefore, it should be incorporated into the on admission scoring systems in AP.
Disclosure: Nothing to disclose

P0721 PRE-EXISTING DIABETES ELEVATES RISK OF RENAL FAILURE AND LOCAL COMPLICATIONS IN ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is an inflammatory condition which commonly requires hospitalization and shows increased incidence. The prevalence of diabetes mellitus (DM) has duplicated in the last 35 years. Acute pancreatitis may result in pancreatic exocrine insufficiency and DM, but nowadays the influence of pre-existing DM in AP patients represents a hot research topic.
Aims and Methods: The aim of our meta-analyses is to understand the influence of DM on the outcomes of AP including mortality, length of hospitalization,

incidence of organ failures and intensive care unit admission. The meta-analysis was performed using the PRISMA Protocol. PubMed, EMBASE and Cochrane databases were searched, articles with AP patients including DM and non-DM groups were included, and complications, length of hospitalization (LOH), intensive care unit (ICU) admission and mortality were analyzed. The odds ratio (OR) and standardized mean difference (SMD) with 95% confidence intervals (CI) were calculated with Comprehensive Meta-Analysis software.
Results: 1417 articles were found, of which 9 articles involving 354,880 patients were analyzed. More systemic complications were seen in diabetic patients, than in non-DM patients (OR = 1.553 [CI:1.266–1.904], $p < 0.001$). ICU admission (OR = 1.799 [CI:1.442–2.243], $p < 0.001$) and renal failure (OR = 1.585 [CI:1.278–1.966], $p < 0.001$) were more frequent in DM patients than in non-DM patients. There was a tendency of higher mortality and local complications (OR = 1.276 [CI: 0.991–1.643], $p = 0.059$; and OR = 1.267 [CI:0.964–1.659], $p = 0.090$, respectively) in the pre-existing DM group. LOH was longer in DM patients than in non-DM patients (SMD = 0.217 [CI:0.075–0.360], $p = 0.003$).
Conclusion: Pre-existing DM negatively influences the outcome of AP and increases the risk of renal failure, ICU admission, local complications and mortality. More attention is necessary for AP patients with pre-existing DM.
Disclosure: Nothing to disclose

P0722 ALTERED LEVEL OF CONSCIOUSNESS DETERIORATES THE SEVERITY OF ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is an inflammatory disease often requiring hospitalization. In the moderate and severe form of the disease organ failure and altered level of consciousness (ALC) may develop, which is often alcohol related (AR-ALC). However, the influence of ALC on the outcome of AP has not been examined yet.
Aims and Methods: We aimed to investigate the influence of ALC and AR-ALC on the outcomes such as severity, mortality and length of hospitalization (LOH) of AP. Out of the 1449 subjects in the Hungarian Pancreatic Study Groups' AP register 1220 contained the exact data on ALC. Patients were separated to non-ALC and ALC, whereas ALC was further separated to non-alcohol related ALC (NAR-ALC) and AR-ALC groups. Statistical analysis was performed by SPSS 24 Software Package, Chi-Square, Mann-Whitney, One-Way-ANOVA and Kruskal-Wallis tests were used.
Results: From the 1220 patients 47 (3.85%) developed ALC from that 23 (48.9%) cases were AR-ALC, whereas 24 (51.1%) cases NAR-ALC. ALC showed significantly higher incidence in men than in women (70.2% vs 29.8%, $p = 0.045$). Age was significantly higher in the ALC vs non-ALC group (62.19 ± 18.69 vs 56.52 ± 16.97, $p = 0.025$). The incidence of severe AP was significantly higher in the ALC compared to non-ALC group (19.15% vs 5.29%, $p < 0.001$). The mortality was significantly higher in the ALC vs non-ALC group (14.89% vs 1.71%, $p < 0.001$). LOH was significantly longer in ALC vs non-ALC group (Me: 11; IQR: 8–17 days vs Me: 9; IQR: 6–13 days, $p = 0.049$). AR-ALC showed significant correlation with the gender, it developed more frequent in men than women (91.30% vs 8.70%, $p = 0.002$), while in NAR-ALC no difference was seen between the genders. Patients with NAR-ALC were older than patients with AR-ALC (70.5 ± 18.38 vs 53.52 ± 14.95 years, $p = 0.002$). Patients with AR-ALC developed more frequently moderate severe AP vs NAR-ALC (43.48% vs 12.5%), while the incidence of severe AP was significantly higher in NAR-ALC vs AR-ALC group (33.33% vs 4,35%) ($p < 0.001$). Concerning the LOH, patients with NAR-ALC shows a tendency for longer hospitalization (Me: 13; IQR: 7–20 days vs Me: 9.5; IQR: 8–15.5 days, $p = 0.119$).
Conclusion: ALC during AP elevates the risk of moderate and severe AP and enhances the risk of mortality, therefore ALC should be avoided during hospitalization due to AP.
Disclosure: Nothing to disclose

P0723 OPPOSITE EFFECTS OF YOUNGER AND OLDER AGES ON SEVERITY AND MORTALITY IN ACUTE PANCREATITIS. A META-ANALYSIS BASED ON 191 678 PATIENTS

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Introduction: Acute pancreatitis (AP) is one of the most common cause of hospitalization among gastrointestinal diseases worldwide. Although most of the cases are mild, approximately 10%–20% of patients develop a severe course of disease with higher mortality rate. Scoring systems consider age as a risk factor of mortality and severity (BISAP; >60 yrs, JPN>70 yrs (Japanese severity score), RANSON; >55 yrs, APACHE II >45 yrs). If there is a correlation between ageing and the clinical features of AP, how does age influence mortality and severity?
Aims and Methods: In this study we aimed to investigate whether ageing has any effects on severity or mortality in AP.
Comprehensive literature searches were conducted using Embase, Cochrane and Pubmed databases. A meta-analysis was performed using the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P). The searching terms were (age and acute pancreatitis and (clinical trial or cohort)). There were 502 articles found in Embase, 340 in PubMed, and 17 in the Cochrane database. After removing duplications and unsuitable articles altogether 27 articles containing 191,678 AP patients, 179,180 for mortality and 21,573 AP patients for severity were analyzed. Seven subgroups were determined: under 20 yrs (U20), 10 yrs ranges from 20 to 70yrs and above 70 yrs (A70).
Results: Concerning the risk for mortality, there was a clear elevation from paediatric to elderly people: U20: 0.9% (510/55266; pooled event rate: 0.009 CI:0.008–0.010), 20–29: 0% (0/1720), 30–39: 1.3% (137/11375), 40–49: 5.4% (76/1411), 50–59: 2.0% (825/41634), 60–69: 8.5% (2153/25452) A70: 17.3% (7312/42322; pooled event rate: 0.107 CI: −0.026–0.239). This significant elevation was also confirmed by meta-regression (coefficient: 0.038 CI:0.017–0.058, $p = 0.001$; adjusted r^2: 35.41%) and with the conventional regression analysis also ($p = 0.005$, r^2: 0.906).
Concerning severity, there was no severe AP U20, 20–29: 0%(0/36), 30–39: 6.7%(5/75), 40–49: 8.3%(586/7028), 50–59: 11.3%(1352/11933), 60–69: 16.6%(390/2344), A70:9.6% (15/157; pooled event rate: 0.098 CI: −0.054–0.142). This elevation was not confirmed by meta-regression (coefficient: 0.021 CI: −0.022–0.065, $p = 0.322$; adjusted r^2: −3.16%). In case the conventional regression analysis an exponential tendency could be observed ($p = 0.069$, r^2: 0.778).
Conclusion: Our meta-analyses shows that younger age (U20) has protective effects in acute pancreatitis, whereas ages above 50 elevates the risk for mortality and severity.
Disclosure: Nothing to disclose

P0724 CLINICAL EVALUATION OF INTERVENTIONAL EUS DRAINAGE AND SEQUENTIAL DIRECT ENDOSCOPIC NECROSECTOMY USING A NEW BIFLANGED METAL STENT FOR PANCREATIC FLUID COLLECTION

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Introduction: EUS-guided transluminal drainage (EUS-TD) and sequential direct endoscopic necrosectomy (DEN) for pancreatic fluid collections (PFCs) using a dedicated biflanged metal stent (BFMS) has been reported as a useful alternative to using plastic stents or a conventional metal stent. However, current dedicated BFMSs [lumen-apposing metal stent (LAMS) such as AXIOS stent or SPAXUS stent and flared metal stent (FMS) such as Nagi stent] have limitations. Recently, a new BFMS with solidly constructed biflanges and various stent lengths (Plumber stent, 14-mm in diameter and 20-mm or 30-mm in length) matched to the PFC condition has been developed. The feasibilities and safety of the new Plumber stents are being clinically tested and discussed.
Aims and Methods: Plumber stent has both advantages of the LAMS and FMS, the so-called "hybrid BFMS". Herein, we show the prospectively evaluated clinical outcome of this new BFMS for the treatment of PFCs. From July 2015 to March 2018, EUS-TD using Plumber stent was performed in 25 patients for PFCs (5 patients with pancreatic pseudocysts; 20 patients with walled-off necrosis (WON)). When clinical resolution could not be achieved within a few days after EUS-TD, DEN was performed the following day.

Results: Plumber stent was deployed successfully with a median procedure time of 18 min (range, 11–38 min) and with no procedure-related adverse events in all the patients (25/25, 100%). DEN (n = 7) and/or additional drainage procedure (n = 6) via the stent were achieved in all the patients in whom they were attempted (10/10,100%). Stent dislocation during DEN was not observed in any of the patients, but in one patient spontaneous stent migration was observed about 4 months after stent placement. The migrated stent has been already discharged outside the body. Two WON patients died from spontaneous pseudoaneurysm rupture occurred between the endoscopic necrosectomy sessions and from multiple organ failure although hemostasis was achieved by coil embolization. The PFCs in the other 23 patients completely resolved (the clinical success 23/25, 92.0%), and later the stent was removed with no difficulty in 21 patients after a median time of 56 days (range, 30–196 days). PFC recurrence or stent-related late adverse event was not observed for a median follow-up time of 550 days (range, 83–941 days).
Conclusion: The new BFMS (Plumber stent) is technically feasible and safe for the treatment of PFCs. Though, further studies using randomized-controlled, well-designed, adequately powered studies comparing the new BFMS with previous BFMSs (LAMS or FMS) are required to validate its efficacy.
Disclosure: Nothing to disclose

P0725 METABOLIC SYNDROME ELEVATES THE RISK FOR MORTALITY AND SEVERITY IN ACUTE PANCREATITIS

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Introduction: Several studies have confirmed that obesity (BMI > 30) increases the severity and mortality of acute pancreatitis (AP), however, no information is available whether its effect is independent or joint with the components of metabolic syndrome (MS).
Aims and Methods: Our aim is to understand whether obesity is an independent risk factor for mortality and severity of AP.
The Hungarian Pancreatic Study Group has prospectively collected clinical data from patients suffering from AP between 2012 and 2017. Our cohort contains 1435 cases of which 906 cases from 26 centers had information on all four components of MS. Patient groups were formed retrospectively based on the WHO classification of BMI and the presence of the components of MS, namely obesity, hypertension, hyperlipidemia and diabetes. Logistic regression was performed to analyze the independent effects of these four factors.
Results: The obesity prevalence in our AP cohort is 29.5%, therefore it is representative of the Hungarian population (prevalence of obesity: 30.0%). High BMI is directly associated with higher rates of severity, mortality and necrosis of AP, respiratory and renal failure and more severe comorbidities. The prevalence of diabetes, hypertension and hyperlipidemia are growing with higher BMI. The rate of severe AP elevates with the number of affected components of MS (2.6%, 4.7%, 6.1%, 8.5% and 6.0% with 0, 1, 2, 3 and 4 components respectively), however, the increase was significant only in case of three components of MS compared to cases without any MS components (OR = 3.439 95% CI: 1.145–10.328). In a logistic regression model, out of the four components only hypertension is a predictive factor for severity (OR = 3.895 95% CI: 1.704–8.902) and mortality (OR = 5.900 95% CI: 1.330–26.165). Concerning complications, hyperlipidemia elevates the risk of diabetes as a complication (OR = 2.373 95% CI: 1.195–4.711) and obesity increases the risk of renal failure (OR = 2.968% CI: 1.343–6.559). Hypertension is a strong predictive factor for respiratory failure (OR = 2.667 95% CI: 1.139–6.243) and renal failure (OR = 7.565 95% CI: 1.760–32.516).
Conclusion: Metabolic syndrome, in particular hypertension factor, strongly deteriorates the outcome of AP. Obesity, hyperlipidemia and diabetes are not independent risk factors for severity and mortality in AP, however strongly elevate each other's detrimental effects.
Disclosure: Nothing to disclose

P0726 NSAIDS AMELIORATES PANCREAS INJURY AND INHIBITS INFLAMMATORY CYTOKINES IN RAT POST-ERCP PANCREATITIS

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is a kind of advanced technology for the diagnosis and therapy of biliary-pancreatic diseases. However, various postoperative complications have constrained the widespread application of the technology to some extent. Post-ERCP pancreatitis (PEP) is the most common complication of ERCP. To date, although several clinical studies have suggested prophylactic use of nonsteroidal anti-inflammatory drugs (NSAIDs) is effective on PEP prevention, the effects of NSAIDs on PEP prophylaxis are still in debate. Meanwhile, the underlying mechanism by which NSAIDs prevents PEP remains poorly understand. As cyclooxygenase-2 (COX-2) is implicated in inflammatory response, thus we speculate that NSAIDs exert its protective effect mainly through inhibiting COX-2 expression.
Aims and Methods: In the present study, we aimed to determine the prophylactic effects of two different types of NSAIDs, indomethacin (COX-1 and COX-2 inhibitor) and parecoxib (selective COX-2 inhibitor) on PEP occurrence in rat model and investigate the underlying mechanisms. Thirty-two Wistar rats were equally and randomly assigned to 4 groups: PEP model group, indomethacin group, parecoxib group and pseudo-operation group. PEP rat models were established via retrograde injecting 0.4ml 30% omnipaque into bile ducts at 50mmHg pressure. NSAIDs prophylaxis rats received rectal administration of indomethacin suppository at 10mg/kg or intramuscular parecoxib injection at 4mg/kg 30min prior to surgical operation. The serum amylase, IL-6, IL-10 and TNF-α were tested, and the pancreas histological alteration were assessed. For mechanism study, the expression of COX-1, COX-2 and apoptosis-relative protein BAX was further determined.
Results: The amylase level in PEP rats dramatically increased compared with pseudo-operation rats ($p < 0.05$). Indomethacin and parecoxib treatment decreased 14% and 13% amylase levels compared with PEP rats, respectively, but without significant difference. Histological assessment showed that compared with the pseudo-operation rats, the pancreatic edema, hemorrhage, acinar necrosis and inflammatory cell infiltration scores in PEP rats obviously increased, respectively. However, indomethacin and parecoxib prophylaxis effectively declined the histological scores above mentioned ($p < 0.05$). Likewise, the serum IL-6, IL-10 and TNF-α levels in PEP rats dramatically increased compared to pseudo-operation rats, respectively ($p < 0.05$), and indomethacin and parecoxib remarkably declined the serum inflammatory cytokines levels ($p < 0.05$). Western blot analyses revealed that compared with PEP rats, indomethacin markedly inhibited COX-1 (0.99 ± 0.11 vs. 1.51 ± 0.13, $p < 0.05$) and COX-2 (1.04 ± 0.13 vs. 1.50 ± 0.12, $p < 0.05$) proteins expression while parecoxib selectively inhibited COX-2 expression (0.90 ± 0.08 vs. 1.50 ± 0.12, $p < 0.05$) Furthermore, indomethacin and parecoxib treatment decreased the expression level of BAX proteins (1.17 ± 0.13 vs. 1.62 ± 0.12, $p < 0.05$; 1.03 ± 0.09 vs. 1.62 ± 0.12, $p < 0.05$).
Conclusion: Prophylactic use of indomethacin and parecoxib could histologically mitigate pancreas injury and suppress inflammatory cytokines levels in PEP rats. NSAIDs could protect pancreatic acinar cells from apoptosis via inhibiting COX-2 expression.
Disclosure: Nothing to disclose

P0727 CHRONIC USE OF STATINS AND AMINOSALICYLIC ACID AND INCIDENCE OF POST-ERCP ACUTE PANCREATITIS. PRELIMINARY DATA FROM THE STARK STUDY, A PROSPECTIVE INTERNATIONAL, MULTICENTER, COHORT STUDY

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Introduction: Acute Pancreatitis is the most frequent complication of Endoscopic Retrograde Cholangiopancreatography (ERCP). Some prophylactic strategies have been investigated to prevent it, such as the use of pancreatic stents or the use of peri-procedural NSAIDs; the incidence of Post-ERCP Acute Pancreatitis (PEP) in patients consuming aminosalicylic acid (ASA), a NSAID, is unclear. Statins are widely used lipid-lowering drugs and recent studies suggest that chronic statin intake may be associated to a lower incidence of acute pancreatitis.
Aims and Methods: Our aim is to investigate whether chronic statin and/or ASA intake is associated to a lower incidence of PEP.
Stark project (Statin and ASA for Ris k of PEP) is a prospective, international, multicenter, cohort study, developed under the auspices of the Pancreas 2000 educational program. Consecutive patients undergoing ERCP were included

prospectively. Demographic and medical data were retrieved by anamnesis. The patients were followed-up to detect those with PEP. Outcomes for PEP were retrieved from medical records. The final sample size was estimated to be 1,016 participants. A multivariate analysis (binary logistic regression) was performed; the variables included in the model were: statin intake, ASA intake, sex, age, center, difficult cannulation, procedure time, sphincter of Oddi dysfunction or previous episodes of acute pancreatitis. Adjusted odds ratios (aOR) were calculated.

Results: 638 patients were included for this preliminary analysis. Median age was 68.7 years (67.7-69.8), 333 (52.2%) patients were male, 41 patients developed PEP (6.4%), 16 patients (8.6%) under statin treatment versus 25 patients (5.6%) who were not consuming statins ($p = 0.160$). The multivariate analysis showed an aOR of 1.86 (0.874–3.986), $p = 0.107$ for PEP incidence in statin users. Regarding ASA consumption, 6 patients (5,8%) under ASA treatment versus 35 patients (6.6%) who were not consuming ASA developed PEP ($p = 0.782$). The multivariate analysis showed an aOR of 0.837 (0.292–2.399), $p = 0.740$ for PEP incidence among ASA users.

Conclusion: Our preliminary data suggest that chronic use of statins and/or ASA is not associated to a lower incidence of PEP.

Disclosure: Nothing to disclose

P0728 META-ANALYSIS AND TRIAL SEQUENTIAL ANALYSIS OF PROPHYLACTIC ANTIBIOTICS FOR ACUTE PANCREATITIS

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Introduction: Prophylactic antibiotics (AB) are not recommended for treatment of acute pancreatitis (AP). Their use is still widespread despite several trials showing no firm evidence of efficacy.

Aims and Methods: To evaluate the effects of prophylactic antibiotics (PAB) for AP in a meta-analysis and investigate the need for further research by trial sequential analysis (TSA). Medline, Scopus and Web of Science were searched for randomized clinical trials assessing prophylactic use of AB in AP. Primary outcomes were all infectious complications and mortality. Secondary outcomes comprised infected pancreatic necrosis (IPN) and other specific infections, organ failure, surgical interventions and length of hospital stay. TSA was performed for primary outcomes, and secondary outcomes with significant results at a level of $\alpha = 0.05$ and power of 80%. Risk of bias was assessed using the Cochrane tool for bias assessment. Results for dichotomous outcomes were expressed as risk ratios (RRs) with 95% confidence intervals (CIs) and continuous results were expressed as mean differences (MDs) with 95% CIs.

Results: A total of 18 trials with 1134 pts were included in the analysis. PAB were received by 576 pts, while 558 were assessed as controls. Most of trials were assessed as being of high risk of bias. Overall mortality rate was similar in both groups with RR 0.85 (95% CI 0.64–1.14; $p = 0.27$; $I^2 = 0\%$), but the risk for infectious complications was significantly reduced in pts receving PAB (RR 0.34; 95% CI 0.22–0.51; $p < 0.00001$; $I^2 = 59\%$). This reduction was mainly due to the decreased risk of sepsis (RR 0.36; 95% CI 0.19–0.68; $p = 0.002$; $I^2 = 15\%$) and urinary tract infections (RR 0.46; 95% CI 0.25–0.86; $p = 0.02$; $I^2 = 11\%$), while a trend in risk reduction of IPN was shown with RR 0.78 (95% CI 0.60–1.00; $p = 0.05$; $I^2 = 0\%$). There was no significant difference in risk of other infections, fungal infections, organ failure and surgical interventions. Length of hospital stay was diminished in the intervention group by MD −6.65 (95% CI −8.86 to −4.43; $p < 0.00001$; $I^2 = 0\%$) days. For the detection of RRR of 30% in a 10% mortality rate among controls the required sample size is 2714 pts, while the number of included pts is 1076. A 30% RRR of 15% rate of IPN among controls requires 1725 pts, while only 959 are included so far. A 30% RRR of 30% rate of infectious complications has been achieved at 428 included pts, although the estimated sample is 1923. To show a minimally relevant mean shortening of hospital stay of 3 days requires a sample size of 391 pts and according to TSA this has already been achieved at the level of 351 included pts.

Conclusion: PAB clearly decrease the rate of infectious complications in AP, but mainly due to RRR of extrapancreatic infections, which requires no further research. No significant effect is shown on IPN and mortality, although firmer evidence requires additional trials and a larger sample size.

Disclosure: Nothing to disclose

P0729 SERUM TATI, TRYPSINOGENS 1-3, AND COMPLEX OF TRYPSIN-2 AND α_1-ANTITRYPSIN IN THE DIAGNOSIS OF ACUTE PANCREATITIS

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Introduction: Human pancreatic juice contains three trypsinogen isoenzymes: Trypsinogen-1 (cationic, T-1), trypsinogen-2 (anionic, T-2), and trypsinogen-3 (mesotrypsinogen, T-3). Tumor-associated trypsinogen inhibitor (TATI), also called pancreatic secretory trypsin inhibitor (PSTI) inhibits activated T-1 and -2 within the pancreas. Acute pancreatitis (AP) occurs when the inhibitory capacity of TATI is exceeded. Inflammation leads to leakage of pancreatic enzymes into the circulation. This can lead to 100-fold increases in the serum concentrations of TATI and trypsinogens in plasma and urine a few hours after onset of the disease. Concentrations of T-2 may stay elevated for weeks. α-macroglobulin and α--antitrypsin form complexes with and inactivate trypsin. When their inhibitory capacity exceeds, other proteolytic enzymes activates which lead to complications and organ dysfunctions (OD).TATI, T-1, T-2, T-3, and complex between trypsin-2 and α--antitrypsin (trypsin-2-AAT) have been studied as markers for AP but their prognostic value in detecting developing OD has not been cleared.

Aims and Methods: Our aim was to explore if on-admission serum levels of TATI, trypsinogens 1, −2, and −3, and trypsin-2-AAT can be used to evaluate the severity of AP and predict development of OD in AP patients, with and without OD.

We measured from 239 AP patients with onset of the disease within 72h the serum concentrations of TATI,T-1, T-2, T-3, and trypsin-2-AAT. As a normal hospital routine serum C-reactive protein, creatinine, and pancreatic amylase served as reference markers. Severity of AP was defined according to the revised Atlanta criteria.

Results: At admission, the serum concentrations of TATI ($p = 0.000$), T-1 ($p = 0.001$), T-2 ($p = 0.000$), trypsin-2-AAT ($p = 0.000$), and creatinine ($p = 0.000$) correlated with the severity of AP. The median concentrations of serum TATI ($p = 0.000$) T-1 ($p = 0.009$), T-2 ($p = 0.000$), trypsin-2-AAT ($p = 0.001$), and creatinine ($p = 0.035$) were higher in patients with developing OD than in those who did not. The diagnostic accuracy distinguishing patients who will develop persisting OD (severe AP) was estimated by receiver operating characteristic (ROC) curve analysis: TATI had the largest area under ROC curve (0.742, SD 0.062), T-2 (0.726, SD 0.063), trypsin-2-AAT (0.657, SD 0.056), creatinine (0.656, SD 0.063), T-1 (0.652, SD 0.071), T-3 (0.557, SD 0.069), and CRP (0.499, SD 0.075). TATI and T-2 were the most accurate in diagnoses. With a cutoff 166 µg/l specificity for TATI was 93%, sensitivity 48%, and DOR 11.52. With a cutoff for T-2 of 1375 µg/l, specificity was 93%, sensitivity 38%, and diagnostic odds ratio (DOR) 7.8. In multivariate logistic regression analysis, TATI was only independent predictor of severe AP among patients presenting without OD on admission ($p = 0.001$).

Conclusion: To our best knowledge this is the first study comparing the performance of TATI, T-1, T-2, T-3, and trypsin-2-AAT in distinguishing the development of OD in AP patients. We found that TATI was an independent marker of severe AP in patients who presented without OD on admission. The markers studied here, and especially TATI and T-2, are of great potential utility for diagnosis of AP and for prediction of later development of persistent OD. This could facilitate the early recognition of patients prone to develop severe AP in order to early initiation of intensive care and prevention of OD development.

Disclosure: Nothing to disclose

P0730 INFLAMMATION PLAYS A KEY ROLE IN PANCREATIC CARCINOGENESIS INDUCED BY ELECTROPORATION

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Introduction: Pancreatic cancer (PC) is one of the deadliest cancers. Because of the high lethalness, PC becomes a hot spot of research. Over the last decade, many experimental models for PC have been developed. It is worth noting that PC is not a paediatric disease which may make us pay more attention to adult animal models, such as lentivirus-infected (LI) model and another model which induced by electroporation (EP). By using genetic alterations of *Kras* and *P53*, the EP model has induced PC. However, the LI model can not format PC by altering cancer genes above *Kras*, *P53*, until *Cdkn2A* and *Cdkn2B* are added. They indicate that the mechanisms of tumour formation between the two adult PC models are not similar. Moreover, inflammation, a tumour risk factor, can contribute to carcinogenesis when combined with characterized mutational events.

Aims and Methods: To investigate the difference in cancer formation mechanism of the two new humanized genetically-modified adult mouse model of PC. A reporter plasmid driven by green fluorescent protein (GFP) expression was constructed. After laparotomy, it is possible to make the pancreas accessible for intraparenchymal injection of vector DNA which co-deliver sleepy beauty (SB)13-transposase with the GFP-expressing transposon. GFP was detected by immunofluorescence staining for testing the efficiency of transfection. At day 7 and 14, after intra-parenchymal administration, H&E-stained sections and immunofluorescence of some inflammatory cells were utilized, by using antibodies against T-lymphocytes (CD3 antibodies), macrophages (F4/80 antibodies), B-lymphocytes (Pax5 antibodies), neutrophils (MPO antibodies), to determine the existence of pancreatitis. The characteristic of acinar-to-ductal metaplasia (ADM) was detected by co-immunofluorescence staining for Cytokeratin 19 (CK-19), a duct cell-specific marker, and Carboxypeptidase A1 (CPA1), an acinar cell-specific marker. Cell proliferation was detected by the immunofluorescence of Ki67.

Results: The transfected-DNA vectors could stably express in pancreatic cells between the two PC model groups. In spite of day 7 or 14, the EP pancreas had higher level of kinds of inflammatory cells than LI pancreas, although both of them showed more visible immune cells than normal mice pancreas. In addition, a few co-positive cells displayed acinar cells into a persistent duct-like state showed structures of ADM. Moreover, the expression of Ki67 in EP and LI group is stronger than normal pancreas.

Conclusion: These observations suggest the difference of process for cancer inducement between the two adult animal PC models. Apart from the mutation with *Kras* and *P53*, the EP model requires inflammation cooperated with genomic aberrations to build tumour. However, only if altering several cancer genes, PC in LI model can be induced. These findings provide considerable insight that for different research purposes, the proper use of animal model is an important step for gaining significant scientific observation. Additionally, inflammation inhibition might be a potential target in treating parts of PC whose formation required inflammation.
Disclosure: Nothing to disclose

P0731 INCREASED CATHEPSIN D EXPRESSION HAS A NEGATIVE PROGNOSTIC EFFECT ON SURVIVAL IN GEMCITABINE TREATED PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

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Introduction: The lysosomal aspartic protease Cathepsin D (CatD) is overexpressed and hypersecreted in many cancers and hereby influences cell death. Previously, in the ESPAC-3 cohort we determined a significantly increased median overall survival in cathepsin D low expressing PDAC patients. Gemcitabine treatment was significantly less effective in patients with high CatD expression compared to 5FU treated patients. Here, we present a prospective validation study.
Aims and Methods: Sample size calculation based on the $c2_{LR,\ 1DF}$ [3.58] from our previous study warranted 76 gemcitabine treated patients asking for a power of 0.8 and $p < 0.05$. Tumor tissue microarrays of 79 patients from the ''informative patients'' with PDAC receiving adjuvant gemcitabine treatment recruited at a single center were stained with anti-CatD (C-20) antibody. Patients were dichotomously distributed in lower and higher H-scores (H-score cut-off: 22.35) for generating Kaplan-Meier curves and to perform log-rank testing and Cox proportional hazards models. All statistical tests were two-sided.
Results: In our independent validation cohort with 237 cores from 79 patients (97.4%) median overall survival of patients was reported with 30.6 months (95%CI, 23.27–36.82). Median survival for patients for low CatD expression in the validation cohort was 39.8 (95%CI, 19.06–49.11) months vs 26.10 (95%CI, 18.77–34.19) months for high CatD expression, $c^2_{LR,1DF} = 5.3$; $p = 0.02$ confirming our null hypothesis. Multivariate analysis with sex, lymph node status, tumor staging and Cathepsin D expression revealed CatD expression as independent predictive marker in gemcitabine treated patients with a hazard ratio of 2.02 (95% CI, 1.03–3.97, $p = 0.04$).
Conclusion: Subject to prospective validation within a randomized trial, gemcitabine is less effective for patients with high CatD expression and could serve as a stratification marker for biomarker driven pancreatic cancer therapy.
Disclosure: Nothing to disclose

P0732 THE IMPORTANCE OF BIOMARKERS IN EARLY DIAGNOSIS OF PANCREATIC CANCER: GLYPICAN 1

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Introduction: Pancreatic cancer (PC) is one of the most important life-threatening cancers all over the world. It is ranked fourth in deaths from cancer. In case it is diagnosed early, albeit it is infrequent, there would be a chance of long-term life expectancy. Glypican (GPC) 1 is a cell membrane protein that have an important role in oncogenesis. We aimed to investigate if there is a role for GPC1 in the diagnosis of PC.
Aims and Methods: Pancreatic cancer patients who were operated between January 2016 and January 2017 in our center and healty volunteers were included in the study. Blood samples were taken. centrifuged and stored at −80° until GPC1 measurement. ELISA and RT-PCR were used in measurement. Mann Whitney U test and Chi-square tests were used to compare the groups. Optimal cut-off value for diagnosis was calculated.
Results: Fifty patients with pancreatic cancer and 50 healthy individuals enrolled. Patients with pancreatic cancer were found to have an average protein content of 101.24 ng / ml and healthy subjects had an average protein content of 92.68 ng / ml. The optimal cut-off vale was 96.6 ng/ml. In according ROC curve sensitivity was 83.1% and specificity was 74.0%.
Conclusion: GPC 1 level was significantly higher in patients with pancreatic cancer. Considering the moderate sensitivity and specificty, it is yet to be a perfect marker. However it seems promising in comparison to existing markers. Its levels in cyst fluids may provide better prediction that is the subject of a study we are currently pursuing.
Disclosure: Nothing to disclose

P0733 RINT1 IS ESSENTIAL TO PANCREATIC DUCTAL ADENOCARCINOMA (PDAC) HOMEOSTASIS

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Introduction: The diagnosis of pancreatic ductal adenocarcinoma (PDAC) is associated with high mortality rates. High numbers of oncogenic mutations are commonly found. RINT1 (RAD50-interacting protein 1) is a multifunctional protein playing a role in cell cycle regulation, genomic stability, telomere maintenance, ER-Golgi trafficking and autophagy. All factors that are of high relevance in PDAC homeostasis.
Aims and Methods: Here we aim to decipher the role of RINT1 in PDAC, by in-depth characterization of primary PDAC cell lines.
Results: We can show that RINT1-depletion in PDAC cell lines leads to severe growth defects associated with massive Golgi fragmentation and G2/M cell cycle arrest leading to genomic instability. These data suggest that RINT1 homeostasis is essential for PDAC survival and represents therefore a putative therapeutic target. To characterize more in details the mechanisms of RINT1 regulation and to ultimately identify RINT1-dependent pathways that could be targeted in PDAC, we performed an extensive interaction study through yeast-two hybrid assay and mass spectrometry. We discovered hundreds of new RINT1-interaction partners including proteins involved in mitotic events supporting our preliminary data indicating an increase in genomic instability in PDAC cell lines. Moreover, we identified E3 ligases interacting with RINT1 allowing a better understanding of RINT1 biological function. In addition, we identify several post-translational modifications including ubiquitination and sumoylation and demonstrated that ubiquitination is a key regulator of RINT1 stability and biological function.
Conclusion: The data presented reveals a key role of RINT1 in PDAC homeostasis and identified multiple RINT1-post-translational modifications and protein-protein interaction partners that could be targeted in novel therapeutic approaches.
Disclosure: Nothing to disclose

P0734 PANCREATIC CANCER AND PANCREATIC PRE-MALIGN LESIONS HAVE DISTINCT POLYAMINE PROFILE

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Introduction: Recently ion mobility spectrometry-based electronic nose has been shown to detect pancreatic cancer from urine (1). Until now it is not known which volatile compounds in urine are specific for pancreatic cancer. Polyamines are volatile organic compounds with strong odour and play important roles in cell proliferation, signaling, gene expression, apoptosis and organ development. Urine polyamine concentrations increase in malignant and proliferating cells (2).
Aims and Methods: To determine if pancreatic cancer can be detected from urine sample by quantitative analysis of urinary polyamines with liquid tandem mass spectrometry (LC-MS/MS).
For a proof-of-concept study in two Finnish hospitals, patients with pancreatic cancer, pancreatic pre-malign lesions, acute pancreatitis and chronic pancreatitis were prospectively recruited between January 2014 and June 2016. Patients provided urine sample at the time of the diagnosis. Controls were patients undergoing hernia reparation or elective cholecystectomy and were recruited during the same time period. Midstream urine was collected before the operation and stored in −70C° until analysis the urinary concentration of 14 polyamines including their mono- and diacetylated forms in a single run with LC-MS/MS (3). To our knowledge, this is the widest panel of polyamines analysed in a single run. Results were calculated as both absolute concentration and urinary creatinine-normalized concentration. To find optimal polyamine profiles for detection of cancer, the data was analyzed with linear discriminant analysis and cross-validated with leave-one-out cross-validation.
Results: 82 patients with pancreatic cancer, 36 with acute pancreatitis, 17 with chronic pancreatitis and 8 with pre-malign pancreatic lesion and 44 controls were recruited. 72% had stage III-IV pancreatic cancer and 27% went to radical pancreatectomy. A profile of five specific polyamines in urine putrescine,

acetylputrescine, spermide, diacetylpermide, cadaverine, and spermine distinguished pancreatic cancer from controls with a sensitivity of 79% and specificity of 79% and area under curve (AUC) was 0.86. We also compared pancreatic cancer and pancreatic pre-malign lesions with controls when LC-MS/MS revealed a sensitivity of 80% and specificity of 83% and AUC was 0.88.
Conclusion: We specified urine volatile compounds associated with pancreatic cancer and pancreatic pre-malign lesions. This novel finding has important implications when developing a non-invasive test for early diagnosis of pancreatic cancer.
Disclosure: Nothing to disclose

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P0735 PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY ASSESSMENT OF PANCREATIC DUCTAL ADENOCARCINOMA, N EX-VIVO STUDY WITH PATHOLOGICAL CORRELATION

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Introduction: Pancreatic ductal adenocacinoma (PDAC) is one of the most aggresive tumors, with a five-year survival rate of less than 5%. Probe based confocal laser endomicroscopy (pCLE), with various miniprobes available is being used as a prehistopathological tool for different types of lesions. However, in PDAC there is limited experience in imaging studies.
Aims and Methods: *Ex-vivo* freshly surgical removed PDAC specimens were assessed using pCLE and then processed for paraffin embeding and histopathological diagnostic on a pursuit of delivering new methods of assessing and differentiating pancreatic adenocarcinoma from other structures Twelve patients diagnosed with PDAC on endoscopic ultrasound and FNA confirmation underwent surgery. Removed samples from each patient were selected and sprayed with acriflavine as contrast agent, underwent pCLE with an experimental probe and compared with previous recordings of normal pancreas. Consecutively, all samples were subjected to cross-sectional histopathology, including surgical resection margins for controls. pCLE records, as well as anti-mesothelin Alexa488 labelled antibody corespondant and cytokeratin-targeted immunohistochemistry were processed on Image ProPlus AMS image analysis software.
Results: After histopathological confirmation of adenocarcinoma areas, on mesothelin fragments the proliferating ducts were clearly expressed, compared to no signal in the normal ducts and acini. On cytokeratin immunohistochemistry and pCLE correspondants the morphological classifiers clearly differentiated between tumor and non tumor areas.
Conclusion: Our study confirms that pCLE imaging might be used to differentiate between tumor and non tumor tissue with similar correspondant when using mesothelin antibody or cytokeratin immunohistochemistry imaging classifiers. This enhances the potential of chosing pCLE as a potential tool for future *in-vivo* studies for live diagnosis.
Disclosure: Nothing to disclose

P0736 PANCREATIC CYST SURVEILLANCE IMPOSES LOW PSYCHOLOGICAL BURDEN: PRELIMINARY RESULTS OF THE PACYFIC STUDY

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Introduction: Neoplastic pancreatic cysts are identified with increasing frequency, mainly as incidental findings. Because some have malignant potential, yearly lifelong surveillance is globally recommended and executed, even though evidence on effectiveness is lacking. A prerequisite for any surveillance program to be feasible is adherence, in which psychosocial aspects play an important role. However, the impact of such intensive surveillance on participants and their willingness to participate has hardly been studied.
Aims and Methods: To evaluate the perception and psychological burden of pancreatic cyst surveillance from a participant's perspective.
The present patient survey is part of an international cohort study (PACYFIC study, www.pacyfic.net), which prospectively records the outcome of pancreatic cyst surveillance. Participants with a newly diagnosed pancreatic cyst (<6 months) are invited to complete questionnaires after diagnosis (baseline) and each subsequent control visit (follow-up). The questionnaires contain the Hospital Anxiety and Depression Scale (HADS, with both subscale scores ranging from 0–21 and a score <7 indicating a low level of anxiety or depression) and questions concerning patients' perception of surveillance and wishes regarding follow-up frequency and duration.
Results: 103 patients with a newly diagnosed cyst returned the baseline questionnaire (median age 69 years (IQR 62–76), 35% male). 86 participants (84%) agreed or strongly agreed that surveillance reduces their concerns about pancreatic cancer and 81 (80%) confirmed that it contributes to their sense of security. Although 26 participants (25%) reported that it leads to worries and 23 (22%) found it burdensome, almost all (99 respondents, 96%) agreed that the advantages outweigh the disadvantages 'somewhat', 'rather' or 'very much'. The majority (77 participants, 75%) wanted surveillance to continue for the rest of their lives, with a yearly or even 6-monthly frequency.
In the 20 patients who already completed a second questionnaire, median HADS scores (2 for anxiety (IQR 1–6.75) and 2 for depression (IQR 0–5.75)) were unaffected by the follow-up visit ($p = 0.551$ for anxiety and $p = 0.487$ for depression, paired T-test).
Conclusion: The majority of respondents reported a highly positive attitude towards pancreatic cyst surveillance. HADS scores were low to begin with and appear unaffected by subsequent follow-up, presuming a low psychological burden. Based on these preliminary results, the adherence in a pancreatic cyst surveillance program is predicted to be high, and annual surveillance such as currently recommended in the guidelines seems feasible.
Disclosure: Nothing to disclose

P0737 PANCREATIC DUCTAL ADENOCARCINOMA RESECTABILITY ASSESSMENT: WHAT ARE THE REALLY REQUIRED PREOPERATIVE IMAGING MODALITIES?

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Introduction: However, assessment of pancreatic ductal adenocarcinoma (PDAC) resectability relies on different preoperative imaging modalities, no consensus about the best approach has been reached so far [1].
Aims and Methods: We aimed to evaluate the diagnostic efficacy of different imaging modalities in the preoperative resectability assessment of non-metastatic PDAC.

A retrospective comparative study including non-metastatic PDAC patients who were subjected to surgery at Nagasaki University Hospital between January 2014 and December 2017. Data obtained by different preoperative imaging modalities including contrast enhanced computed tomography (CECT), magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) were compared with the final postoperative pathologic diagnosis. The included parameters for comparison were: tumor size, common bile duct (CBD)/gall bladder (GB) invasion, duodenal wall (DU) invasion, regional lymph node (LN) spread, adjacent organs infiltration including stomach, colon, spleen, left adrenal, retroperitoneal fat and coeliac plexus, portal vein (PV) invasion/encasement, arterial (ART) invasion/encasement including coeliac artery (CA), hepatic artery (HA) and superior mesenteric artery (SMA), and the overall tumor resectability. Sensitivity, specificity, PPV, NPV and diagnostic accuracy (DA) with the corresponding 95% confidence interval (95% CI) were calculated for each individual imaging modality. Tumor invading the PV, CA, HA and SMA was defined as unresectable. When the lesion was assessed as resectable by the imaging modality, the test was defined as positive.

Results: A total of 64 PDAC patients, 28 females, with mean age 70 years ± 7 was included. Tumor size assessment was more accurate by EUS than CECT and MRI with DAs of 65% (CI: 41–85), 61% (CI: 46–74) and 59% (CI: 39–76) respectively. For CBD/GB infiltration, EUS was superior than MRI and CECT with DAs of 95% (CI: 75–99), 83% (CI: 64–94) and 78% (CI: 65–89) respectively, while for assessing DU infiltration, CECT had the best DA of 74% (CI: 60–85) versus 70% (CI: 46–88) for EUS and 65% (CI: 46–82) for MRI. All modalities had 100% specificity and PPV for ruling in adjacent organ infiltration, but the DAs was very low: 34% (CI: 18–54) for MRI, 29% (CI: 17–44) for CECT and 15% (CI: 3–38) for EUS. For evaluation of regional LN affection, CECT had the highest specificity (90%, CI: 68–99) and PPV (82%, CI: 52–95) while MRI had the highest sensitivity (31%, CI: 11–59) and NPV (50%, CI: 40–60), with comparable DAs of 53% (CI: 38–67), 55% (CI: 36–73) and 55% (CI: 31–77) for CECT, MRI and EUS respectively. Compared to CECT and MRI, EUS was the best modality for ruling in PV invasion and ART invasion. For PV invasion, DA of EUS, CECT and MRI was 89% (CI: 65–99), 80% (CI: 67–90) and 76% (CI: 56–90) respectively, while that for ART invasion was 89% (CI: 67–99), 88% (CI: 76–95) and 73% (CI: 67–89) respectively. For the overall resectability assessment, EUS had the highest DA of 85% (CI: 62–97), the lowest overstaging rate (0%) and the lowest understaging rate (15%) versus 76% (CI: 62–87), 5.8% and 17.6% for CECT, and 72% (CI: 53–87), 6.8% and 20.6% for MRI respectively. Our study was a retrospective one on a small number of patients and it did not include a cost minimization analysis.

Conclusion: For non-metastatic PDAC, CECT is the most useful preoperative imaging modality for assessing DU infiltration and ruling in regional LN spread, while EUS is the best modality for assessing tumor size, CBD/GB infiltration and the overall tumor resectability with the lowest overstaging and understaging rates.

Disclosure: Nothing to disclose

Reference

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P0738 PROGNOSTIC SIGNIFICANCE OF ADIPOSE TISSUE-DERIVED HORMONS IN PANCREATIC CANCER PATIENTS

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Introduction: Evidence is increasing that various obesity-related cancers are associated with changed plasma levels of adipokine-derived hormons. We recently demonstrated an association between adiponectin levels and tumor stage in patients with pancreatic cancer (PC) suggesting its potential role in risk prediction and tumor proliferation. However, the prognostic role of adipokines in PC patients has not been well studied before.

Aims and Methods: The aims of the study were to analyze the possible associations between adipokines and clinicopathological parameters of PC patients and to investigate their potential role as prognostic indicators of PC disease.

Baseline levels of serum adiponectin and leptin were determined in 51 consecutive patients with PC and followed up for the median period of 2 years.51 Control subjects were matched to case patients by age, sex and BMI. The association between variables were evaluated using nonparametric Spearman's correlation test. Receiver operating characteristics (ROC) analysis was employed to calculate the area under the curve (AUC). Survival analysis used the Kaplan-Meier curve and the Cox proportional hazards model.

Results: In PC patients serum leptin levels were higher than i controls ($p < 0.0001$); adiponectin levels were lower than in controls ($p < 0.001$) and inversely correlated with tumor size ($rho = -0.834$, $p < 0.01$). Leptin levels were inversely correlated with adiponectin levels ($rho = -0.727$,$p < 0.01$). Thus, leptin concentrations were corrected by adiponectin values (L/A ratio). At ROC analysis the diagnostic profile of L/A (AUC 0.874; sensitivity 84%;specificity 80%) in detecting pancreatic cancer stage was superior to that of leptin alone (AUC 0.675;sensitivity 86%;specificity 50%). High L/A ratio was the only independent predictor of metastatic disease ($beta = 0.112$,$p = 0.03$). Kaplan-Meier global survival analysis revealed a low L/A ratio was associated with an increased survival compared to patients with high L/A ratio (Cox F test = 2.788, $p < 0.05$).

Conclusion: This study identified, for the first time, that the combined measurement of leptin and adiponectin (L/A ratio) might represent a better prognostic indicator than individual parameters in patients with PC. Our results support the hypothesis linking adipose-tissue derived hormon levels to tumor growth and progression of obesity-associated cancers.

Disclosure: Nothing to disclose

P0739 K-RAS MUTATION ANALYSIS BY DIGITAL PCR IN EUS-GUIDED FNA CYTOLOGY SPECIMENS AND CTDNA IMPROVE PANCREATIC CANCER DIAGNOSIS

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Introduction: Pancreatic cancer is a dismal disease and the fourth leading cause of cancer-related death in western countries. Novel methods for early diagnosis is the necessary path forward to improve the situation for patients with pancreatic cancer. Our primary aim in this study is to explore the possibility of detecting the K-ras gene mutation to supplement histo/cytopathologic evaluation of pancreatic masses. Our secondary aims of the current study were to compare the quantities of K-ras mutation of ctDNA in the circulation with FNA tissue samples in pancreatic mass of the same patients and investigate the prognostic value of K-ras gene mutation in advanced pancreatic adenocarcinoma.

Aims and Methods: Our study comprised 149 consecutive patients who underwent EUS-FNA of pancreatic solid masses between September 2014 and May 2016 at the Endoscopy Center of Tongji Hospital. After lesions were identified by EUS; aspirated samples were separated into 2 parts each for cyto/histopathological evaluation and K-ras point mutation analysis. ctDNA in serum was extracted from cell-free ctDNA in serum blood samples from these patients. We used droplet digital PCR (ddPCR) to analyse K-ras mutations (G12V, G12D, and G12R). The final diagnosis was based on pathological examinations of specimens obtained by surgical resection or following up for at least 2 years.

Results: We prospectively evaluated 149 patients, including 105 pancreatic ductal adenocarcinoma (PDAC) patients [age 58.38 ± 11.01 years; male 69/105 (65.71%)] and 44 cases with non-malignant pancreatic masses [age 52.66 ± 13.81 years; male 36/44 (81.82%)]. The sensitivity, specificity, PPV, NPV, and accuracy of the cyto/histopathological examination alone were 71.4%, 86.4%, 92.6%, 55.9% and 75.8%, respectively, whereas these values of the K-ras mutation ddPCR analysis combined with Cyto/histopathological analysis were 93.3%, 79.1%, 91.6%, 82.9% and 88.6%, respectively. The sensitivity and accuracy of EUS-FNA increased by 21.9% ($p < 0.001$) and 12.8% ($p < 0.001$), respectively, when K-ras mutation ddPCR analysis was added to standard cyto/histopathological assessment. Aiming for further investigation in a non-invasive method in highly sensitive detection of KRAS mutations, we evaluated K-ras mutation ddPCR analysis of ctDNA in all matched plasma samples. We identified KRAS mutations in 56.2% of the ctDNA in plasma samples from patients with pancreatic cancer. 26.3% of the plasma ctDNA were positive for G12D, 8% for G12V, and 3.5% for G12R. The sensitivity and accuracy of combined KRAS mutations in plasma ctDNA and CA1-19 were 78.9% and 76.2%, respectively. The median survival time was significantly shorter in patients with G12D mutations (180 days) compared with patients with other mutations (240 days) in their EUS-FNA tissue samples and ctDNA sample (long-rank test, $p = 0.001$ and $p = 0.0008$, respectively). Multivariate analysis demonstrated that both G12D mutation in EUS-FNA tissue samples (HR, 0.495, 95% CI, 0.325–0.753, $p = 0.0010$) and ctDNA (HR, 0.417, 95% CI, 0.199–0.870, $p = 0.0199$) were independently associated with poor overall survival.

Conclusion: We observed that combining K-ras mutation qPCR analysis and histo-/cytopathological findings increases the accuracy in diagnosing pancreatic cancer. The K-ras mutation in plasma ctDNA complements the use of other diagnostic techniques in the diagnosis of pancreatic cancer in clinical practice. G12D mutation in EUS-FNA tissue samples and ctDNA were independent risk factors for poor prognosis of pancreatic cancer.

Disclosure: Nothing to disclose

P0740 COST-EFFECTIVENESS OF PANCREATIC CANCER SURVEILLANCE IN HIGH-RISK INDIVIDUALS: AN ECONOMIC ANALYSIS

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Introduction: Surveillance of high-risk individuals (HRI) with magnetic resonance (MRI) or endoscopic ultrasound (EUS) can detect resectable pancreatic cancer (PC) and may reduce cancer-related mortality. There is controversy whether systematic screening and surveillance is cost-effective or not.

Aims and Methods: We aim to perform an economic analysis to identify the different clinical and cost determinants of PC screening in HRI. Three strategies

Abstract No: P0740

		No screening	*EUS-based screening*	*MRI-based screening*
Baseline: Higher risk of PC Relative risk : 5–120	Cost (U.S. dollars)	$54,741	$47,750	$27,617
	Effectiveness (QALYs gained)	19.477	21.225	21.532
	ICER ($/QALY)	-	$13,200	Dominant strategey
Highest risk of PC Relative risk : >20	Cost (U.S. dollars)	$110,441	$64,875	$66,639
	Effectiveness (QALYs gained)	14.815	20.622	20.010
	ICER ($/QALY)	-	Dominant strategy	$7,847

[Incremental cost-effectiveness ratios (ICER) for pancreatic cancer screening in high-risk individuals]

were compared: no screening, EUS-based screening and MRI-based screening. A Markov model was created with yearly interventions starting at age 40. Patients were considered HRI according to the Cancer of the Pancreas Screening (CAPS) consortium recommendations. Average lifetime risk for developing PC, survival and cost of care data were obtained from SEER Cancer Prevalence and Cost of Care Projections database and from Center for Medicare Services data. Screening effectiveness (i.e. adenocarcinoma and high-risk dysplasia cases detected) was obtained from a recent systematic review. EUS and MRI sensitivity, specificity and probabilities of developing complications after surgical or medical treatment were obtained from published literature. Only direct costs were considered. Outcomes were adjusted for utility indices with discounting.

Results: Baseline analysis of a cohort with five-fold relative risk (RR) of PC higher than the general U.S. population showed that MRI screening is the cheapest strategy and yielded highest QALYs. While this was valid for conditions with relative risk of PC < 20 (i.e. familial pancreatic cancer with 1 or 2 first degree relatives (FDR) affected, HNPCC syndrome, FAP and BRCA2 mutations), for those with the highest relative risk (≥ 3 FDR, hereditary pancreatitis, Peutz-Jeghers, and CDKN2A mutations (p16)), EUS became the dominant strategy (Table).

Sensitivity analyses showed that the model is impacted by cost and imaging performance, but still cost-effective within the range reported in published literature. Threshold analysis in the baseline scenario showed that if MRI cost is > $1,600, EUS becomes more cost-effective. Once patients reached 76 years 'no screening' was the favored strategy.

In the Monte Carlo simulation over the lifetime of the baseline cohort; 443 (12% resectable), 130 (40% resectable) and 127 (51% resectable) patients developed PC under no screening, EUS and MRI screening strategies, respectively. A relative risk reduction of 70% and a number needed-to-screen of 32 (95% CI, 27–38) were seen in both imaging strategies. The screening strategies were cost-effective in the vast majority of simulation trials over a wide range of willingness to pay.

Conclusion: Surveillance of HRI for pancreatic adenocarcinoma is cost-effective favoring MRI over EUS in moderate risk cases but EUS-based screening in those with highest relative risk. Screening should be offered starting at age 40 until 75 years old.

Disclosure: Nothing to disclose

P0741 IMPACT OF INCONCLUSIVE OR NEGATIVE ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION RESULTS IN THE MANAGEMENT OF SUSPICIOUS SOLID PANCREATIC MASSES

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Introduction: Endoscopic ultrasound (EUS) plays a key role in the evaluation of solid pancreatic masses, obtaining tissue for diagnosis through EUS-fine needle aspiration (EUS-FNA). However, the diagnostic accuracy is variable, with relatively high rate of inconclusive results after the first EUS-FNA.

There are currently no consensus regarding the best diagnostic method after negative or inconclusive EUS-FNA of a highly suspicious solid pancreatic mass.

Aims and Methods: The aim of this study was to evaluate the diagnostic methods and predictive factors of malignancy after a negative or inconclusive EUS-FNA of a highly suspicious solid pancreatic mass.

Retrospective study of all cases of EUS-FNA of highly suspicious solid pancreatic masses in a tertiary center (from Jan/2012 to Dez/2016), with inconclusive or negative result for malignancy.

Results: We included 118 EUS-FNA in a total of 277 EUS-FNA, of 85 patients, 65.9% male, with mean age of 60,31 ± 14,27 years. The majority of the pancreatic masses were located in the head (56.8%) and 54.2% had an estimated size between 2 and 4 cm.

The mean number of passes were 3.0 (+/−1.4) and the most common needle size was 25G (55.9%).

Ninety-four (79.7%) of the 118 EUS-FNA were inconclusive and the other 24 EUS-FNA were negative for malignancy. After this result, 41.5% repeated EUS-FNA, 17.8% underwent surgical exploration, 16.1% kept in close follow-up and 13.6% were referred to palliative care.

More than 3 passes in EUS-FNA was statistically associated with malignancy (p = 0.022), as well as higher values of CA 19.9 (p = 0.025). The size of the lesion was statistically associated with obtaining tissue for diagnosis (p = 0.016).

After a first negative/inconclusive EUS-FNA, 72% of the cases were diagnosed as malignant (75.4% as pancreatic adenocarcinoma), being EUS-FNA and surgery the main methods for the diagnosis. Seven patients (33%) that were submitted to surgery due to high suspicion of malignancy, revealed benign lesions.

Conclusion: EUS-FNA is the best method for the evaluation of pancreatic solid masses. However, in some cases, EUS-FNA does not lead to conclusive cytological diagnosis.

After a negative or inconclusive EUS-FNA of a highly suspicious solid pancreatic mass EUS-FNA appears a reasonable choice to achieve the definite diagnosis.

Disclosure: Nothing to disclose

P0742 SURVIVAL TRENDS FOR RESECTABLE PANCREATIC CANCER USING A MULTIDISCIPLINARY CONFERENCE

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Introduction: Patients with resectable pancreatic ductal adenocarcinoma (PDA) have improved survival compared to unresectable PDA. It has been shown that multidisciplinary pancreas cancer conferences (MDPC) implementation results in selection of candidates for surgery with higher stage PDA compared to patients not presented at MDPC. In addition, patients are taken to surgery earlier through MDPC management. Rates of survival after MDPC management is limited.

Aims and Methods: We aim to determine survival of resectable pancreas cancer of patients that underwent pancreatic resection after consensus from a MDPC and assess the parameters on survival time. A total of 64 patients in a MDPC group underwent upfront surgical resection from May 2013 to August 2016 at an experienced surgical PDA center. Patients were followed prospectively till November 2017 and rates of survival from the date of surgical resection were recorded. Survival analysis was performed using Kaplan Meier for age, tumor size, tumor differentiation, T-Stage and lymph node status. Log-rank tests were used to compare the difference on survival time. Independent predictors of survival were determined using Cox model. Proportional hazard assumptions were checked and a p-value < 0.05 was considered statistically significant.

Results: 64 patients were identified with successful resection of PDA. The majority (61) had a Whipple's procedure, and 3 had pancreatectomy. The average age of the Whipple's group was 69.1 years ± 10.1. 1-year survival was 78.13%, 2-year survival was 46.30% and 3-year survival was 27.27%. Overall, survival times after surgery were different according to age group (p = 0.01), tumor size (p = 0.002), tumor differentiation (p = 0.05), T-Stage (p = 0.008) and lymph node status (p = 0.001). Tumor size (p = 0.002) and lymph node status (p = 0.008) remained statistically significant after multivariate Cox regression model with all the variables included. The largest tumor size (≥50mm) had almost 53 fold mortality risk compared to patients with smaller size (<20mm). Patients with N1 lymph node status had more than 3-fold mortality risk compared to patients with N0 lymph node status.

Conclusion: Survival trends following resected PDA were followed after consensus from an experienced MDPC. Log-rank test revealed that age, tumor size, tumor differentiation, T-stage, and lymph node involvement can influence the survival pattern in the years following surgery. Tumor size and lymph node involvement were the only significant predictors of mortality. This study suggests that patients with PDA with tumor size ≥ 50 mm and/or lymph node involvement have poor survival despite being surgically resectable. Consideration for alternative management such as down-staging with neoadjuvant therapy should be investigated.

Disclosure: Nothing to disclose

Abstract No: 0742

Parameter	p-value	Hazard Ratio (HR)	95% HR Confidence Lower Limit	95% HR Confidence Upper Limit
Age 60–69	0.8219	0.877	0.280	2.745
Age 70–79	0.6140	1.313	0.455	3.790
Age ≥ 80	0.1441	2.808	0.703	11.225
Tumor Size 20–29 mm	0.1272	7.291	0.568	93.659
Tumor Size 30–39 mm	0.2378	5.109	0.341	76.628
Tumor Size 40–49 mm	0.1244	8.031	0.563	114.458
Tumor Size ≥ 50	0.0043	53.724	3.478	829.890
Moderate Differentiated Tumor	0.1939	0.551	0.224	1.354
Well Differentiated Tumor	0.8535	1.226	0.141	10.661
T2-Stage	0.2689	0.208	0.013	3.366
T3-Stage	0.1624	0.161	0.012	2.085
T4-Stage	0.2202	0.124	0.004	3.489
Lymph Node Status (N1 vs N0)	0.0077	3.437	1.386	8.523

[Multivariate Cox regression Model Estimates]

P0743 A COMPOSITE LIQUID BIOMARKER FOR NON-INVASIVE DIAGNOSIS OF RESECTABLE PANCREATIC DUCTAL ADENOCARCINOMA

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) has a dismal prognosis. Biomarkers are needed to facilitate early and preferably noninvasive detection of PDAC, which may enable early diagnosis and therefore influence patients' prognosis. Circulating tumor DNA (ctDNA) was examined several times in metastatic PDAC. Its value in resectable disease with lower tumor load has not been sufficiently analyzed. CA19-9 is used as a serum marker to assess disease progression in PDAC patients but is not recommended for general screening due to lack of sensitivity and specificity. Recently it has been reported that elevated levels of thrombospondin-2 (THBS2) protein are detectable in several stages of PDAC. Here we aimed at improving sensitivity and specificity of THBS2-based detection of early PDAC by combining THBS2 analysis with further markers.
Aims and Methods: 39 patients with histologically or cytologically proven PDAC, which were enrolled to the NEONAX trial (Neoadjuvant plus adjuvant or only adjuvant nab-Paclitaxel plus Gemcitabine for resectable pancreatic cancer, clinical trial identifier: NCT02047513), were selected for this study-independent retrospective translational analysis. Mean age was 67 ± 10 years, gender 19 female/20 male, mean tumor size 31 ± 12mm, primary tumor location 27 head, 7 body, 2 tail, 1 body/tail, 2 not determined. 15 patients with benign pancreatic disease (intraductal papillary-mucinous neoplasms, IPMN) served as controls. Mean age of the IPMN-cohort was 66 ± 13 years; mean tumor size 11 ± 6 mm; location 4 head/body/tail, 6 head/body, 3 body/tail, 2 tail; gender 10 female/5 male. Blood samples were collected at the time point of disease diagnosis. Plasma was separated within 1 hour after blood draw and stored at $-80°C$ until further analyses. *KRAS* genotyping was performed after isolation of ctDNA (QIAamp MinElute ccfDNA Kit, Qiagen) by digital droplet PCR (QX200 system, Bio-Rad) for the 7 most frequently occurring *KRAS* mutations in PDAC (*KRAS* G12A, G12C, G12D, G12R, G12S, G12V, G13D; ddPCR™ KRAS Screening Multiplex Kit, Bio-Rad). Clinical data and CA 19-9 levels of PDAC and IPMN cohort were routinely assessed at initial disease diagnosis by ELISA (Roche, threshold 55 U/ml). The levels of THBS2 were assessed by Quantikine ELISA Human Thrombospondin-2, R&D Systems (threshold: 42 ng/ml). Statistical analyses followed a descriptive, hypothesis-generating approach and were done by using GraphPad Prism Version 7.00, GraphPad Software Inc.
Results: Median cfDNA level in plasma of PDAC patients (12.6 ng/ml, range: 1.1–270) was significantly higher ($p = 0.0006$, Mann-Whitney) than that of the IPMN cohort (5.5ng/ml, range: 1.7–12.6). Only 2/39 PDAC patients (5%) and 1/15 IPMN patients (6%) had *KRAS* mutations in ctDNA detectable by highly sensitive ddPCR. CA19-9 level was elevated in 22/39 PDAC patients (56%) and in none of the IPMN patients. THBS2 was elevated in 17/39 PDAC patients (44%) and in none of the IPMN patients. In contrast, parallel assessment of both, THBS2 and CA19-9 levels, was found to be most suitable to discriminate the PDAC% cohort from the IPMN cohort, with a sensitivity of 77% and a specificity of 100%.
Conclusion: THBS2 and CA19-9 panel assessed in human blood using a conventional ELISA assay may improve the definition of pancreatic lesions as PDAC even at early stages of disease. While total cfDNA amount differs between patients with benign and malignant pancreatic lesions, ctDNA genotyping for *KRAS* mutations failed to improve non-invasive diagnostic strategies in resectable PDAC most likely due to a low tumor load.
Disclosure: Nothing to disclose

P0744 EARLY DETECTION OF PANCREATIC CANCER IN PATIENTS WITH CHRONIC LIVER DISEASE UNDER SURVEILLANCE FOR HEPATOCELLULAR CARCINOMA: A RETROSPECTIVE COHORT STUDY FROM JAPAN

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Introduction: Pancreatic cancer (PC) is a deadly disease typically diagnosed at advanced stages and its prognosis is the worst among various cancers (5-yr survival 5–10%) due to the lack of an algorithm to diagnose the disease at an early stage. Recent study showed detection of a dilated pancreatic duct or cystic pancreas lesions may facilitate an early diagnosis. Patients with chronic liver disease caused by the hepatitis B virus (HBV) or hepatitis C virus (HCV) have an increased risk of developing hepatocellular carcinoma (HCC). Thus, the guidelines strongly recommend that these patients routinely undergo abdominal imaging surveillance for HCC, regardless of whether they have symptoms.
Aims and Methods: This study aimed to evaluate whether patients with HBV- and HCV-related chronic liver disease were diagnosed with PC at early stages during abdominal imaging surveillance for HCC. This retrospective study examined 520 consecutive patients with PC who were diagnosed at the Ehime University Hospital and its affiliated centers (including a cancer institute, tertiary care hospital, and community hospital) between 2011 and 2013. Data were collected regarding HBV and HCV status, likelihood of PC diagnosis, and Union for International Cancer Control (UICC) stage. Based on the aim of the present study, 73 patients without test results for viral hepatitis markers were excluded. The chi-square test and Student's t-test were used for statistical analysis, where appropriate. Outcomes were analyzed using the Kaplan-Meier method and Cox proportional hazards regression. Differences in survival analyses were determined using the log-rank test. Local ethic boards approved the study but written consent form was waived due to the retrospective manner.
Results: The cohort included 447 patients (240 men and 207 women) with PC, who had a mean age of 72 ± 10 years (range: 33–91 years). Forty-five patients (10.0%) were positive for either HBsAg (N = 18, 4.0%) or anti-HCV (N = 27, 6.0%), although none of them had coinfection. Among the 45 patients, 26 patients had newly diagnosed HBV/HCV infections at the PC diagnosis. Among the other 19 patients, 16 patients were undergoing periodical HCC surveillance, based on HBV- or HCV-related chronic liver disease, at their PC diagnosis (the HCC surveillance group). The UICC stage distribution among the HCC surveillance group (N = 16) was stage 0 (N = 2, 12.5%), stage IA (N = 3, 18.8%), stage IB (N = 2, 12.5%), stage IIA (N = 2, 12.5%), stage IIB (N = 1, 6.3%), stage III (N = 2, 12.5%), and stage IV (N = 4, 25%). The UICC stage distribution among the non-surveillance group (N = 431) was stage 0 (N = 4, 0.9%), stage IA (N = 28, 6.5%), stage IB (N = 27, 6.3%), stage IIA

(N = 86, 20.0%), stage IIB (N = 48, 11.1%), stage III (N = 56, 13.0%), and stage IV (N = 182 patients, 42.2%). The HCC surveillance group had significantly more patients with stage 0 disease, compared to stages IA-IV (p = 0.0166). A dilated pancreatic duct led to the diagnosis of PC in all 6 patients with stage 0 disease. Similar results were observed for cut-offs of stage IA (p = 0.0066) and stage IB (p = 0.0043), but not stage IIA (p = 0.1042).
Conclusion: Patients with HBV- and HCV-related chronic liver disease had an early diagnosis of PC during HCC surveillance. Careful evaluation of the pancreas is warranted during HCC surveillance.
Disclosure: Nothing to disclose

P0745 IMAGING AND HISTOLOGICAL DIAGNOSTIC ABILITY OF PANCREATIC NEUROENDOCRINE NEOPLASMS LESS THAN 20 MM IN SIZE

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Introduction: For diagnosis of pancreatic neuroendocrine neoplasms (PNENs), the usefulness of various imaging examinations has been reported. However, the diagnostic ability of imaging and pathological examinations for small lesions is uncertain.
Aims and Methods: The aim of this study was to examine the diagnostic ability of ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), endoscopic US (EUS)/EUS fine-needle aspiration (FNA) for PNENs < 20 mm in size. From April 2004 to December 2017, 93 patients with PNENs were treated in our hospital. Thirty-four patients (48 lesions) who underwent surgery after US, CT, MRI, and EUS/EUS-FNA and whose tumours had pathological diameters of < 20 mm were included this study. The primary endpoints were detectability of each imaging modalities and calculated the cut-off line of detectable size of PNENs and the secondary endpoint was accuracy of the pathological examinations and concordance rate of the World Health Organization (WHO) grade by EUS-FNA.
Results: Ten lesions were in the pancreatic head, and 38 were in the pancreatic body or tail. The median tumour diameter was 10 mm (2–20). Four lesions were functional PNENs, and 44 were non-functional PNENs. The pathological diagnosis was based on WHO classification, and 41 lesions were G1 and 7 were G2. We performed US for 46 lesions and detected 24 (52%). On CT, 38 lesions (79%) were observed. Thirty-six lesions were contrasted in the early phase, and 2 showed delayed enhancement. MRI revealed 29 lesions (60%), of which 26 showed high signal intensity in diffusion-weighted images. On EUS, 44 lesions (83%) were detected. The boundary was clear/unclear in 43/1 lesions, the surface was adjusted/irregular in 42/2, and the internal echogenic gain was hypoechoic/hyperechoic/isoechoic in 38/4/2.
The diameters of the 38 lesions detected on CT were all ≥ 5 mm, and lesions of < 5 mm could not be detected. The cut-off size of the detectable lesions in the receiver-operating characteristic curve analysis was 8 mm on US (sensitivity, 0.87; area under the curve [AUC], 0.82), 8 mm on MRI (sensitivity, 0.86; AUC, 0.84), and 3.5 mm on EUS (sensitivity, 0.95; AUC, 0.97). EUS-FNA was performed for 26 lesions, and 25 (96%) were diagnosed as PNEN. The Ki-67 index was evaluated for 23 lesions. Regarding the pathological classification of the FNA specimens, 17 lesions were G1 and 2 were difficult to assess. However, after surgery, 17 lesions were diagnosed as G1 and 6 as G2. In the analysis of pathological classifications, 16 lesions (70%) were properly assessed using FNA specimens.
Conclusion: The most useful examination for the diagnosis of small PNENs was EUS. Although the pathological diagnostic ability of EUS-FNA was high, the grading classification tended to be underestimated.
Disclosure: Nothing to disclose

P0746 IGF2BP RNA-BINDING PROTEINS: POTENTIAL REGULATORS OF EPIGENETIC FACTORS IN PANCREATIC NEUROENDOCRINE TUMOR-CELLS

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Introduction: Pancreatic neuroendocrine tumors (PNET) are highly angiogenic tumors which – despite of various systemic targeted options including mTOR and VEGF inhibition – frequently develop secondary drug resistance. IGF2BP (IGF2 mRNA-binding proteins) represent a family of RNA-binding proteins (RBP) comprised of three members (IGF2BP1-3) which have been described as potentially oncogenic factors in different solid tumors. As posttranscriptional regulators of gene expression they control the transport, translation and degradation of their target mRNAs, thereby influencing proliferation, migration and chemoresistance of tumor cells. However, the oncofetal proteins IGF2BP1 and IGF2BP3 are well known to be associated with highly aggressive carcinomas, e.g. pancreatic ductal adenocarcinoma (PDAC), but their role and function in PNETs is still unknown.
Aims and Methods: We aim to analyze the functional role and clinical potential of IGF2BPs in PNETs to identify novel therapeutic avenues overcoming therapy resistance. Thereby the methods RNA interference, Flow Cytometry, Migration-Assay, CFU, Western Blot, qRT-PCR, RNA-IP, RNA-decay were used.
Results: In the PNET cell line BON1, we observed an exuberant expression of IGF2BP1 and MYC. Remarkably, IGF2BP1 depletion in BON1 cells significantly extenuated cell proliferation, migration and colony formation by posttranscriptional reduction of c-MYC, PCNA, CCNE1, CCNA2, CCNB1 and the methyltransferase EZH2. Simultaneously, mRNA and protein levels of p21, p27 and BCL-2 were upregulated, resulting in a G1 cell cycle arrest. Interestingly, no sign of apoptosis, senescence or reduced viability where observed. Using RNA Immunoprecipitation (RIP) we could confirm binding of IGF2BP1 to the EZH2 mRNA as well as to its known target mRNA MYC. The posttranscriptional regulation of EZH2 and MYC could explain the derepression of cell cycle arrest genes and BCL-2 in BON1 cells. In contrast to our findings on IGF2BP1, the depletion of IGF2BP2 and IGF2BP3 had no effect on the oncogenic capacity of BON1 cells. These data on EZH2 indicate a novel signaling mechanism by which the RNA-binding protein IGF2BP1 regulates methyltransferase activity and thereby influences epigenetic repression systems.
Conclusion: Our findings suggest that IGF2BP1 acts as a posttranscriptional modulator of oncogenic and epigenetic factors in PNET-cells, thereby enhancing or sustaining oncogenic hallmarks in support of an aggressive and chemoresistant phenotype.
Disclosure: Nothing to disclose

P0747 EXENDIN-IRDYE700DX FOR PHOTODYNAMIC THERAPY OF GLP-1R POSITIVE LESIONS

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Introduction: Insulinoma and focal lesions in congenital hyperinsulinism (CHI) are GLP-1R positive lesions that are characterized by excessive insulin production and thereby causing severe hypoglycaemia. The therapy of choice is surgery, however, these surgical procedures are challenging because of the necessity to preserve as much healthy pancreatic tissue as possible and in some cases due to the localization of lesions near the ducts or large vessels. Targeted photodynamic therapy (tPDT) could provide selective destruction of tumour tissue without causing damage to surrounding tissues. The glucagon-like peptide-1 (GLP-1) analogue exendin specifically binds the GLP-1R expressed on pancreatic beta cells. GLP-1R imaging using ^{68}Ga-labelled exendin is a successful pre-operative imaging technique for insulinoma and is under investigation in CHI. We hypothesize that tPDT using exendin labelled with the near-infrared (NIR) sensitive photosensitizer IRDye700DX enables specific destruction of GLP-1R positive cells.
Aims and Methods: Exendin-IRDye700DX was characterized *in vitro* and *in vivo*. A competitive binding assay was performed using CHL-cells transfected with the GLP-1R. The feasibility of inducing specific cell death was assessed by incubating different cell-types (CHL-GLP-1R cells, INS-1 cells and PANC-1 cells) with 300 nM exendin-IRDye700DX and exposing them to various intensities of NIR LED light. Cell viability was measured using a cell titer glo assay. Tracer biodistribution was determined in BALB/c nude mice bearing subcutaneous GLP-1R positive tumours. To determine therapy response, tumours of 2 groups of mice (N = 8 per group, 1 group injected with 20 µg exendin-IRDye700DX and 1 control group injected with PBS) were exposed to 120 J/cm^2 of NIR LED light of 690 nm. Mice were sacrificed when tumours reached a size of 1000 cm^3.
Results: Exendin-IRDye700DX has a high affinity for the GLP-1R with an IC_{50} value of 6.3nM, which is comparable to unlabeled exendin. In CHL-GLP1R cells as well as INS-1 cells, NIR light reduced cell viability in a dose-dependent manner with 0% viability reached at 175 J/cm^2. PANC-1 cells, which do not express the GLP-1R remained 100% viable with this tracer dose and light-intensity. Injection of 0.3 µg exendin-IRDye700DX resulted in an *in vivo* tumour uptake of 12.8 ± 6.4%ID/g, which decreased with increasing peptide doses. The survival of mice treated by PDT with exendin-IRDye700DX was significantly increased compared to control mice ($p < 0.05$).
Conclusion: These data show *in vitro* as well as *in vivo* evidence for the efficacy of tPDT using exendin-IRDye700DX. This could be a promising new therapeutic option for GLP-1R positive lesions.
Disclosure: Nothing to disclose

P0748 LOCALIZATION OF INSULINOMAS WITH ^{68}GA-NODAGA-EXENDIN-4 PET/CT

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Introduction: Insulinomas are usually small, single benign tumors. Surgery is the therapy of choice and precise preoperative anatomical localization of the tumor is essential. Imaging techniques like CT, MRI as well as somatostatin receptor (SSTR) imaging have limited sensitivity (1,2). The stable glucagon like peptide-

1 (GLP-1) analog exendin specifically binds to the GLP-1 receptor (GLP-1R) (3), which is markedly upregulated/overexpressed in insulinomas (4).
^{68}Ga-DOTA-exendin-4 PET/CT has been shown to be feasible in detecting insulinomas. Replacing the chelator DOTA by NODAGA in the labeling process ensures higher specific activities, allowing imaging with sub-pharmacological peptide doses. We propose ^{68}Ga-NODAGA-exendin-4 PET/CT as a promising new method for improved localization of insulinomas.
We here present the first data of a multi center prospective imaging study to evaluate the effectiveness of ^{68}Ga-NODAGA-exendin-4 PET/CT.
Aims and Methods: 33 adults aged 24-65 with biochemically proven hyperinsulinemic hypoglycemia were included. PET/CT images were obtained one and two hours after injection of (5–7 μg) 95–105 MBq ^{68}Ga-NODAGA-exendin-4. Current standard imaging was performed within 8 weeks of ^{68}Ga-NODAGA-exendin-PET in all patients, consisting of CT or MRI and SSTR PET imaging.
Results: ^{68}Ga-NODAGA-exendin-4 PET imaging confirmed insulinoma, i.e., GLP-1R positive lesions, in 25 of the 33 patients with suspected insulinoma. In 15 of these patients, insulinoma were also confirmed by conventional imaging as well as Sst-receptor PET. In two patients, conventional imaging could not confirm the presence of an insulinoma while Sst-receptor PET as well as ^{68}Ga-NODAGA-exendin-4 PET were positive. In one patient, an insulinoma was found using conventional imaging and ^{68}Ga-NODAGA-exendin-4 PET, while Sst-receptor PET was negative In 5 patients, all other imaging modalities were negative and an insulinoma could only be visualized by ^{68}Ga-NODAGA-exendin-4 PET. In one MEN1 patient, multiple NETs were visualized by conventional imaging and Sst-receptor PET, but no decisive answer could be given on which of these lesions produced insulin leading to recurrent hypoglyceamias. In this patient, ^{68}Ga-NODAGA-exendin-4 PET/CT confirmed only one GLP-1R positive lesion. In all patients, GLP-1R positive lesions were pathologically confirmed to be insulinoma. In 7 patients, insulinoma could not be confirmed despite a positive Whipple's triad with any of the imaging techniques applied, including ^{68}Ga-NODAGA-exendin-4 PET. This result may indicate that false positive results can be excluded following ^{68}Ga-NODAGA-exendin-4 PET.
Conclusion: In conclusion, ^{68}Ga-NODAGA-exendin-4 PET/CT performed better than standard imaging methods, which indicated it is a promising new technique for non-invasive pre-operative detection of insulinomas.
Disclosure: Nothing to disclose

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P0749 CLINICAL AND PATHOLOGICAL CHARACTERIZATION OF GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS: RETROSPECTIVE SINGLE-CENTER STUDY

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Introduction: Gastroenteropancreatic neuroendocrine tumours are a rare group of neoplasia, with an incidence of approximately 2.5–5/100000 people. These tumours can be non-functioning or functioning, consisting of a clinical and biochemically heterogeneous group of tumours.
Aims and Methods: In this retrospective single-center study, clinical, pathological and prognostic characteristics of gastroenteropancreatic neuroendocrine tumours were evaluated and compared with current medical knowledge. 70 patients diagnosed with an histological diagnosis of gastroenteropancreatic neuroendocrine tumours between 2008 and 2017 were included
Results: Pancreas was the most common primary location (48.6%), followed by small intestine (27.1%), ileocecal appendix (8.6%), stomach (7.1%), colon (2.8%), mesentery (1.4%) and liver (1.4%). Metastasis were detected by the time of diagnosis in 25 patients (35.7%), which had a mortality of 24%, higher than the mortality between patients without metastasis by diagnosis (15.5%). Female patients had metastasis more often than males (42.4% vs 29.7%); however, mortality was higher in male than female patients (21.6% vs 15.2%). According to primary location, metastasis were more commonly encountered in small intestine tumours (42.1%), followed by stomach (40%), pancreas (29.4%) and ileocecal appendix (16.7%). Mortality was higher in gastric tumours (60%), followed by pancreas (20.6%) and ileocecal appendix (16.7%). No patients with small intestinal tumours died during the follow-up. Patients were treated with surgery (61.4%), surgery and chemotherapy (27.1%) or isolated chemotherapy (7.1%).
Conclusion: Survival was higher in patients whose treatment included surgery, compared to those where surgery was not performed. Retrospective studies including patients with gastroenteropancreatic neuroendocrine tumours contribute to identify patients with worse prognosis and the most effective therapies, therefore allowing a more individualized, tailor made approach to these tumours.
Disclosure: Nothing to disclose

P0750 THE DIAGNOSTIC YIELD OF EUS-GUIDED FINE-NEEDLE ASPIRATION REGARDING PANCREATIC NEUROENDOCRINE NEOPLASM

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Introduction: Endoscopic ultrasound-*fine needle aspiration* (EUS-*FNA*) has a significant role in diagnosing pancreatic tumors. Pancreatic neuroendocrine neoplasm (P-NEN) accounts for about 2–3% of pancreatic tumors, and the usefulness of EUS-FNA in P-NEN is has recently been reported. However, the ability of EUS-FNA to assess the degree of malignancy of P-NEN in pathologic diagnosis remains an issue.
Aims and Methods: This retrospective study evaluated data from clinical records that were collected prospectively. During April, 2012 to March, 2018, 169 consecutive patients with pancreatic lesions underwent EUS-FNA, 12 patients from whom a pathologic diagnosis of P-NEN was obtained were studied. Patient background and factors related to the procedure were studied. Regarding 8 patients to whom EUS-FNA was performed, the concordance rate between EUS-FNA and the operated samples in diagnosing the degree of malignancy were evaluated.
Results: The background of the 12 patients with PNEN were: male to female ratio, 4 to 8; median age, 61 yrs. [range: 31–81 yrs.]; site of lesion, pancreatic head/body and tail: 6/4; median longest diameter of the lesion: 18mm [range 8–50mm]. As factors associated with the procedure: diameter of the needle, 19G/20G/22G/25G, 5/1/7/2 (2 cases with combined use of 19G and 22G, and 1 case with combined use of 22G and 25G); median number of punctures, 4 times [range 3–6 times]; with/without side port, 6/6; slow pull/aspiration, 9/3; median procedure time, 43 min. [range 16–64 min.]. There were no complications associated with EUS-FNA.
The diagnosis made regarding malignancy were compared between that by EUS-FNA and that by the operated sample in 8 patients who received the procedure; they were G1, 6/4; G2, 2/4. The concordance was k coefficient 0.5.
Disagreement was found in 2 cases; both of the cases were diagnosed as G1 by EUS-FNA but as G2 with the operated sample. The sites of the lesion of the disagreed cases were the pancreatic head in 1 and the pancreatic body in 1. Regarding puncture needles, combined use of 22G/25G was in 1 and 22G in 1.
Conclusion: EUS-FNA has been performed safely for P-NEN. There was no problem in EUS-FNA in its histological diagnostic yield of P-NEN, but regarding diagnosis of malignancy, the concordance rate with operated samples was low, indicating the need for further devise.
Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00

Endoscopy and Imaging II – Hall X1

P0751 ENDOSCOPIC APPLICATION OF AUTOLOGOUS PLATELET RICH PLASMA ON GASTRIC ULCER AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION: A PILOT STUDY

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Introduction: Platelet-rich plasma (PRP) is a concentrate of platelet-rich plasma protein derived from whole blood, centrifuged to remove red blood cells. Although PRP has been shown to promote healing and regeneration in various of tissue, little is known about its effect on gastric ulcer. This study aimed to investigate the efficacy of endoscopic application of autologous PRP on artificial gastric ulcer after endoscopic submucosal dissection (ESD).
Aims and Methods: A prospective randomized placebo-controlled trial was conducted at a single tertiary hospital. Consecutive patients who underwent ESD for gastric neoplasm were randomly assigned to the PRP or control group. Immediately after ESD, prepared autologous PRP or saline was applied to artificial ulcer. The ulcer diameter was measured immediately after ESD, 2nd week, and 4th week after the procedure using endoscopic ruler. The efficacy of PRP for healing of artificial ulcer was evaluated based on the ulcer size and the occurrence of post ESD complications between the two groups.
Results: Overall, twenty patients were enrolled in this pilot study (PRP group 10, control 10, age, mean ± SD, 61.00 ± 10.15, male 11). Baseline characteristics did not differ between the two groups. The mean size of long diameter of ulcer immediately after ESD was significantly larger in the PRP group than in the control (51.00 ± 11.26 vs. 38.50 ± 8.52, $p = 0.012$). When the changes in ulcer size were compared between the two groups, the mean ulcer size decreased more in the PRP group than in the control group at 2 weeks (1648.20 ± 1004.66 vs. 851.60 ± 502.53, $p = 0.043$), and 4 weeks (1898.20 ± 1021.18, 1096.30 ± 553.40,

p = 0.047) after ESD. Post ESD bleeding rate was not different between the groups. No adverse events related to the application of PRP were occurred.
Conclusion: Endoscopic application of PRP may be effective treatment modality for artificial gastric ulcers after ESD. Further larger studies are required to apply it to the clinical setting.
ClinicalTrials.gov (NCT03220334)
Disclosure: Nothing to disclose

P0752 ENDOSCOPIC VACUUM THERAPY FOR THE TREATMENT OF UPPER GASTROINTESTINAL TRANSMURAL DEFECTS: INITIAL EXPERIENCE

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Introduction: Upper gastrointestinal transmural defects are associated with a high morbidity and mortality. Stents are the first-line endoscopic approach, however, their efficacy varies considerably and are associated with important adverse events (AEs). Endoscopic vacuum therapy (EVT) is a new approach to this condition.
Aims and Methods: The objective of this study was to evaluate the preliminary efficacy and impact of EVT in the treatment of upper gastrointestinal transmural defects.
Single-center retrospective study that evaluated patients with upper gastrointestinal transmural defects undergoing EVT. EVT was performed using the Endo and Eso-Sponge system (B. Braun, Melsungen, Germany). Continuous negative pressure of 100 mmHg, generated by an electronic vacuum pump system was applied. Whenever possible the sponge was placed in an intracavitary position. Sponge replacement was performed every 3–7 days.
Results: Five patients (3 males) with a median age of 58 years were referred for EVT due to anastomotic leak after distal esophagectomy (n = 2), gastrojejunal leak following Roux-en-Y gastric bypass (n = 1), gastropleural fistula post-sleeve gastrectomy (n = 1) and esophageal-pleural fistula after esophageal diverticulectomy (n = 1). In 60% of cases, the size of the cavity was greater than 20 mm. EVT was used as the first-line endoscopic treatment in 1 patient and in the remainder after stent failure. Stent-over-sponge technique was performed in one patient. After a median of 5 procedures (IQR 4–6), complete closure of the defect was seen in 2 patients (40%). In another patient, after almost complete reduction of the cavity, effective closure was achieved after application of an OTSC (Ovesco, Tuübingen, Germany). These 3 patients were discharged after a median of 43 days (IQR 39–50) since the beginning of EVT therapy. In the remaining 2 patients, there was a decrease in dimensions of the defect, without closure, with placement of a biodegradable stent in one and need of revision surgery in the other patient.
Conclusion: EVT is a promising approach in the treatment of upper gastrointestinal transmural defects, even after stent failure. It appears to be most effective when performed intracavitarily. Despite the need for multiple procedures, it can lead to complete closure of the defect, avoiding the need for surgery.
Disclosure: Nothing to disclose

Reference

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P0753 A PROSPECTIVE, RANDOMIZED CONTROLLED TRIAL OF VONOPRAZAN VERSUS LANSOPRAZOLE IN THE TREATMENT OF ARTIFICIAL GASTRIC ULCERS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) has been established as a standard therapy for treating early gastric cancer and adenoma. After ESD, artificial gastric ulcers are created. These ulcers sometimes cause complications, such as delayed bleeding and perforation. Therefore, they should be healed at the earliest. Conventional proton pump inhibitors (PPIs) have been widely used for treating ESD-induced gastric ulcers. Although PPIs are proven to shrink such ulcers, some ulcers fail to heal. Therefore, a more effective therapy is needed. Vonoprazan is a novel suppressant of gastric acid secretion and an active potassium-competitive acid blocker (P-CAB). Similar to PPIs, P-CABs inhibit gastric H+/K+-ATPase; however, unlike PPIs, P-CABs inhibit the enzyme in a K+-competitive and reversible manner. Thus, vonoprazan is more potent with a more long-lasting effect than PPIs. Although vonoprazan is expected to be superior to PPIs, and to heal ESD-induced gastric ulcers earlier than the conventional PPI-based therapy, its efficacy in treating these ulcers remains unclear.
Aims and Methods: We aimed to evaluate the effectiveness of vonoprazan in healing artificial ulcers after ESD. Patients with gastric tumor were randomly assigned to the vonoprazan group (group V) or the lansoprazole group (group L) after ESD. The exclusion criteria were as follows: remnant stomach, administration of antithrombotic agents, complication during and after ESD, need for additional surgery, and unwillingness for study participation. Patients were administered 30 mg intravenous lansoprazole twice on the day of ESD. From postoperative day2, patients in group V received 20 mg/day vonoprazan and those in group L received 30 mg/day lansoprazole. Esophagogastroduodenoscopy was performed 4 and 8 weeks after the ESD. During the following endoscopy, the length and width of the artificial ulcer were evaluated using measure forceps. The ESD ulcer index was calculated by multiplying the length with the width of the resected specimen. The 4- and 8-week ulcer indices were also calculated by multiplying the length with the width of the artificial ulcer at 4 and 8 weeks after ESD, respectively. The primary endpoint was the healing rate for the artificial ulcer at 4 weeks after ESD. Secondary endpoints were the healing rate at 8 weeks,; shrinkage rates for the artificial ulcers at 4 and 8 weeks; and complications, such as delayed bleeding and perforation.
Results: Of the 263 patients who underwent ESD from April 2015 to December 2017, 182 patients (90 in group V and 92 in group L) were eligible for the study. Thirteen patients were excluded during follow-up because of complications or the need for additional surgery. Finally, 85 patients were allocated to group V and 84 to group L. The age, sex, status of *Helicobacter pylori* infection, tumor location, and ESD ulcer index of the two groups did not differ significantly. The 4-week healing rate for artificial ulcers was not significantly higher in group V (17/85, 20.0%) than in the group L (14/84, 16.7%). Further, there were no significant differences between the 4-week shrinkage rates of group V (92.4%) and group L (92.5%). Delayed bleeding was observed in 3 subjects of group L; however, no subject of group V had delayed bleeding. One patient in group V presented delayed perforation 2 days after ESD.
Conclusion: Vonoprazan was not superior to lansoprazole in its ability to heal artificial gastric ulcer after ESD.
Disclosure: Nothing to disclose

P0754 THE EFFECTIVENESS AND SAFETY OF ORAL PHLOROGLUCIN AS PREMEDICATION FOR NON-SEDATIVE ESOPHAGOGASTRODUODENOSCOPY: A DOUBLE BLINDED, PLACEBO-CONROLLED, RANDOMIZED CLINICAL TRIAL

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Introduction: : Gastrointestinal (GI) peristalsis during esophagogastroduodenoscopy (EGD) commonly requires antispasmotic agents which are administered by intravenous or intramuscular injection. Oral Phloroglucin (Flospan®) is a smooth muscle relaxant that is currently used as anti-spasmodic treatment.
Aims and Methods: This study aimed to evaluate the effectiveness and safety of oral Phloroglucin (Flospan®) as premedication for non-sedative EGD. A Prospective, double-blinded, placebo-controlled, randomized clinical trial was conducted at a single tertiary hospital. Subjects who scheduled to undergo non-sedative EGD were randomly assigned to receive oral Phloroglucin (Flospan®) and placebo at 10 minutes before EGD. The primary outcome was the degree of peristaltic movement which was graded from 1 (none) to 5 (very severe). The secondary outcomes include the degree of endoscopist's subjective difficulty for peristalsis and adverse effect.
Results: Overall, 140 subjects were included in the study (Phloroglucin 70, placebo 70, age mean ± SD, 66.31 ± 9.37, male 47.8%). The degree of peristalsis was significantly lower in phloroglucin group at initial of test. (Phloroglucin vs Placebo, 1.97 ± 0.92 vs 2.39 ± 1.15, p = 0.02). But there was no significant difference at last of test. (Phloroglucin vs Placebo, 2.27 ± 1.17 vs 2.63 ± 1.10, p = 0.064) The degree of endoscopist's subjective difficulty for peristalsis in phloroglucin group was also lower than placebo. (Initial of test : Phloroglucin vs Placebo, 1.93 ± 0.77 vs 2.34 ± 0.81, p = 0.002 / Last of test: Phloroglucin vs Placebo, 2.13 ± 0.96 vs 2.53 ± 0.83 p = 0.009). There was no difference in the willingness to take this premedication at next examination between two groups (Phloroglucin vs Placebo, 94.3% vs. 98.6%, p = 0.366). Most of subjects in each group answered the taste of the drug was good or very good. There were no significant adverse events besides each one participants who complained of dry mouth or dizziness in the placebo group.
Conclusion: Oral Phloroglucin (Flospan®) significantly suppress peristalsis during non-sedative EGD with no adverse drug reactions compared with placebo. (Clinical trial registration number: NCR03342118)
Disclosure: Nothing to disclose

P0755 RISK FACTORS ASSOCIATED WITH TREATMENT FAILURE OF SOFT-MODE THERMAL COAGULATION FOR BLEEDING PEPTIC ULCERS

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Introduction: Endoscopic therapy is effective in achieving hemostasis of bleeding peptic ulcers. Based on a systematic review, hemoclips or the combined use of injection therapy with thermal coagulation is recommended for the treatment of bleeding peptic ulcers. Recently, monopolar electrocoagulation using a soft-mode coagulation system and hemostatic forceps has been applied for the treatment of patients presenting with acute peptic ulcer bleeding. In this method, it is possible to control the bleeding by grasping with hemostatic forceps the hard base of the ulcer, and coagulation is achieved without carbonization or sparking because the voltage is held below 200V, thereby preventing perforation due to excess damage compared with conventional thermal coagulation. Several randomized controlled studies showed the efficacy of soft coagulation for hemostasis of peptic ulcer bleeding. However, there are few reports on the risk factors for treatment failure because the sample size is small. The aim of this study was to clarify the risk factors for hemostatic failure of soft coagulation.
Aims and Methods: This retrospective study included all 313 patients with peptic ulcers who were treated using monopolar soft coagulation in our department between January 2005 and December 2015. Endoscopic hemostasis with soft coagulation was performed if a patient with hematemesis or melena was admitted and presented with an actively bleeding ulcer (spurting or oozing), a non-bleeding visible vessel, or an adherent clot. Endoscopic hemostasis with soft coagulation was performed using monopolar hemostatic forceps (FD-410LR, Olympus Co.,Tokyo,Japan or HDB2418W, Pentax Co., Tokyo, Japan) and an electrosurgical unit (ICC-200, ERBE, Tübingen, Germany) at soft-mode coagulation with a 70W current. If hemostasis was not achieved using this method, injection of hypertonic saline-epinephrine, hemoclip, heater probe or argon plasma coagulation was applied. If the additional endoscopic treatment was still unable to stop the bleeding, intervention radiology or surgical treatment was performed. Rebleeding was defined as blood in the stomach and stigmata of a recent hemorrhage at the ulcer base when second-look endoscopy was performed, or fresh hematemesis and/or melena accompanied by either instability of vital signs or reduction in hemoglobin level of greater than 2g/dl within 24 hours. Factors associated with treatment failure of soft coagulation were analyzed.
Results: The study subjects were 207 men and 106 women at a median age of 69 (range, 28–97) years, with 242 gastric ulcers and 71 duodenal ulcers. Initial hemostasis with soft coagulation was achieved in 296 patients (94.6%). Of the 17 patients with treatment failure, additional endoscopic methods were required in 15, intervention radiology in 1 and surgery in 1. Rebleeding occurred in 21 patients (6.7%). Minor perforation occurred in 2 patients, and was managed conservatively in both patients. Three patients died of ulcer bleeding within 30 days of the occurrence of initial bleeding. Initial hemostasis with soft coagulation was significantly associated with an exposed vessel. In multivariate analysis, rebleeding was significantly related to duodenal ulcer and elderly patients.
Conclusion: Soft coagulation using a monopolar hemostatic forceps is effective and safe for patients with gastroduodenal ulcer bleeding. However, duodenal ulcer bleeding, exposed vessels and elderly patients are risk factors for treatment failure.
Disclosure: Nothing to disclose

P0756 LAUNCHING AN ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) PROGRAM IN A EUROPEAN ACADEMIC HOSPITAL: REVIEW OF THE FIRST 34 MONTHS OF EXPERIENCE

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Introduction: Launching a professional program of endoscopic submucosal dissection (ESD) for the treatment of early gastrointestinal neoplasia in Western countries may be fastidious and is still debated.
Aims and Methods: After practicing few ESDs in selected indications, we sought to develop a structured ESD program by sending two advanced endoscopists (AL, VH) for 7 weeks to Japan (2015, Keio Cancer Center, Pr Yahagi) for lesion recognition and ESD learning, watching 95 ESD procedures, and performing 18 ESD on isolated pig stomach models. Further hands-on was performed on living pigs before treating patients. All ESDs were from then concentrated on these 2 operators, starting treating patients following European guidelines in June 2015. Here, we analyse the safety and efficacy of ESD from the beginning of our program. Clinical and technical data were prospectively collected from June 18th 2015 to April 10th 2018, excluding ESD performed by guest experts during live demonstrations. R0 resection rate was defined as clear margins (no dysplasia / no adenoma for lateral margins and clear vertical margin). Curative resection was defined following European ESD guidelines. All ESD were performed under general anaesthesia using a 20% glycerol submucosal injection solution and for 98% of them an adjustable tip electrosurgical knife for dissection.
Results: One hundred ESDs were performed in 98 patients (40% female; aged 68(27–98) years old) by two operators (AL,VH). Lesions were located for 29% in the oesophagus (11/29 squamous cell carcinoma), 21% in the stomach, 41% in the rectum and 9% in the colon. En-bloc resection rate was 98%, complete endoscopic resection rate was 95%. R0 resection rate was 67% globally (8% with positive vertical margin; 2% with carcinoma in the lateral margin). In detail, R0 resection rate was 79%, 84% and 57% for oesophageal, gastric and colorectal lesions respectively. Median specimen size was 40 (15–160) mm. Median procedure duration was 120 (IQR 90–180) min. In 92% of cases, there were none or conservatively managed complications. Two patients needed endoscopic hemostasis for delayed bleeding, 4 presented secondary stenosis requiring dilations, one urgent surgery for sepsis after colonic perforation. Pathological analysis revealed a carcinoma in 82% of oesophageal lesions (18 pTis/pT1a; 6 pT1b), in 28% of gastric lesions (3 pT1a; 3 pT1b) and 32% of colorectal lesions (7 pTis/9 pT1). A neuroendocrine tumor was present in 1 oesophageal, 5 gastric and 2 rectal cases. Curative ESD was obtained in 70% of cases and 15 patients required complementary oncological surgery with 61% of them having no residual tumor in the organ and negative lymph nodes. When endoscopic follow-up was recommended, data were obtained in 71% of cases with a median of 7 (range 1–24) months length and no recurrence of the lesion observed in 95% of cases. Pathological specimen processing was revised after the first 6 months implementing Japanese standards and increasing the rate of free lateral margins from 47 to 75%. For the rectum, despite a 29% positive (adenoma) lateral margin rate, 100% of patients were free of residual adenoma at the end of endoscopic follow-up, suggesting coagulation artefact effect on the specimen.
Conclusion: Nowadays, launching an ESD program in an academic European Center by experienced therapeutic endoscopists, after an observation period in an expert Japanese center, is possible, safe and quick with good results in terms of en-bloc resections and outcomes. Technical and pathological analysis efforts must be done to decrease positive lateral margins.
Disclosure: Nothing to disclose

P0757 A COMPARISON STUDY WITH ENDOSCOPIC ROBOT MANIPULATOR IN ESD : NOVICE AND EXPERT

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Introduction: Endoscopic submucosal dissection (ESD) is a difficult procedure due to lack of counter traction for unskilled endoscopists. Recently, auxiliary devices have been developed to alleviate the difficulties of ESD. We also developed new endoscopic technique using robotic manipulator. The purpose of this study is to evaluate the efficacy and safety of endoscopic detachable auxiliary manipulator (EDAM) *in vitro* animal study
Aims and Methods: A novel robotic manipulator is composed of a control panel and a working arm, which grasp and move objects at the end of scope. A total of 40 porcine stomachs were used for the test. Endoscopists were classified as expert or novice. As a preliminary work, operation time and perforation rate of the experts and novices were recorded when ESD was performed by the conventional method. (C-Expert group, C-Novice group). The same experiment was performed using EDAM (M-Expert group, M-Novice group). During this procedure, robotic manipulator lifts up dissected tissue of stomach to make better visibility. The results were compared.
Results: The safety of the operation was greatly improved when using the EDAM. Perforation rate of the EDAM method was significantly lower than that of the conventional method in the novice group. (10% vs 60%, $p = 0.002$) There was no significant difference between the conventional method and the EDAM in the operation time in the novice group.
Conclusion: As a result of this *In-vitro* test, the EDAM significantly improved the safety of ESD in the case of the novice, with no increase in operation time.
Disclosure: Nothing to disclose

P0758 DOES SECOND-LOOK ENDOSCOPY PREVENT POSTOPERATIVE BLEEDING IN HIGH-RISK PATIENTS AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION?: A PROPENSITY SCORE-MATCHING ANALYSIS

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Introduction: Postoperative bleeding (POB) is the most common and highly frequent complication in gastric endoscopic submucosal dissection (ESD). Several reports have shown that second-look endoscopy (SLE) does not significantly prevent POB in low-risk patients for bleeding (LRPs) [1], whereas it is currently performed in most institutions for high-risk patients for bleeding (HRPs). However, no studies have reported the use of SLE for HRPs. Therefore, this study aimed to evaluate the prophylactic effect of SLE on POB in HRPs.
Aims and Methods: [Study 1] HRPs who underwent gastric ESD without SLE between May 2017 and February 2018 were assigned to the non-SLE group. HRPs were defined as patients who were continuously administered low-dose aspirin, those in whom treatment was changed from warfarin or direct oral

anticoagulants to heparin replacement, and those who underwent hemodialysis. This non-SLE group was compared with a historical control group that included patients who underwent SLE after gastric ESD between November 2013 and March 2017 (the SLE group). Data were analyzed using propensity score-matching methods. We used the size of the ESD specimen and comorbidity of diabetes mellitus as covariates according to previous reports [2, 3]. The primary endpoint was POB.
[Study 2] In the entire cohort, the risk factors for POB were analyzed.
Results: [Study 1] Eighty-two patients (96 specimens) underwent gastric ESD, among whom eight (8.3%) encountered POB. After propensity score-matching, 38 subjects (19 subjects in each group) were enrolled. Significantly fewer specimens were detected at the upper location of the stomach in the SLE group than in the non-SLE group ($p = 0.03$), whereas there were no differences in the other background factors between the two groups. No significant differences were observed in the rate of POB between the two groups (SLE group, 5.3%; non-SLE group, 10.5%).
[Study 2] In the entire cohort, the rate of POB of HRPs with two risk factors for bleeding was significantly higher than that of HRPs with one risk factor (30.0% vs. 5.8%, $p = 0.04$; chi-squared test). However, multivariate analyses revealed no independent predictors of POB.
Conclusion: SLE did not reduce the rate of POB after gastric ESD in HRPs. SLE may not be recommended after gastric ESD in HRPs, as is the case in LRPs; however, it is necessary to accumulate and analyze more cases.
Disclosure: Nothing to disclose

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P0759 OLGA AND OLGIM STAGE ACCORDING TO AGE AND RISK FACTORS INFLUENCE HIGH RISK OF GASTRIC CANCER

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Introduction: Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) are superordinate stages system for Gastric risk stratification.
Aims and Methods: The study aimed at evaluating the distribution of OLGA and OLGIM staging and the ralationship with age and other risk factors analysis. 632 patients who underwent endoscopy for functional dyspepsia. *Helicobacter pylori* status and histologic changes were assessed using the updated Sydney system. At least three biopsy pieces (one from the lesser curvature of antrum and corpus,respectively, one from incisura angularis) were acquired. *Helicobacter pylori* status and histologic changes graded by senior gastrointestinal pathologists according to the updated Sydney system. Stage III and IV OLGA or OLGIM stages were considered as high-risk stages.
Results: The proportion of Stage III and IV OLGA or OLGIM stages was remarkably increased with older age. Old age (OR = 4.85 (95% CI: 1.09–21.67, $p = 0.039$), 5.79 (95%CI : 1.30–25.71, $p = 0.021$),and16.61 (95% CI:3.63–76.10, $p < 0.001$) for ages in the 50's, 60's, and older than 70 years, respectively), smoking (OR = 2.07, 95% CI: 1.09–3.95, $p < 0.001$), and *H. pylori* infection (OR = 2.46,95% CI:1.37–3.95, $p = 0.002$) were independent risk factors for high-risk OLGA stages. These risk factors were also for high-risk OLGIM stages. The *H. pylori* infection was positive correction with the OLGA and OLGIM staging, the *H. pylori* positive rate of OLGA and OLGIM Stage 0-IVand IV was 23.1 and 22.4%, 22.9% and 23.9%, 31.4% and 30.8%, 39.5% and 39%, 45.0% and 50.0%, respectively, the proportion of high-risk OLGA stages was low (6.9%) before the age of 50, but increased to 9.5%, 11.7%, and 25.7% for those in their 50s, 60s, and older than 70 years, respectively. High-risk OLGIM stages showed a similar trend.
Conclusion: High-risk OLGA and OLGIM stages are uncommon under the age of 50, The *H. pylori* infection was positive correction with the OLGA and OLGIM staging,thus eradication of *H. pylori* before that age may reduce the requirement for endoscopic surveillance for gastric cancer.
Disclosure: Nothing to disclose

P0760 ARGON PLASMA COAGULATION FOR SUPERFICIAL SQUAMOUS CELL CARCINOMA IN THE RESIDUAL ESOPHAGUS AFTER ESOPHAGECTOMY

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Introduction: Patients with esophagectomy for esophageal squamous cell carcinoma (SCC) often develop metachronous SCC in the residual esophagus. Although most of the lesions are detected as superficial SCC at follow-up endoscopy, it is difficult to perform endoscopic resection for lesions near the anastomosis. We have performed argon plasma coagulation (APC) for such superficial SCC in the residual esophagus. The aim of this study is to evaluate the usefulness of APC for superficial SCC in the residual esophagus after esophagectomy.
Aims and Methods: The aim of this study is to evaluate the usefulness of APC for superficial SCC in the residual esophagus after esophagectomy. Twelve patients (15 lesions) with superficial SCC in the residual esophagus after esophagectomy underwent APC at our institution, from September 2007 to October 2016. The indications for APC was tumor in situ or mucosal cancer in the residual esophagus. We retrospectively evaluated the treatment outcomes after APC. The median of follow-up duration after the initial APC was 43 months (range: 28–103 months).
Results: The median number of treatment courses per lesion was 1 (range, 1–12 courses). The median treatment time of APC was 17 minutes (range, 4–33 minutes). There were no treatment-related complications. Complete remission (CR) was achieved in 13 (86.7%) of 15 lesions; 11 lesions (73.3%) achieved CR after the first APC course, and 2 lesions (13.3%) achieved CR after 2 or more APC courses. Of the 2 patients with residual tumor, 1 patient received 12 courses of APC over 6 years and achieved local control without metastasis. Another patient received radiotherapy (60Gy) after treatment failure with APC. He later developed local recurrence after 2 years of complete response. He underwent cervical esophagectomy and free jejunal graft reconstruction. Death occurred in 2 patients: 1 died of non-cancer-related cause and the other died of other primary malignancy.
Conclusion: APC was a safe and effective treatment, and was technically easy to perform. APC might be an alternative to endoscopic resection for superficial SCC in the residual esophagus after esophagectomy.
Disclosure: Nothing to disclose

P0761 THE EFFECTIVENESS OF "HANDMADE MULTI-BENDING SYSTEM OF THE ENDOSCOPE" FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF THE DIFFICULT-TO-APPROACH SUPERFICIAL GASTRIC NEOPLASMS

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Introduction: Maintaining good operative field is crucial in performing endoscopic submucosal dissection (ESD) for early stage gastrointestinal tumors, but it often requires high skill or special equipment depending on the lesion location. In ESD for the lesions at the lesser curvature of the gastric body, it is often difficult to approach the lesions, although early gastric cancers are often detected at this area. A multi-bending endoscope (Olympus) is a good option for such a situation, but it is difficult for most operators to prepare it due to its particularity or cost.
Aims and Methods: We therefore recently developed handmade multi-bending system (HMBS) and performed ESD using it for 11 lesions which were located at the lesser curvature of the gastric body and tended to be difficult to approach. A fishing line was passed through the external tube (Crusher catheter, Zeon Medical, Japan), and the tip of external tube was fixed about 15–20 cm apart from the tip of the gastroscope (Olympus or Fujifilm). The fishing line was bound and fixed at the original first bending portion. Second bending portion was created by pulling the fishing line through the external tube, and fixed with three-way stopcock according to the situation during the procedure. HMBS were used at our hospital between February 2017 and August 2017. In this study, we retrospectively investigated the treatment outcome of ESD with HMBS (N = 11) for the lesions located at the lesser curvature of the gastric body and difficult to approach, and compared it with the treatment outcome before the adoption of HMBS (Conventional, N = 11). ITknife2 (Olympus), Flushknife BT (Fujifilm), or both endoknives were used for ESD. This study was approved by the ethical committee.
Results: Average tumor diameter and resected specimen diameter of Conventional and HMBS were 16.6mm vs 16.5mm, and 36.2mm vs 37.8mm (not significant), respectively. In all cases to which we applied HMBS, the tip of the endoscope could be closely approached to each lesion just after using HMBS, although it was difficult to approach the lesion without HMBS. Procedure time of HMBS (34.3minutes) was significantly shorter than that of conventional (61.5 minutes) ($p = 0.01$). In all cases, en bloc resections were achieved, and no perforation or other complication occurred.
Conclusion: This study demonstrates our handmade multi-bending system may greatly shorten the procedure time of ESD for the lesions which are located at the lesser curvature of the gastric body and difficult to approach.
Disclosure: Nothing to disclose

P0762 CLINICAL EFFICACY OF THE OVER-THE SCOPE CLIP DEVICE: A SYSTEMATIC REVIEW

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Introduction: The over-the-scope clip (OTSC) is a technology that is increasingly incorporated into endoscopic practice and is utilized for applications including fistula closure, control of bleeding, perforation, management of anastomotic

leaks, endoscopic full thickness resection (EFTR), and luminal stent fixation. Our study evaluated a large body of literature to determine the overall efficacy and safety of OTSC.

Aims and Methods: A Medline search was conducted from inception to October 1st, 2017. The following search terms were used: ''over the scope clip'', ''OTSC'', ''Ovesco'', ''endoscopic fistula closure'', ''over the scope clip bleeding'', and ''endoscopic perforation closure''. Publications selected for inclusion consisted of case reports, case series, as well as prospective and retrospective single-arm clinical studies. Data were collected from each study on technical success, clinical success, and reported adverse outcomes. Weighted means (Table 1) were calculated to adjust for sample size.

Results: 238 papers were selected that met the search criteria: 81 case series/retrospective reviews/prospective studies (Group A) and 157 case reports (Group B). In Group A, technical success of OTSC placement was 95.3%, with a clinical success of 77.2% (n = 2285 patients). Indications for OTSC placement were fistula closure (30.6%), bleeding (28.9%), perforation closure (16.3%), leaks (15.1%), EFTR (8.4%) and stent fixation (0.7%). Clinical success for each indication (weighted means) is listed in Table 1. Complete luminal obstruction (one) was the only reported adverse event across all studies. 24/81 papers reported the need for surgery despite OTSC placement. In these 24 papers, total of 90/673 (13.4%) patients required surgery despite OTSC placement.

In Group B, OTSC was deployed in 177 patients. Indications for OTSC placement were fistula closure (37.9%), perforation closure (33.9%), bleeding (14.1%), EFTR (7.9%) and leaks (6.2%). Pooled technical success in this group was 99% and clinical success was 96.0%. 7/177 (4%) patients required surgical intervention despite OTSC placement. Complete luminal obstruction in 1/177 patients and small bowel fixation with pneumoperitoneum in 1/177 patients were the only OTSC-related adverse events reported.

Conclusion: OTSC is a safe and effective, surgery-sparing, endoscopic tool in today's GI practice with 77–96% of patients achieving clinical success without the need for further intervention. Technical success of > 95% has been reported across all indications. Surgical salvage is still needed in a minority of patients.

	Sample Size	Weighted Mean
Overall Clinical Success	2285	77.2%
Fistula Closure	700	61.7%
Bleeding	660	84.3%
Perforation	373	86.3%
Anastomotic Leak	346	72.9%
EFTR	191	92.5%
Stent Fixation	15	80.0%

[Table 1: Observation Studies Pooled Sample Sizes and Weighted Means of Overall Clinical Success and Individual Indications for OTSC placement]

Disclosure: Nothing to disclose

P0763 CONFOCAL LASER ENDOMICROSCOPY IN THE ASSESSMENT OF PERSISTENT OR RECURRENT INTESTINAL METAPLASIA/NEOPLASIA AFTER ENDOSCOPIC TREATMENT OF BARRETT'S ESOPHAGUS RELATED NEOPLASIA

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Introduction: Patients after endoscopic treatment of Barrett's esophagus (BE) related neoplasia (BORN) should undergo regular endoscopic surveillance with biopsies to detect recurrent intestinal metaplasia (IM) or neoplasia (N). Probe-based confocal laser endomicroscopy (pCLE) offers detailed examination of cellular structures and may examine larger areas compared to standard biopsy. The role of pCLE in the surveillance of patients after endoscopic treatment of BORN has not been systematically assessed.

Aims and Methods: The aim of this prospective study was to evaluate the efficacy of pCLE (vs. standard biopsies) in detection of persistent/recurrent IM/neoplasia in patients after endoscopic treatment of BORN.

A single center, prospective, controlled and pathologist-blinded (still ongoing) study in patients undergoing surveillance endoscopy after endoscopic treatment of BORN. pCLE images were obtained from the neo-Z-line (in few cases including macroscopically visible tongues), the cardia and the esophagus. Thereafter, standard biopsies were taken and sent for histopathological analysis (minimally 4 biopsies from macroscopically normal neo-Z-line, 2 biopsies from the cardia and the esophagus and targeted biopsies from visible abnormalities, if present).

Intestinal metaplasia (IM) on pCLE was defined by the presence of regular capillaries in upper and deeper parts of the mucosal layer along with identification of dark (''non-refractile'') mucin in goblet cells in columnar-lined mucosa. The dysplastic BE was characterized by black cells with irregular borders and shapes, high dark contrast to the surrounding tissue, and irregular leaking capillaries in the mucosa.

Results: We examined 39 patients (33 males, 6 females), from these 15 patients (38.5%) had the initial diagnosis of low-grade intraepithelial neoplasia (LGIN), 9 patients (23%) had high-grade intraepithelial neoplasia (HGIN) and 15 patients (38.5%) had an early adenocarcinoma (EAC). Four patients (10%) underwent endoscopic resection (ER), in 21 patients (54%) we performed ER or dissection of all visible lesions followed by radiofrequency ablation (RFA), and 14 patients (36%) had RFA as a single treatment modality.

Persistent/recurrent IM was detected only at the level of neo-Z-line in 10 patients (26%, 10/39 pts) by both standard biopsies and pCLE.

pCLE but not biopsies detected persistent/recurrent IM in 2 patients (5%, 2/39), another 2 patients had IM present in biopsies but not in pCLE.

pCLE diagnosed one patient with recurrent LGIN in a macroscopic visible tongue arising from neo-Z-line, which was not confirmed in biopsies.

Sensitivity and specificity of pCLE in detection of persistent/recurrent IM was 83% (95% CI 51.6–97.9) and 93% (95% CI 75.7–99.1), respectively, with a positive predictive value of 83% (95% CI 56.3–95.1) and a negative predictive value of 93% (95% CI 77.8–97.8). Agreement of pCLE and histopathological findings was 90%.

Conclusion: pCLE seems comparable to standard biopsies in detection of persistent/recurrent IM after endoscopic treatment of BORN.

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ClinTrial registration: NCT02922049.

Disclosure: Nothing to disclose

P0764 THE ROLE OF ENDOSCOPIC DILATION AND STENTS IN THE REFRACTORY BENIGN ESOPHAGEAL STRICTURES: A RETROSPECTIVE ANALYSIS

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Introduction: To alleviate the symptoms of dysphagia, in addition to frequent endoscopic dilation, the esophageal stents more and more were used for patients with refractory benign esophageal strictures (RBES). Our objective was to explore the role of endoscopic dilation and stents in the long-term management of RBES.

Aims and Methods: This study including patients with RBES (recurrence of dysphagia despite endoscopic therapy more than 3 sessions) by dilation and stents between January 2009 and December 2017. Endoscopic therapy success was defined as: before the end of the follow-up, no need for endoscopic interventions for at least 6 months. The primary outcome was to establish a risk-scoring model predicting RBES in benign esophageal strictures, and clinical effectiveness and adverse events. Secondary outcome was to identify factors that predicted the dysphagia-free period (the time interval of two subsequent endoscopic interventions). Multivariate analysis was used to establish a risk-scoring model and the treatment success. To explore the trend of dysphagia-free period along with times used hierarchical linear models.

Results: In the study, 469 patients with benign esophageal strictures were eligible for the inclusion criteria. The number and length of strictures, age and etiology were independent risk factors for the refractory performance of esophageal benign strictures. According to risk factors of benign esophageal strictures, a risk-scoring model for predicting RBES in benign esophageal strictures was established: the risk score ranged from 0 to 9 points, and the risk scores were divided into low risk (0–2 points), intermediate risk (3–5 points) and high risk (6–9 points). The proportions of RBES in the corresponding risk categories were 10.2%, 42.4% and 87.5%, respectively. Among 469 patients, 75 patients with RBES were eligible for the inclusion criteria. In 75 patients with RBES (54 male; median age, 59 years), 39 (52%), 20 (26.7%), 3 (4%), 10 (13.3%), and 3 (4%) were post-surgical, post-ESD, achalasia of cardia, caustic and mixed etiology, respectively. The median times of endoscopic therapy was 5 times (range 3, 21). Self-expandable metal stents were placed in 20 patients (26.7%), and the success rate of patients treated with dilation (70.9%, 39/55) was higher than with stents (35%, 7/20). Fifteen patients died during follow-up. Nineteen patients had adverse events after endoscopic therapy. In total, the mean dysphagia-free period was 3.4 months (95% CI, 2.5–4.3). The dysphagia-free period of patients treated with dilation was 3.7months (95% CI, 2.7–5), and with stents was 2.3 months (95% CI, 1.5–3). The dysphagia-free period has linear growth trend with times, increased by 12 days per endoscopic therapy.

Conclusion: In this study, 22.6% (106/469) patients with benign esophageal strictures had RBES in our hospital. The risk-scoring model predicting RBES in benign esophageal strictures could predict the long-term outcome of patients with strictures ahead. The main causes of RBES was anastomotic strictures and post-ESD strictures. The etiology of the strictures could affect the outcome of treatment, in which the anastomotic strictures were the prognostic factor for the failure of treatment. After dilation and stents, the dysphagia-free period of RBES increased by 12 days per endoscopic therapy, so the endoscopic therapy tended to be effective in patients with RBES. Compared with the simple dilation, the success rate of RBES with stents was lower and the dysphagia-free period was shorter, so stents therapy tended to not reduce the times and frequency of dilation.

Disclosure: Nothing to disclose

P0765 ENDOSCOPIC SUBMUCOSAL DISSECTION IN EARLY GASTRIC CANCER WITH PAPILLARY HISTOLOGICAL TYPE

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Introduction: Gastric papillary adenocarcinoma has been regarded as differentiated-type adenocarcinomas along with well- or moderately-differentiated tubular adenocarcinomas in current endoscopic submucosal dissection (ESD) indication. We aimed to investigate safety of ESD in patients with papillary early gastric carcinoma (P-EGC).

Aims and Methods: 4,264 patients with early gastric cancer (EGC) underwent curative gastrectomy between 2000 and 2017 at National Cancer Center, Korea. Among them, 45 patients were confirmed with P-EGC. We compared clinicopathological factors among differentiated-type EGC except P-EGC (n = 2,106), undifferentiated-type EGC (n = 2,113), and P-EGC. Logistic regression model was used to investigate risk factors of lymph node metastasis (LNM).

Results: Frequency of mucosal cancer of P-EGC (22.2%) was significantly lower than those of differentiated-type (48.8%) and undifferentiated-type EGC (60.4%, $p < 0.001$). Angiolymphatic invasion and LNM occurred most frequently in P-EGC (46.9% and 20.0%, respectively) compared to differentiated-type (18.9% and 9.2%, respectively) and undifferentiated-type EGCs (10.9% and 11.7%, respectively; $p < 0.001$ and $p = 0.004$, respectively). P-EGC that was not mixed with other pathological type tended to have increased risk of LNM referent to differentiated EGC. (Odds ratio [OR] 2.53, 95% confidence interval [CI], 0.99–6.50). Among 45 patients with P-EGC, 13 met the current ESD indication; 3 absolute and 10 expanded indications. One out of 13 had LNM and met expanded indication with submucosal invasion less than 500 μm. In multivariate analysis, OR for LNM meeting expanded indication of P-EGC was 40.67 (95% CI, 2.54–702.76) compared to LNM meeting expanded indication of non-papillary EGC (10.28, 95% CI, 1.37–77.04).

Conclusion: When ESD was applied to P-EGC, it should be carefully performed because of high rate of submucosal invasion and high risk of LNM even in with submucosal invasion less than 500 μm.

Disclosure: Nothing to disclose

P0766 A STUDY OF THE POSSIBILITY OF COMPUTER-AIDED DIAGNOSIS USING MULTIPLE MACHINE LEARNING MODELS FOR THE DIAGNOSIS OF UPPER GASTROINTESTINAL ENDOSCOPIC IMAGING

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Introduction: There is much diversity in location, disease, the condition of background mucosa, the distance from lesion and magnification percentage in the endoscopic examination of upper gastrointestinal (GI) examination. We reported that computer-aided diagnosis (CAD) with machine learning (ML) was useful for the diagnosis of the location of the upper GI tract in UEGW 2017. However, it is unknown whether it is useful for the diagnosis of disease of the upper GI tract.

Aims and Methods: The aim of this study was to clarify the possibility of CAD using multiple ML models for the diagnosis of disease in the upper GI tract. 15,852 endoscopic images containing 603 images of laryngopharynx, 2,907 images of esophagus, 10,779 images of stomach and 1,563 images of duodenum were selected from a collection of 2,000,000 images, which were taken in our hospital between 2010 to 2017. The imagery was 0.8% of 2,000,000 images described above. In the imagery, there were 1,282 images of early gastric cancer (EGC), 559 images of advanced gastric cancer, 6,006 images of other diseases, and 8,005 images without abnormal findings. They were used as training imagery.

We trained one ML model for the detection of location, and four ML models for the diagnosis of disease of each location (laryngopharynx, esophagus, stomach, and duodenum).

817 endoscopic images were taken in 17 upper GI endoscopic examinations at our hospital in one day of January 2018. There were 26 images of EGC, 65 images of other diseases and 726 images without abnormal findings. They were used as test imagery.

We examined the test imagery by the ML model for the detection of location and then by the ML model for the diagnosis of the disease of the detected location.

Results: Overall, 673 (82%) of 817 images were diagnosed correctly. 18 of 26 images of neoplasm were diagnosed as neoplasm (all of them were EGC) and 8 images were diagnosed as non-neoplasm. 40 of 791 images of non-neoplasm were diagnosed as neoplasm and 751 images were diagnosed as non-neoplasm. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of the CAD using multiple ML models were 94%, 69%, 95%, 31%, and 99%, respectively.

Conclusion: This study revealed the possibility of CAD using multiple ML models for the diagnosis of upper GI endoscopic imaging. However, the training imagery contains only 15,852 images (0.8% of 2,000,000 images described above). It is necessary to collect more images, and to consider how to classify the image, and how to use ML model.

Disclosure: Nothing to disclose

P0767 SIZE DISCREPANCY BETWEEN ENDOSCOPIC AND PATHOLOGIC ESTIMATES AFTER ESD IN GASTRIC EPITHELIAL NEOPLASM

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Introduction: Endoscopic submucosal dissection (ESD) is the effective treatment method in the gastric adenoma or superficial adenocarcinoma. The one of major parameter to determine the resection method is the size of the lesions. Previous study showed that there were a significant discrepancy between endoscopic and pathologic sizes.

Aims and Methods: The aim of the study was to find the factors affecting size discrepancy occured after formalin fixation, propectively. 69 lesions including 50 gastric adenomas and 19 adenocarcinomas were analyzed for age, sex, location, gross shape, histologic finding, complete resection of ESD, and size immediately after excision and after fixation in formalin.

Results: Size of resected specimen decreased after formalin fixation (37.5mm vs 35.8mm, $p < 0.05$). Mean size of long diameter of the lesion was 20.3 ± 7.7mm in the time of pre-fixation, 13.4 ± 7.9mm after fixation. Size discrepancies in the lesions between endoscopic and pathologic estimate were 7.6 ± 5.7mm in adenomas and 4.6 ± 5.7mm in adenocarcinomas. In the lesions smaller than 20mm, size differences between Pre-fixation and post-fixation were larger significantly compared to that more than 20mm (7.6 ± 5.6 vs 2.5 ± 5.8, $p < 0.01$). In multivariate anlaysis, tumor size $\geq$ 20mm of the lesion was independent factor affecting size increases after formalin fixation ($p < 0.05$).

Conclusion: Endoscopic evaluation of horizontal extent of the lesions before ESD may be incorrect in large tumor more than 20mm in size. It must be resected with more careful approach to prevent incomplete resection.

Disclosure: Nothing to disclose

P0768 THE DIAGNOSIS OF INVASION DEPTH IN SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA: EFFICACY OF ENDOSCOPIC ULTRASONOGRAPHY — A SINGLE CENTER TRIAL

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Introduction: The diagnosis of cancer invasion depth is crucial for selecting the optimal treatment strategy for esophageal cancer. In Japan, magnifying endoscopy with narrow-band imaging (ME-NBI) has been used for diagnosis by observing the esophageal microvasculature architecture. This modality represents a rapid and simple diagnostic procedure without the need for additional equipment. However, some lesions have microvascular patterns which cannot be observed because the intra-epithelial papillary capillary loop is inaccessible.

Endoscopic ultrasonography (EUS) is regarded as the standard modality for diagnosing esophageal cancer invasion depth in the West. EUS is an effective modality, but needs additional endoscopy, is time-consuming, and its cost effectiveness is unknown. We investigated the role of EUS in diagnosing invasion depth in superficial esophageal cancer.

Aims and Methods: Patients with superficial esophageal squamous cell carcinoma (SESCC) and suspected muscularis mucosa or submucosal invasion in non-magnifying white light imaging (WLI) were included. All patients received WLI and ME-NBI observation followed by EUS. WLI was classified into protrusion, granular change, irregular surface, and depression. ME-NBI observation was performed by endoscope with magnification based on the Japan Esophageal Society (JES) classification. EUS was performed using a high-resolution probe by jelly-filled method [1]. Cancer invasion depth was diagnosed as T1a or T1b using each modality. Tumors without changes in the nine-layered structure, or changes involving only the first three layers, were staged as mucosal carcinoma. Tumors involving the first four layers were staged as submucosal carcinoma. All EUS images were assigned a level of confidence to the prediction (high or low). T1b High Confidence was defined as low echoic area in 4/9 layers with repeatability. T1b Low Confidence was defined as low echoic area in 4/9 layers without repeatability.

The diagnostic accuracy of WLI, ME-NBI, and EUS was analyzed while the histologic diagnosis of resected specimen served as reference standard.

Results: From May 2015 to January 2018, 119 patients with esophageal SCC with suspected muscularis mucosa or submucosal invasion in WLI were examined. Of the 119 patients, 31 were excluded from analysis because histologic specimens were not obtained. Eighty-eight patients with 88 lesions treated either by esophagectomy (n = 26) or endoscopic resection (n = 62) were included in the final analysis. Histologic diagnosis was T1a in 44 lesions and T1b in 44 lesions. The accuracy of invasion depth in WLI followed by ME-NBI and WLI, ME-NBI followed by EUS was 70% and 77% ($p = 0.30$), respectively. The overall accuracy of diagnosing invasion depth for lesions with granular change, irregular surface, and depression in WLI followed by ME-NBI and WLI, ME-NBI followed by EUS was 67% (33/49 lesions) and 71% (35/49 lesions) ($p = 0.66$), respectively. The overall accuracy of diagnosing invasion depth for lesions with protrusions in WLI followed by ME-NBI and WLI, ME-NBI followed by EUS was 74% (29/39 lesions) and 85% (35/49 lesions) ($p = 0.26$), respectively. The positive predictive value (PPV) in EUS T1b High Confidence and T1b Low Confidence was 47% (9/19) and 79% (19/24) ($p = 0.06$).

Conclusion: EUS showed a possible additional benefit to WLI followed by ME-NBI for lesions with protrusions. T1b High Confidence in EUS showed higher PPV compared with T1b Low Confidence in EUS which showed marginal

statistical benefit. Therefore, the confidence level in EUS may affect the diagnosis of invasion depth for SESCC.
Disclosure: Nothing to disclose

Reference

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P0769 EVALUATION OF FACTORS TO DECIDE ON ESD INDICATION FOR GASTRIC ADENOMAS DIAGNOSED WITH ENDOSCOPIC BIOPSY

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Introduction: Although the adenoma is a benign neoplasm, those diagnosed with a biopsy specimen sometimes prove to be malignant by pathological evaluation after ESD, indicating that the accuracy of the diagnosis for neoplasm based on a small biopsy specimen is limited. Thus, it is difficult to decide on the indication of endoscopic submucosal dissection (ESD) for adenomas. In addition, therapeutic strategy for gastric adenoma has not been well established and none has reported the appropriate approach to adenomas for the future metachronous multiple lesions. In this study, factors contributing to the decision for removing gastric adenomas diagnosed preoperatively with biopsy specimen were evaluated.
Aims and Methods: Five hundred and thirty-nine lesions of gastric epithelial tumor pathologically diagnosed after complete *en-bloc* curative resection by ESD between 2009 and 2017 were retrospectively reviewed. Among 539 lesions, 62 lesions, diagnosed preoperatively as adenomas, were enrolled in this study. The preoperative endoscopic findings under white light (WL), known as signs of potential cancer, such as a size over 20 mm, red color, tall protrusion, central depression, and positive finding in the assessment under magnified-NBI (M-NBI) were analyzed using Fisher's exact test. The assessment under M-NBI was based on VS classification system by Yao. The removed specimens, pathologically assessed by cutting with every 2 mm of interval, were classified as either cancer or adenoma. In addition, the specimens of well differentiated adenocarcinoma (tub1) were classified into 2 groups, low-grade tub1 and regular tub1. While adenomas are characterized of lesions without A (dysplasia of nucleus and disappearance of differentiation in superficial area) and B (dysplasia of glandular structure with or without invasion to submucosal layer), regular tub1 was characterized of that with A and B. Low-grade tub1 was defined as lesion with A but without B.
Results: Among 62 lesions preoperatively diagnosed as adenoma, 24 (38.7%) proved to be cancer by detailed pathological assessment after ESD. These 24 lesions (tub1) were all pathologically classified as low-grade intestinal type tub1. Among 24 lesions diagnosed as tub1 after ESD, the 4 preoperative endoscopic findings described above under WL were found in 10/2/4/2 lesions (41.7/8.3/16.7/8.3%), respectively. On the other hand, among 38 lesions diagnosed as adenoma, those were found in 9/3/2/1 lesions (23.7/7.9/5.3/2.6%), respectively, indicating that the rate of each factor was higher in tub1 than adenoma although no statistically significant difference was observed. However, the rate of above factors with more than 1 preoperative finding was significantly higher in tub1 group (62.5%(15/24) vs 34.2%(13/38), $p = 0.038$). The rate of positive findings under M-NBI was also higher in tub1 group (54.2%(13/24) vs 23.7%(9/38), $p = 0.028$). We experienced 2 metachronous cases with a scar of previous ESD for benign adenoma. The treatment time was extremely long (252, 323 min, respectively) because of the technical difficulty.
Conclusion: It is important to evaluate macroscopic findings under white light as well as magnified-NBI assessment to decide on the ESD indication for lesions with a preoperative diagnosis of benign adenoma with biopsy specimens. Considering the difficulty to remove lesions with an ESD-related scar in case with metachronous multiple lesion, lesions without risk factors of cancer can be carefully followed-up to avoid the consequent ESD-related scar because of pathologically low-grade malignancy in all cancer lesions diagnosed postoperatively.
Disclosure: Nothing to disclose

P0770 HOW DOES LINKED COLOR IMAGE (LCI)WHICH IS ONE MODALITY OF IMAGE ENHANCED ENDOSCOPY (IEE) CONTRIBUTE TO DETECT OF THE MINUTE TO SMALL EARLY GASTRIC CANCER? A PILOT STUDY

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Introduction: How can you detect minute to small early gastric cancer effectively? It is the theme that is the most important to gastric cancer screening.
If minute to small early gastric cancer is detected by untechnical Endoscopist it is effective at all.
Therefore we examined whether a detection rate of the early gastric cancer was raised by using LCL which was one of the modality of IEE which Fuji Film Company developed.
Aims and Methods: LCI expands color differences so that reddish color becomes redder and whitish color becomes whiter for image obtained by simultaneously irradiating laser light and white light with appropriate balance. Therefore, LCI enhances slight color differences close the mucosal color and may increase the visibility of the lesion as compared with the conventional white light observation.
Detectability of neoplastic lesions in stomach using ultra slim endoscope and LCI : a randomized comparison trial.
The aim of this study is to evaluate usefulness of LCI compared with White light observation for detectability of neoplastic lesions in Stomach.
Registered cases:
- WLI 750 cases
- LCI 750 cases
Total 1500 cases
Study term: March, 2017∼Feb. 2022 (5 years)
Pilot Study (100 cases) is finished
Results: In Japan, the differentiated type early gastric cancer with *H. pylori* (+) was said to tend to be multiple around 10–15% and did field setting of this study after early gastric cancer endoscopic treatment primarily. We report pilot study at a point in time when 100 registration completed it in 1,500 aims. There was four cancer detected group and was one three LCI group xenon group. There are three cases in LCI group one case in xenon group in cancer detected group. Three LCI group was recognized it as redness with a depression type together and wasgroup of xenon recognized as fading by a flat elevation. Each these cases was *H. pylori*-negative. Whereas there are 12 registration cases in the adenoma detected group, and eight cases in LCI group, xenon group was four. Only one case of LCI was *H. pylori* (+) infection, but all others were infected. One case of the LCI group was a depressive type, but all the others were flat elevations. Six of eight LCI group discoloration, and two patients recognize it as redness. In four xenon group, two cases redness, two cases discoloration. From these, eradication was done in the case of cancer group, the LCI function seems to become easy to be recognized as redness regardless of depression and flat elevation. Whereas, in the case of adenoma, there are many flat elevation.
It seems to become easy to recognize a flat elevation as fading more.
Conclusion: Both cancer and adenoma were a few in the LCI group, but were the tendency that a discovery rate was high in with a significant difference.
We may contribute to detect of the minute∼ small early gastric cancer by LCI in the detection of the early gastric cancer after eradication in future while *H. pylori* eradication states increase.
Disclosure: Nothing to disclose

P0771 COMPARATIVE STUDY OF ESD AND SURGICAL RESECTION FOR GASTRIC SETS ORIGINATED FROM MUSCULARISPROPRIA

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Introduction: Endoscopic resection for gastric subepithelialtumors (SETs) originated from the muscularispropria (GSET-PM) has offered less invasive alternatives to surgical resection.
Aims and Methods: The aims of this study were to compare endoscopic subtumoraldissection (ESD) with surgical resection for the removal of GSET-PM. This study involved 17 patients with GSET-PM removed by ESD and 76 patients who underwent curative surgical resection. ESD was attempted in GSET-PM with well marginated tumors which was below 5cm and showed an endoluminal growth pattern according to endoscopic ultrasound (EUS) finding.
Results: ESD group were more likely to have upper portion (10/17, 58.8%) and surgery group were more likely to have mid portion (41/76, 53.8%, $p = 0.039$). ESD group were smaller median tumor size (25.6 mm vs 35.9 mm, $p = 0.037$) and higher endoluminal ratio ($58.5 \pm 9.1\%$ vs $45.8 \pm 15.4\%$, $p = 0.002$). ESD group were mostly to have Yamada type III (10/17, 58.8%) and surgery group were mostly Yamada type I (52/76, 68.4%, $p < 0.001$). Complete resection by ESD was lower than by surgical resection (82.4% vs 100%, $p < 0.001$). In ESD group, 3 performed surgical resection after ESD (1 incompletely resection and 2 uncontrolled bleeding) and 1 showed perforation was completely resected with endoscopic closure. In surgery group, complications occurred in 6 patients (1 leakage, 1 stricture, 1 hernia and bowel obstruction, 1 wound infection and 2 worsened general condition after surgery). Although surgery group were lower in complication rate than ESD group ($p = 0.006$), severity of complications were higher in the surgery group and there were no mortalities in the ESD group compared with 2 in the surgery group. There was no statistical difference of recurrence and the follow-up period between two groups.
Conclusion: ESD can be one of good options for the resection of endoluminal GSET-PM and could be replace treatment by surgical resection in Yamada type III with a high endoluminal ratio.
Disclosure: Nothing to disclose

P0772 SHOULD NARROW BAND IMAGING (NBI) BE ROUTINELY USED DURING ESOPHAGUS INSPECTION? A RANDOMIZED PROSPECTIVE STUDY

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Introduction: Heterotopic gastric mucosal patch of cervical esophagus (gastric inlet patch, GIP) is a common endoscopic finding, however, its origin, prevalence and clinical significance are not well understood. Recently gastric inlet patch detection rate (GIPDR) has been proposed as potential quality indicator of upper gastrointestinal endoscopy [1] and first guidelines mentioned about cervical inlet patches (BSG and AUGIS) [2]. Endoscopists awareness as well as endoscopy using narrow band imaging (NBI) are proposed as main factors that affect its detection, however there is lack of prospective randomized trials that may answer the question if this imaging technique should be used routinely [3–5].

Aims and Methods: The aim of the study was to investigate whether routine use of NBI and endoscopist's attention improves the GIPDR. 1000 patients were randomized into NBI or standard white light endoscopy (WL) in 1:1 ratio. During first 500 endoscopies operators were asked to perform endoscopy with the standard attention. For next 500 endoscopies the same endoscopists were asked to step up with attention on GIP presence. The difference in imaging technique was applied to esophagus inspection during withdrawal of the scope. Results were compared with 460 endoscopies performed during one year before the research (control group).

Results: Eighty GIPs were found during the study (47 NBI, 33 WL), GIPDR obtained at 8%.

There was neither significant difference in GIPDR between NBI and WL groups (9.4% vs 6.6%, $p = 0.1$), nor in 'attentive' and 'inattentive' groups (9.4% vs 6.6%, $p = 0.1$). Attention did not improve GIPDR in WL and NBI groups (WL inattentive 5.6% vs WL attentive 7.6%, $p = 0.37$; NBI inattentive 7.6% vs NBI attentive 11.2%, $p = 0.17$). NBI and enhanced attention improved GIPDR in comparison to WL and standard attention (11.2% vs 5.6%, $p = 0.001$). GIPDR in the study was greater than in control group (8% vs 4.1%, $p = 0.006$), however only increased attention was superior to the control group (inattentive $p = 0.09$; attentive $p = 0.001$). NBI was superior to the control group (NBI total $p = 0.001$, NBI inattentive $p = 0.047$, NBI attentive $p = .0003$), in WL group only increased attention was superior to the control group (WL total $p = 0.09$, WL inattentive $p = 0.36$, WL attentive $p = 0.047$).

Conclusion: NBI enables CIP detection at the same level as standard endoscopy with enhanced attention. Increased attention of GIP enhances GIPDR especially when using NBI.

Disclosure: Nothing to disclose

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P0773 EFFICACY OF HAEMOSPRAY THERAPY ON RE-BLEED AND MORTALITY RATES – A UK SINGLE-CENTRE EXPERIENCE

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Introduction: Dual endotherapy including epinephrine injection, thermal and mechanical methods have been shown to be superior to monotherapy in reducing the risk of re-bleed (20% vs 10%) and need for surgery in patients with upper gastrointestinal bleed (UGIB) [1]. Heamospray, an inorganic powder is a chemical mechanism to achieve haemostasis. The aim of the study was to describe a single centre district hospital experience in the United Kingdom with haemospray both as monotherapy and dual therapy in UGIB.

Aims and Methods: Retrospective data for all patients who were treated with haemospray for UGIB were collected retrospectively between January 2016 to June 2017 using EndoSoft®, Sunquest ICE®, Medisec and case notes. The primary endpoints were short-term haemostasis (24 hours), long-term haemostasis (7 days) and mortality in patients where haemospray was used either as primary haemostatic agent or combination therapy with a second haemostasis modality.

Results: Haemospray was applied during 50 examinations in 48 patients – 21 male (44%) and 27 female (56%), mean age 71.9 (range 40 to 92) years. The mean Blatchford score was 9.6 (range 0–18). 33 (69%) patients were treated for peptic ulcer. The rest were used for treating 2 (4%) gastric antral vascular ectasia, 2 (4%) oesophagitis, 2 (4%) post sphincterotomy, 8 (16%) non-specific bleeding source and 1 (2%) gastric tumour. Of the 48 procedures, re-bleeding occurred in 8 patients. Overall, short-term haemostasis was achieved in 46 (95%) patients and long-term haemostasis was achieved in 42 (87.5%). A total of 12 (25%) patients died, out of which 4 (8%) died due to a re-bleed and 2 (4%) failed to achieve initial primary haemostasis. The reminder 6 patients died from non-UGIB cause.

Conclusion: In this single-centre audit, the role of haemospray as combination and monotherapy in achieving haemostasis has been shown to be comparable to other modalities of endotherapy with statistical significance. This data needs to be replicated in a larger number of patients across other centres.

Disclosure: Nothing to disclose

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P0774 MUCOSAL LOSS IS THE CRITICAL MECHANISM OF ESOPHAGEAL STRICTURE AFTER MUCOSAL RESECTION: A PILOT EXPERIMENT IN A PORCINE MODEL

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Introduction: Esophageal stricture is a major complication of endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). To date, the critical mechanism of esophageal stricture has not been fully elucidated and there is no effective treatment.

Aims and Methods: We designed this experiment to explore the underlying mechanisms of esophageal stricture after mucosal resection in a porcine model. Twelve swines were used for this study and were randomly divided into two groups. Firstly, In all the swines, two submucosal tunnels, 5 cm in length and 1/3rd in width, were made on the anterior and posterior wall of the esophageal circumference. After that,we resected the mucosa along the edge of the tunnel in the first group meanwhile mucosal incision was made on the covered mucosa to expose the submucosal layer over each tunnel In the second group. The process of stricture formation was evaluated by endoscopic inspection after one, two and four weeks respectively. Histological examination were performed after humanely execution

Results: Ulcer formation was inspected on endoscopic observation and incisional edges tended to grow and conglutinate with each other in each group after one week. All of the swines in the first group developed mild to severe esophageal stricture with weight loss whereas no esophageal stricture was evident in the ones of the second group after two and four weeks respectively.

Conclusion: The loss of esophageal mucosa should be the crucial factor for esophageal stricture after mocosal resection. Inflammation and scar formation slightly attribute to esophageal stricture formation. These results are important for developing a suitable treatment method for esophageal stricture.

Disclosure: The two authors were involved in this work, agreed to submit it to UEGW 2018, and assumed responsibility for the accuracy and completeness of the data. The authors declare that there are no conflict of interest.

Abstract No: P0773

	Mean age	Blatchford score	Short-term haemostasis (24hrs)	Long-term haemostasis (7days)	Deaths due to primary UGI bleed	Deaths due to Re-bleed
Monotherapy n = 21	75	9.57	21/21 (100%) [OR 0.02, 95%CI 0.01–0.41, p < 0.01]	19/21 (90%) [OR 0.10, 95%CI 0.02–0.51, p < 0.01]	0/21 (0%)	1/21 (4.7%)
Dual therapy n = 27	70	9.59	25/27 (93%) [OR 0.08, 95%CI 0.02–0.37, p < 0.01]	23/27 (85%) [OR 0.17, 95% CI 0.05–0.57, p < 0.01]	2/27 (7%)	3/27 (11%)

[Summary of monotherapy vs dual therapy including haemospray]

P0775 ENDOSCOPIC SUBMUCOSAL DISSECTION WITH SPLASH M-KNIFE: A SINGLE-CENTER CONSECUTIVE CASE SERIES

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Introduction: Endoscopic submucosal dissection (ESD) is widely accepted as a standard endoscopic treatment for early stage gastrointestinal (GI) neoplasms having a small risk of lymph-node metastasis, which could not resect by traditional endoscopic resection methods. However, completion of the procedures is very laborious in some cases due to bleeding and fibrosis. The Splash M-knife is a new multifunctional ESD device with water irrigation function. In addition, a metal plate attached to its distal sheath is better for hemostasis and cutting the fibrotic tissue during the procedure than conventional devices.
Aims and Methods: We aimed to elucidate the technical outcomes of ESD for GI neoplasms by using the Splash M-knife, because no consecutive case series in the whole GI tract have been reported so far. A retrospective single-center study was conducted at the University of Tokyo Hospital between January 2015 and December 2017 in patients who had received ESD with the Splash M-knife in the esophagus, stomach or colon. Procedure time, en bloc and complete resection rates, post procedure bleeding rates and perforation rates were evaluated in each organ.
Results: During the study period, 435 patients (esophagus (E)/stomach (S)/colon (C): 89/146/200) were treated by ESD with the Splash M-knife. The gender ratio (M/F), mean age, specimen size and tumor size in E/S/C were 7.1/3.4/1.2, 67.4/71.1/65.0 years, 37.0/40.2/38.9 mm, and 21.7/18.8/29.4 mm, respectively. As for the short-term outcomes, procedure time, en bloc resection rate, complete resection rate, post procedure bleeding rate and perforation rate in E/S/C were 73.3/123.9/95.2 mins, 91.0/98.6/96.0%, 84.3/84.9/83.0%, 0.0/4.1/2.0%, and 1.1/2.7/6.0%, respectively.
Conclusion: ESD with splash M-knife resulted in favorite outcomes through the GI tract. Further prospective comparative studies are needed to elucidate the advantages of this knife over other conventional knives.
Disclosure: Nothing to disclose

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P0776 DEVELOPMENT AND VALIDATION OF ENDOSCOPIC PREDICTION MODEL FOR GASTRIC CYTOMEGALOVIRUS INFECTION IN PATIENTS WITH RENAL TRANSPLANTATION

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Introduction: Cytomegalovirus (CMV) is a very common viral pathogen after organ transplant patients. However, endoscopic characteristics of gastric CMV infection have not been established.
Aims and Methods: We aimed to develop and validate a prediction model using endoscopic findings for gastric CMV infection in patients with renal transplantation. A retrospective study was performed in a tertiary referral hospital enrolling 354 kidney transplant recipients who received endoscopy with biopsy for suspected CMV infection from Jan. 2005 to Nov. 2015. For the development phase, endoscopic parameters were selected by univariate logistic regression analyses. Then, the prediction model was established on the basis of β coefficients of the multivariate logistic regression. For the validation of the model, the same regression equation was tested on the other group.
Results: Age, days from renal transplantation to endoscopic biopsy, erosion at antrum, erosion with exudate, raised erosion, and ulcer at antrum were selected as the predicting factors for gastric CMV infection. In the development set (n = 176) using these five markers, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 92.23, 80.82, 87.16, and 88.06, respectively. In the validation set (n = 178), the sensitivity, specificity, PPV, and NPV were 83.87, 82.35, 83.87 and 82.35, respectively.
Conclusion: This endoscopic prediction model using 6 risk factors can be a reliable diagnostic tool for gastric CMV infection after renal transplantation.
Disclosure: Nothing to disclose

P0777 AN AUSTRALIAN EXPERIENCE WITH ENDOSCOPIC SLEEVE GASTROPLASTY (ESG) FOR WEIGHT LOSS

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Introduction: The pioneering centres for endoscopic bariatric therapies have demonstrated the strong efficacy and safety profile of endoscopic sleeve gastroplasty (ESG). However, data outside these expert centres remain scant. We report a single-centre experience of ESG performed in Australia (Sydney Adventist Hospital, Sydney).
Aims and Methods: All patients undergoing ESG between May-October 2017 had data prospectively collected. All patients had previous unsuccessful attempts at diet and exercise programs.
ESG was performed by 2 Gastroenterologists. The Apollo OverStitch device (Apollo Endosurgery) was used to place full-thickness endoscopic sutures from the incisura angularis to the fundus, creating a 'sleeve effect' using the technique previously described in detail. All patients received regular follow-up with a multidisciplinary team.
Measured outcomes included absolute weight loss, change in body mass index (BMI), total body weight loss (%TBWL) and excess weight loss (%EWL) at 1 and 6 month follow-up. The proportion of patients achieving ≥10% TBWL, ≥15% TBWL, and ≥25% EWL at 6 months was also assessed. Intention-to-treat (ITT) analysis considered patients lost to 6 month follow-up as failing to meet these thresholds.
Results: A total of 66 patients (75.8% female) underwent ESG. The mean age was 45.2 ± 10.2 years, mean baseline weight was 112.5 ± 17.0kg and mean BMI was 39.3 ± 4.7kg/m^2. The outcomes at 1 and 6 month follow-up (mean ± SD) are summarised in table 1.

	No. of patients	Weight loss (kg)	Δ BMI (Kg/ m^2)	%TBWL	%EWL
1 month	66	9.7 ± 3.3	3.4 ± 1.0	8.6 ± 2.5	25.3 ± 11.7
6 months	64	16.5 ± 7.3	5.8 ± 2.5	14.6 ± 5.7	42.7 ± 20.1

[Weight loss outcomes at 1 month and 6 months post-ESG]

Of the 64/66 (97.0%) of patients with 6 month follow-up data, 81.3% achieved ≥10% TBWL, 45.3% achieved ≥15% TBWL, and 85.9% achieved ≥25% EWL. In the ITT analysis, 78.8% achieved ≥10% TBWL, 43.9% achieved ≥15% TBWL, and 83.3% achieved ≥25% EWL at 6 month follow-up.
There were 2 (3.0%) serious adverse events. Both were a peri-gastric inflammatory collection requiring hospitilisation (4 and 8 days), intravenous antibiotics, laparoscopic washout and percutaneous drainage. Both patients recovered uneventfully without long-term sequelae.
Conclusion: This single-centre study of 66 consecutive patients undergoing ESG demonstrates reproducibility of the strong efficacy and safety profile of ESG outside the core facilities where the procedure was developed.
Patients achieved 14.6% TBWL and 42.7% EWL at 6 months. These results are comparable to the multicentre study across the pioneering centres, in which 248 patients undergoing ESG achieved 15.2% TBWL at 6 months.
In ITT analysis, at 6 months 83.3% achieved ≥25% EWL, which is the 12 month efficacy threshold for a bariatric procedure to be incorporated into clinical practice, as determined by the American Society of Gastroenterology (ASGE) Bariatric Task Force.
The limitations of this study are the lack of control group and limited long-term follow up. Weight loss at 6 months has been shown to be predict weight maintainence and further weight loss at 2 years, so we would anticipate the majority of our patients to have favourable longer-term results.
This study adds to the growing evidence that ESG is a highly effective, reproducible and safe treatment option for patients with obesity.
Disclosure: Nothing to disclose

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P0778 SURFACE IRREGULARITIES OCCURRING IN THE GASTRIC MUCOSA AFTER *H. PYLORI* ERADICATION MAKES IT DIFFICULT FOR ENDOSCOPIC DIAGNOSIS OF GASTRIC CANCER DETECTING

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Introduction: *H. pylori* (Hp) eradication therapy have been thought to be useful on the gastric cancer (GC) detecting more easily before eradication due to disappearance of gastric inflammation. On the other hand, there are various new endoscopic appearances in eradicated stomach which differ from known appearances in Hp-infected stomach. And these new mucosal changes often make difficult to detect GC on eradicated stomach. We can expect that GC will decrease after Hp eradication, but we may confuse to detect GC due to endoscopic diagnostic difficulty with gastric mucosal change after eradication at a certain rate. Although this gastric mucosal change does not occur in all stomach after eradication, endoscopic examination should be done with sufficient consideration that endoscopic diagnosis becomes complicated and becomes difficult in the eradicated stomach.

Aims and Methods: The aim of this study is to elucidate what changes are occurring on the gastric mucosal surface after Hp eradication. Endoscopic images of 352 cases who received Hp eradication therapy were collected (from Jan. 2015 to Nov. 2017). We examined the presence of gastric mucosal changes on all endoscopic files before and after eradication in each case. We checked the presence of irregularities on the gastric mucosal surface, and all cases were examined histologically with biopsy samples. In the histological evaluation, we analyzed the cause of surface irregularity and were measured the thickness of gastric foveolar epithelium and proper gastric glands.

Results: The gastric mucosal change after eradication was classified into three groups (A, B, C) from the viewpoint of easiness (difficulty) of endoscopic observation. Group A is the easy group after eradication: 49.7% (175/352), This group is easy to observe after eradication due to improvement of mucus adhesion and swollen gastric fold. Group B is the unchanged group after eradication: 24.7% (87/352), endoscopic appearance did not change before and after eradication in this group. Group C is the difficult group after eradication: 25.6% (90/352), endoscopic newly appearance occurred after eradication and this change made obviously complicated and difficult to detect GC. The age, sex and other various background of each group had not significant difference in each group. We analyzed this gastric mucosal surface irregularity in histologically. We found that main reasons of gastric mucosal irregularity consisted of gastric foveolar epithelial hyperplasia and intestinal metaplasia after eradication. In other words, gastric surface irregularities after eradication became gradually apparent with foveolar epithelium growth and metaplastic change after eradication. Approximately one fourth of the stomach after eradication, it is considered that endoscopic diagnosis of detecting GC becomes difficult. In the gastric mucosa where proper gastric glands remain, foveolar epithelial hyperplasia occurs in the process of repair and regeneration after inflammation. This is considered that the main cause of surface irregularities in the gastric mucosa after eradication. On the other hand, it seems that such a change does not occur in the gastric mucosa which has been completely replaced by intestinal metaplasia without proper gastric gland remaining.

Conclusion: Surface irregularities occurring in the gastric mucosa after Hp eradication makes it difficult for endoscopic diagnosis of gastric cancer detecting. Therefore, when we examine the stomach after eradication, the endoscopic examination should be done with extremely care as well as stomach before eradication.

Disclosure: Nothing to disclose

P0779 COMBINED TREATMENT OF OVERWEIGHT WITH INTRAGASTRIC BALLOON AND LIRAGLUTIDE AT HIGH DOSE: IS IT WORTH IT?

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Introduction: Intragastric balloon and liraglutide single therapies are used worldwide to treat excess weight and obesity. However, there is no published study with both treatments combined.

Aims and Methods: We aimed to evaluate the efficacy and complications of intragastric balloon therapy alone and combined with liraglutide.

Patients with BMI above 27 kg / m2 were included. Patients at risk of baseline gastroparesis (Type II diabetes, age greater than 60 years) were excluded. Patients were randomly divided into two groups. One group was submitted to the isolated therapy with Orbera intragastric liquid balloon, with permanence of 6 months. The second group, besides the IGB implant, received a daily dose of liraglutide (maximun 3.0 mg (mean). Data were analyzed using descriptive statistical methods, Student's t-test and analysis of variance followed by the Tukey post-test. The level of significance was set at $p < 0.05$.

Results: 90 patients (64 women) were randomly divided into two groups of 45 people with the same composition (32 women and 13 men). The mean age was 34.4 (21–57), the mean initial BMI in group 1 was 33.93 and in group 2, 33.95. 42 patients in group 1 completed treatment compared to 31 patients in group 2. The results regarding the initial and final BMI, TBWL EWL, weight loss in kg are shown in table 1.

	Group 1	Group 2
BMI (Kg/m2)		
initial	33.93 ± 1.94	33.95 ± 1.77
final*	27.72 ± 1.66	26.72 ± 1.65
reduction+	6.21 ± 0.88	7.23 ± 1.07
Weight		
initial	97.98 ± 8.87	97.63 ± 8.63
final*	80.08 ± 7.34	75.92 ± 6.68
Weigh loss (kg)+	17.90 ± 2.87	21.71 ± 3.72
TWL (%)+	18.29 ± 2.16	22.21 ± 2.94
EWL (%)+	71.81 ± 14.50	86.53 ± 17.06

*$p < 0.001$ comparing final and initial values. +$p < 0.001$ between groups

[Table 01]

Conclusion: Both treatments are effective in promoting weight loss; however, the combination with liraglutide seems to promote an even greater weight loss without increasing complication. Liraglutide shows to be a great adjuvant drug for the intragastric balloon therapy.

Disclosure: Nothing to disclose

P0780 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN AMYOTROPHIC LATERAL SCLEROSIS WITH SEVERE VENTILATORY IMPAIRMENT

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Introduction: Weight loss is one of the major bad prognostic factors in amyotrophic lateral sclerosis (ALS). The placement of percutaneous endoscopic gastrostomy (PEG) is of paramount importance in patients with dysphagia to improve the diagnosis. However, there is some fear regarding the possible ventilatory complications during the procedure, as well as the exact timing for placing PEG.

Aims and Methods: The aim of this study was to evaluate the PEG insertion under non-invasive ventilation in patients with ALS and severe ventilatory impairment.

Retrospective study of all consecutive PEGs placed in our department from May/2011 to January 2018 in patients with ALS. The procedure was performed under noninvasive positive pressure ventilation for ventilatory support (oronasal mask).

Results: We included 59 patients with ALS with severe ventilatory impairment, 58% female, with a mean age of 67.2 ± 10.1 years, a median Charlson index of 3 [2–4] and a median follow-up of 6 [2–15] months.

The main indication for PEG placement was dysphagia (98%) and 15% had had a previous episode of aspiration.

The median time for PEG insertion since the established diagnosis of ALS was 12 [6–25] months and 4 [2–18] months since the beginning of bulbar symptoms.

The majority of the patients placed a 20Fr PEG (63%) and under sedation with midazolam (80%), all under non-invasive ventilation (NIV). There were no immediate complications during and after the procedure (no episodes of aspiration or orotracheal intubation) and mortality.

The 30-day, 180-day and 360-day mortality rates were, respectively, 5.1%, 27.1% e 35.6%.

Conclusion: The placement of PEG is a very important in patients with ALS and severe ventilatory impairment, improving not only the nutritious status but also the prognosis. Our collaboration between Gastroenterology and Pneumology permitted the insertion of PEG under NIV, in a safe and effective procedure in this special population, being one of the major series reported in the world.

Disclosure: Nothing to disclose

P0781 DIAGNOSTIC ACCURACY USING ARTIFICIAL INTELLIGENCE-ASSISTED ENDOCYTOSCOPY FOR SESSILE SERRATED ADENOMA/POLYPS

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Introduction: Sessile serrated adenoma/polyps (SSA/Ps) should be resected because they are known to be precursors of CRCs. Accurate endoscopic criteria to differentiate SSA/Ps from Hyperplastic polyps (HPs) are necessary. However endoscopic differentiation with endoscopists' eyes is considered difficult. In this study, we evaluated the performance of the newly developed artificial intelligence (AI) in endoscopic identification of SSA/Ps.

Aims and Methods: We developed the AI system based on the previously proposed model[1].

The AI system was combined with endocytoscopy which enables in vivo observation of cellular images at 500-fold magnification (CF-H290ECI or CF-Y0058, prototype from Olympus Co.). The diagnostic algorithm of the AI consisted of the sequence of image acquisition, extraction of 312 visual features from nuclear images and contrast difference of the whole image, and classification into the two pathological groups (SSA/P and non-SSA/P).

We designed this retrospective study to assess the performance of the AI system for prediction of SSA/Ps by using 18 SSA/Ps (641 images) and 49 HPs (1228 images) resected between Sep. 2017 and Feb. 2018.

The main outcome measures were diagnostic sensitivity specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the AI system in identifying SSA/P in high confidence (probability > = 90%).

Machine learning for the AI was performed by using 28000 images which were acquired from Jan. 2016 to Aug. 2017. In the lesion-based analysis, diagnosis of the target lesion was defined as SSA/P when the AI system shown at least one SSA/P output.

Results: The AI system automatically output the pathological prediction of 527 images (SSA/P 102 images, HP 425 images) out of total 1869 images immediately with high confidence (probability > = 90%). In the image-based analysis, the AI system showed sensitivity of 11.8%, specificity of 99.5%. PPV in high confidence was 85.7% and NPV was 82.5%.

However, in the lesion-based analysis AI system showed sensitivity of 27.8%, specificity of 95.9%.

		Pathology	
		SSA/P	Hyperplastic polyp
AI output	SSA/P	12	2
(High confidence)	non-SSA/P	90	423

[Image-based analysis]

Conclusion: This study revealed AI system diagnosed SSA/P with high specificity, but low sensitivity in high confidence.

However, further accumulation of endoscopic images for machine learning is required to make more robust model for diagnosing SSA/Ps.

Disclosure: Nothing to disclose

Reference

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P0782 A COMPARISON OF PERFORMANCE PARAMETERS FOR COLONOSCOPY FOR USING DIFFERENT ENDOSCOPY SYSTEMS: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: High-definition imaging should be the standard for diagnostic endoscopy and optimized patient care. However, many units still suffer from the high costs of these systems. Most recently, a novel brand offering high-definition imaging was introduced to the market which is significantly less expensive compared to most traditional endoscopy brands.

Aims and Methods: To investigate the performance parameters of colonoscopy between the new brand (Sonoscape) and established competitors (Pentax and Olympus). A prospective, multicentre, randomised controlled, parallel, non-inferiority trial conducted in 5 endoscopy units located in Germany, Italy, Thailand, China and Russia was conducted. Performance parameters assessed were cecal intubation time, withdrawal time, total examination time, number of polyps detected, and average size of polyps.

Results: A total of 252 patients were included. No significant differences were noted between the different groups regarding gender, age, previous surgery or bowel preparation. Cecal intubation time (Sonoscape 8 minutes vs. 7 (Pentax)/ 10 minutes (Olympus); p = NS) and withdrawal time (10.5 minutes vs. 8 (P)/ 9 minutes (O); p = NS) with the new brand was not significantly different to the others. Polyps were detected in 39% of patients with the new brand compared to 33% (P) and 43% (O) with the others (p = NS). Average size of the polyps detected was 5mm for the new brand and 6mm/ 5 mm for the others (p = NS). No complications were recorded.

Conclusion: The performance of the new endoscopy brand is not inferior to that of the other brands studied. Therefore, future research should now focus on the image quality and the applicability for predicting histology. Major advantage of the new system is the low price which makes it even achievable for smaller sized endoscopy units.

Disclosure: Nothing to disclose

P0783 DIAGNOSTIC ABILITY OF BLUE LIGHT IMAGING FOR PREDICTING DEEP SUBMUCOSAL INVASION IN COLORECTAL LESIONS

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Introduction: Blue Light Imaging (BLI) was recently introduced as a novel imaging technology allowing for enhanced visualization of the mucosal surface and vascular pattern morphology. Data regarding the applicability of BLI for prediction of deep submucosal invasion of colorectal lesions is missing.

Aims and Methods: Main study objective was to assess the potential of BLI for prediction of deep submucosal invasion of colorectal lesions.

Consecutive patients undergoing screening or surveillance colonoscopy were prospectively evaluated using a high-definition endoscope with BLI capability. Circumscript lesions were examined with BLI before taking biopsy specimens or performing endoscopic resection. BLI images were graded according to surface and vascular pattern morphology and correlated with conventional histopathology in a prospective and blinded fashion.

Results: 120 cases were included. BLI yielded high-quality images in all cases. Based on pit pattern and vascular alterations BLI could predict the presence of deep submucosal invasion with high sensitivity (95%), specificity (91%) and accuracy (93%). Positive and negative predictive values of BLI for *in vivo* diagnosis of deep submucosal invasion were 88% and 95%, respectively.

Conclusion: BLI is a novel diagnostic tool allowing for real-time prediction of deep submucosal invasion of colorectal lesions with high accuracy. This becomes of crucial importance in clinical practice and could lead to an optimized and rapid diagnosis of neoplasic changes during ongoing endoscopy and an individualized management approach.

Disclosure: Nothing to disclose

P0785 EFFICACY AND SAFETY OF ETOMIDATE-MIDAZOLAM FOR SCREENING COLONOSCOPY IN ELDERLY: A PROSPECTIVE DOUBLE-BLINDED RANDOMIZED CONTROLLED STUDY

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Introduction: Recent studies have shown that etomidate is associated with fewer serious adverse events than propofol and has a non-inferior sedative effect. We investigated whether etomidate-midazolam is associated with fewer cardiopulmonary adverse events and has non-inferior efficacy compared to propofol-midazolam for screening colonoscopy in the elderly.

Aims and Methods: A prospective, single-center, double-blinded, randomized controlled trial was performed. Patients aged over 65 years who were scheduled to undergo screening colonoscopy were randomized to receive either etomidate or propofol based on midazolam. The primary outcome was all cardiopulmonary adverse events. The secondary outcomes were vital sign fluctuation (VSF), adverse events disturbing the procedure, and sedation-related outcomes.

Results: The incidence of cardiopulmonary adverse events was higher in the propofol group (72.6%) than in the etomidate group (54.8%) ($p = 0.040$). VSF was detected in 17 (27.4%) and 31 (50.0%) patients in the etomidate and propofol groups, respectively ($p = 0.010$). The incidence rate of adverse events disturbing the procedure was significantly higher in the etomidate group (25.8%) than in the propofol group (8.1%) ($p = 0.008$). Moreover, the incidence rate of myoclonus was significantly higher in the etomidate group (16.1%) than in the propofol group (1.6%) ($p = 0.004$). There was no statistical significance between the two groups with respect to sedation times and sedation-related outcomes including patients' and endoscopist's satisfaction. In the multivariate analysis, the etomidate group had significantly low odds ratio (OR) associated with VSF (OR: 0.407, confidence interval: 0.179–0.926, $p = 0.032$).

Conclusion: We recommend using etomidate-midazolam in patients with high ASA score or vulnerable to risk factors; propofol-midazolam may be used as a guideline in patients with low ASA score.

Disclosure: Nothing to disclose

P0786 COMPARISON OF THE CLINICAL EFFICACY OF THE COLD SNARE POLYPECTOMY USING A THIN WIRE MINI-SNARE AND THICK WIRE MINI-SNARE FOR SMALL SIZE (5-8 MM) COLORECTAL POLYPS

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Introduction: Cold snare polypectomy (CSP) is established technique for the resection of colorectal polyps up to 10 mm in size without electrical current. However, there is a lack of comparative studies using a thin wire mini-snare (designed for CSP) and thick wire mini-snare during CSP. Thus, the aim of this study was to compare the clinical effectiveness of thin wire mini-snare and thick wire mini-snare during CSP in small colorectal polyps.

Aims and Methods: This study was a prospective, randomized and controlled study. Between September and November 2017, a total of 113 neoplastic colorectal polyps (5 to 8mm in diameter) was removed by CSP and included in this study. The primary outcome was measured by complete resection rate (CRR) by gastrointestinal pathologist based on histopathologic findings. Also, endoscopist experience, polyp characteristics, technical factors during CSP, complication and histopathologic features of resected specimens were carefully analyzed.

Results: A total of 113 eligible polyps were successfully resected using CSP (thin mini-snare group ($n = 48$) and thick mini-snare group ($n = 47$)) by 4 endoscopists. The location, size, and shape of the polyps were not statistically significant difference between the two groups. The CRR was not significantly different between the two groups. (Thin mini-snare group: 75.0% vs thick mini-snare group 89.4, $p = 0.068$) There was no significant difference between the two group in immediate bleeding (18.8% vs 6.4%, $p = 0.070$), tissue retrieval (100% vs 100%), and tissue fly away (2.1% vs 0.0%, $p = 0.32$). Histopathologic features including specimen size, safety margin (996 ± 160 um vs 1358 ± 192 um) and containing submucosa tissue in the resected specimen (6.3% vs 10.6%, $p = 0.442$) were not significant difference between the two groups. Regarding CRR related factors, experience of endoscopists was associated with CRR in univariate regression analysis. (odds ratio 4.037, $p = 0.012$). However, snare type, experience of endoscopists, size of polyp, shape of polyp, location of polyp and pathologic finding were not associated with CRR by multiple logistic regression analysis.

Conclusion: Cold snare polypectomy using thin wire mini-snare is considered to have no additional benefit compared to using thick wire mini-snare in small size (5–8mm) colorectal polyps.

Disclosure: Nothing to disclose

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	Thin wire mini-snare group ($n = 48$)	Thick wire mini-snare group ($n = 47$)	P-value
Complete resection rate (%)	75.0% (36/48)	89.4% (42/47)	0.068
Retrieval rate (%)	48 (100.0%)	47 (100.0%)	–
Fly away (%)	1 (2.1%)	0 (0.0)	0.320
Containing submucosa tissue in the resected specimen (%)	3 (6.3%)	5 (10.6%)	0.441
Size of specimen (μm, Mean ± SD)	8211.61 ± 504.93	8738.86 ± 716.71	0.548
Safety margin (μm, Mean ± SD)	996.05 ± 160.38	1358.89 ± 191.82	0.149
Depth Mucosa Submucosa	87 (91.6%) 8 (8.4%)	45 (93.7%) 3 (6.3%)	0.442
Depth (μm, Mean ± SD)	564.85 ± 304.92	454.96 ± 97.91	0.685
Complication (%) Immediate bleeding Delayed bleeding Perforation	9 (18.8%) 9 (18.8%) 0 (0.0) 0 (0.0)	3 (6.4%) 3 (6.4%) 0 (0.0) 0 (0.0)	0.070 0.070 – -

[Procedure outcomes and adverse events]

P0787 USE OF WATER EXCHANGE (WE) FOR PERFORMANCE IMPROVEMENT TOWARDS ENHANCED ADENOMA DETECTION – IS WE THERE YET?

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Introduction: Water exchange (WE) significantly improved overall adenoma detection rate (ADR) [1–7]. The clinical relevance is lessened by the predominance of diminutive adenomas of low malignant potential accounting for the increase. Advanced adenomas ($\geq$ 10 mm, > 25% villous component or high-grade dysplasia) of all sizes are the most valid surrogate markers of malignant potential [8]. Prevalence of advanced adenomas ranged from 3.4% to 7.6% [9]. Presence of fecal occult blood [10] and surveillance [11] are associated with higher and lower advanced ADR, respectively. Colonoscopists' advanced ADRs are variable, and independent of their non-advanced ADRs [12]. Despite recommendation to use advanced ADR to evaluate new screening technologies, other than split-dose bowel preparation [13], no conclusive data based on randomized controlled trials (RCTs) [14,15] have implicated colonoscopist-dependent methods (e.g., technologies and accessories) in enhancing $\geq$ 10 mm advanced ADR. WE insertion time, prolonged by salvage cleansing, was not a factor influencing ADR [16]. At the 2018 Digestive Diseases Week, we will report that compared to AI, WE significantly increased all sizes advanced ADR (5.7% vs. 8.2%, $p = 0.001$). Since size ($\geq$ 10 mm) is a more robust marker of cancer risk than histological characteristics [17], here we focus on the impact of WE on $\geq$ 10 mm advanced adenomas.

Aims and Methods: To highlight the clinical relevance of WE, the hypothesis that WE significantly increased $\geq$ 10 mm advanced ADR compared to air insufflation (AI) was tested. Data from six RCTs that compared AI to WE were pooled. The current primary outcome is based on previously unreported data.

Results:

Table 1. Demographic and procedural data pooled from six RCTs.

5407 patients were randomized to AI (2699) or WE (2708): screening 35% and 32% ($p = 0.003$); surveillance 9% and 10%; positive fecal occult blood 50% and 50%, respectively. WE showed significantly higher $\geq$ 10 mm advanced ADR (primary outcome) (4.4% vs. 6.5%, $p < 0.001$); higher overall ADR (20.9% vs. 27.4%, $p = 0.001$); higher all sizes advanced ADR (5.7% vs. 8.2%, $p = 0.001$);

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Method (no. of patients)	AI (n = 2699)	WE (n = 2708)	p
Age, year, mean (SD);	54 (12)	54 (12)	0.807
Male, n (%)	1476 (55)	1468 (54)	0.743
Indications: Screening, n (%); {Surveillance, n (%)}; [FIT+ or FOBT+, n (%)]	949 (35); {234 (9)}; [1350 (50)]	863 (32); {270 (10)}; [1366 (50)]	0.010; {0.102}; [0.990]
Cecal intubation (insertion) time, minutes, mean (SD); [Cecal intubation rate, n (%)]	6.9 (5); [2614 (97)]	9.5 (5); [2636 (97)]	< 0.001; [0.293]
Primary outcome: Combined ≥ 10 mm advanced ADR, n (%)	120 (4.4)	176 (6.5)	< 0.001
Combined overall ADR, n (%)	564 (20.9)	742 (27.4)	0.001
Combined all sizes advanced ADR, n (%); [Combined < 10 mm advanced ADR, n (%)]	155 (5.7); [35 (1.3)]	222 (8.2); [46 (1.7)]	0.001; [0.263]

P values were obtained using t-test or Fisher's exact test, as appropriate. ADR, adenoma detection rate; AI, air insufflation; FIT, fecal immunochemical test; FOBT, fecal occult blood test; RCTs, randomized controlled trials; SD, standard deviation; WE, water exchange. Withdrawal time was > 8 minutes in both groups. RCTs included in pooled analysis: 1: *Gastrointest Endosc* 2010;72:693 (unsedated) NCT00747084. 2: *J Interv Gastroenterol* 2013;3:7 (unsedated) NCT01383252. 3. *Endoscopy* 2014;46:212 (On demand minimal sedation) NCT01781650. 4: *Am J Gastroenterol* 2017;112:568 (Unsedated or propofol) NCT02135601. 5. *Gastrointest Endosc* 2017;86:192 (Minimal or propofol sedation) NCT01894191. 6: *Endoscopy* 2017;49:456 (On demand minimal sedation) NCT02041507. 1 and 2 used non-split-dose; 3, 4, 5 & 6 used split-dose. In 1, 2, 3, 4, 5 & 6, WE bowel cleanliness during withdrawal was significantly better than AI. Total number of colonoscopists: 22. The longer cecal intubation time of WE was devoted to insertion salvage cleansing, and not a factor contributing to enhanced ADR. The trends of higher ≥ 10 mm advanced ADR, higher all sizes advanced ADR and higher overall ADR were present in all six RCTs ($p < 0.5$, sign test).

[Water exchange significantly increased ≥ 10 mm advanced adenoma detection rate.]

longer insertion time [6.9 (5) vs. 9.5 (5) min, $p < 0.001$). < 10 mm advanced ADRs (1.3% vs. 1.7%, $p = 0.263$) were comparable.

Discussion: The significantly higher overall ADR confirmed WE provides better quality. Assessment of ≥ 10 mm advanced ADR as previously recommended [8] established WE to be a tool superior to AI. The current difference was not due to variable proportions with blood in the stool or for surveillance. WE is now the only colonoscopist-dependent method that produces a significant increase in ≥ 10 mm advanced ADR. The 2% increase, albeit numerically small, is a clinically significant 47% relative increase. The favorable impact of WE on advanced ADR is primarily due to the significant increase in those ≥ 10 mm.

Conclusion: The proof-of-principle data, significant increase in advanced ADR, primarily those ≥ 10 mm, confirm WE to be highly clinically relevant. The significantly higher overall ADR (albeit mostly diminutive) demonstrates better quality. Taken together, it is appropriate to include WE in colorectal cancer prevention programs.

Disclosure: Nothing to disclose

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P0788 CAP-ASSISTED ENDOSCOPIC MUCOSAL RESECTION VERSUS ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL NEUROENDOCRINE TUMORS: A MULTICENTER RETROSPECTIVE STUDY FROM CHINA

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Introduction: Cap-assisted endoscopic mucosal resection (EMR-C) and endoscopic submucosal dissection (ESD) have been both reported to be effective treatment methods for small rectal neuroendocrine tumor (NET) in limited studies. We aimed to compare the outcomes of EMR-C and ESD to determine which one is better for the treatment of rectal NET.

Aims and Methods: We retrospectively collected 702 patients diagnosed with primary rectal NET from January 2007 to September 2017 in eight tertiary medical centers from China. Clinicopathological characteristics, en bloc resection rate, operating time, estimated blood loss, complications, postoperative hospital days, recurrences were recorded and compared.

Results: Among the 702 patients, 279 meet the criteria and were enrolled in the study. 104 patients (37.28%) received EMR-C and 175 patients (62.72%) received ESD treatment. The demographic characteristics of the patients and the tumor size were well balanced. We did not observe significant difference concerning about en bloc resection rate (100% vs. 98.85%, $p = 0.531$) and pathologic R0 resection rate (97.11% vs. 94.28%, $p = 0.382$) between EMR-C group and ESD group, respectively. However, shorter operating time and less estimated blood loss were observed in EMR-C group (7.00 ± 4.79min vs. 21.73 ± 14.36min, $p = 0.027$; 4.17 ± 2.89ml vs. 6.75 ± 3.22ml, $p = 0.039$, respectively). There was also no significant difference concerning about complications and no serious adverse events were observed. Kaplan-Meier curves for non-recurrence survival and survival analysis showed that there were no significant differences between two groups.

Conclusion: EMR-C may be preferable for removal of small rectal NET (≤10 mm) with shorter operating time and postoperative hospital days, less blood loss and hospitalization cost compared with ESD. Prospective randomized controlled trials are further needed.

Disclosure: Nothing to disclose

Abstract No. P0789

Technique	Location	Size (max)	Histology
EMR	Stomach, posterior wall	31 mm	Adenoma with low-grade dysplasia, R0
EMR	Ascending Colon	45 mm	Adenoma with low-grade dysplasia, 3 fragments
EMR	Transverse Colon	42 mm	Adenoma with high-grade dysplasia, R0
EMR	Sigmoid Colon	45 mm	Adenoma with low-grade dysplasia, 2 fragments
ESD	Stomach, greater curvature	17 mm	pT1a cancer, R0, low risk
ESD	Stomach, posterior wall	37 mm	pT1a cancer, R0, low risk
ESD	Rectum	37 mm	pT1 cancer, R0, low risk
ESD	Rectum	33 mm	Adenoma with high-grade dysplasia, R0

P0789 IMPROVED ENDOSCOPIC RESECTION OF LARGE FLAT LESIONS USING AN EXTERNAL ADDITIONAL WORKING CHANNEL (AWC)

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Introduction: En-bloc resection of lateral-spreading polyps, flat lesions larger than 2 cm in size, or early stages of cancer can be challenging. Endoscopic mucosal resection (EMR) offers the opportunity for resection in piece-meal technique, but completeness (R0) of the resection remains unclear. In contrast, standard endoscopic submucosal dissection (ESD) is complex, time consuming and associated with a significant rate of perforation. Furthermore for standard endoscopes no bi-manual tasks are possible. Additionally resection technique is faced by limited steer-ability and degrees of freedom. The two channel endoscopes are expensive, not available everywhere and have a small distance between the channels.
Aims and Methods: Here, we report our first experience using a new external additional working channel (AWC) (Ovesco, Tübingen, Germany). ESD and EMR with a modified grasp and snare technique was performed. The device can be fixed at the tip of a standard gastroscope or pediatric colonoscope. The distance of the two working channels can be adjusted by the endoscopist. Via the AWC a second endoscopic tool can be inserted and used for bi-manual workflow.
Results: EMR with modified grasp and snare technique was performed successfully in 4 patients (1 upper GI tract, 3 lower GI tract). ESD was performed successfully in 4 patients (2 upper GI tract, 2 lower GI tract) (Table 1). Mean procedure time (scope-in to scope-out) was 68.5 min.
Reported complications were acute arterial bleeding post EMR in two cases. No delayed bleeding or perforation were reported. Passage with the AWC-equipped endoscope was possible in all cases.
Conclusion: So far, based on our preliminary experience, we conclude that a new developed external additional working channel (AWC) enables endoscopic resection of large lesions in the upper and lower GI tract. Potential benefits are its suitability for EMR and ESD, no need for dual-channel endoscope and an adjustable distance of working channels.
Disclosure: Nothing to disclose

P0790 CAN SERT SCORE PREDICT HISTOLOGICAL RECURRENCE IN PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION? COMPARATIVE STUDY WITH SMSA SCORE

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Introduction: Piecemeal endoscopic mucosal resection (pEMR) allows resection of larger non-invasive colorectal lesions. Histological recurrence (HR), determined in surveillance colonoscopy after pEMR, is still a difficult to predict. SERT score (Sydney EMR-recurrence tool) predicts endoscopic recurrence (ER), nevertheless it has not been validated as a predictor of HR.
Aims and Methods: The present study aimed to validate SERT score as a predictor of ER and HR and compare its predictive value to the SMSA score (size, morphology, site, access).
SERT and SMSA score were calculated for all lesions resected by pEMR between 2012–2018. At first surveillance colonoscopy, performed at 3–6 months, RE and RH were evaluated. In the absence of ER, biopsy of pEMR scar was performed in most cases. In patients with ER the removal of the residual lesion was attempted.
Results: 188 pEMR were considered. In the studied population, 61.7% were men and the mean age was 66.1 ± 9.8. Most lesions were located at the right colon (59.0%). The average size was 30.99 ± 13.8 mm. Considering Paris Classification, lesions 0-Is + IIa (42.0%) and 0-IIa (39.4%) were more common.
The overall HR rate was 23.4% (n = 44). ER occurred in 27.1% (n = 51), and in 72.5% of these cases (n = 37) HR was confirmed. In patients without ER, the HR rate was 4.9% (n = 7). There was a strong correlation between the SERT and SMSA scores ($p < 0.001$; $r = 0.61$). There was a significant association between SMSA score and ER ($p < 0.001$) as well as HR ($p < 0.001$). A SERT ≥ 2 score was significantly associated with ER ($p = 0.002$) and HR ($p = 0.015$).
Conclusion: SERT score correlates with the SMSA score and both can be used to predict ER and HR in lesions removed by pEMR. SMSA score showed greater discriminative power for recurrent lesions. SERT score is less complex and allows predicting not only ER as RH.
Disclosure: Nothing to disclose

P0791 CLINICAL OUTCOMES AND PATIENTS' SATISFACTION FOR NOVEL PATIENT REFERRAL SYSTEM CALLED 'SAME-DAY POLYPECTOMY'

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Introduction: Substantial number of patients who diagnosed with polyps on screening colonoscopy undergo subsequent colon polypectomy on a separate day at referral hospital. We developed novel patient referral system called 'Same-day polypectomy' that performs colon polypectomy in tertiary hospital after same day referral from private clinics.
Aims and Methods: The aim of this study was to compare the clinical outcomes between conventional elective polypectomy and 'Same-day polypectomy' and to evaluate the patient's satisfaction with this novel system.
We retrospectively reviewed prospectively enrolled colonoscopy database in a single referral center. A total of 122 patients were referred to Gangnam Severance hospital for polypectomy between July 2017 to December 2017. Among them, 57 patients received 'same-day polypectomy', and remaining 55 patients underwent conventional elective polypectomy. Polyp characteristics, complications, degree of bowel cleanliness using Boston Bowel Preparation Scale (BBPS) were compared between these two groups. Patients' satisfaction for the 'same-day polypectomy' was assessed through questionnaires.
Results: There were no significant differences in the location and average number of resected polyps between two groups. However, the polyps in 'same-day polypectomy' group were smaller in size than those of elective polypectomy group (6.3 ± 3.2 mm vs. 10.9 ± 8.7 mm, $p < 0.001$), and were more frequent in polypoid type. Moreover, mean total BBPS score was lower in 'same-day polypectomy' group than in elective polypectomy group (6.8 ± 1.6 vs. 8.4 ± 1.0, $p < 0.001$). Meanwhile, procedure related complications were not identified in both groups. Regarding patients' satisfaction for 'Same-day polypectomy', 95% of the patients were satisfied with this novel system and most common reason for satisfaction was absence of repeat bowel preparation (70.8%).
Conclusion: Our novel 'same-day polypectomy' is safe and acceptable patient referral system with high patients' satisfaction.
Disclosure: Nothing to disclose

P0792 PHYSICIAN ADHERENCE TO SOCIETAL GUIDELINES FOLLOWING COLONOSCOPY WITH POLYPECTOMY

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Introduction: Colonoscopy with polypectomy reduces incidence and mortality from colorectal cancer. Post-polypectomy surveillance recommendations are aimed at balancing the need for surveillance on one side and ensuring adequate use of medical resources on the other. Surveillance intervals are often determined by features of the removed polyps during the index colonoscopy. Current data on physician adherence to societal guidelines is mixed and limited and to our knowledge none investigated the influence of intervention on adherence.
Aims and Methods: We aimed to improve accuracy and consistency in post-polypectomy surveillance recommendations.
In the first phase of the study we assessed the current practices of 10 gastroenterologist at a tertiary academic center by prospectively collecting colonoscopy reports containing polypectomies over a 3 month period. The exact time frame of data collection was not disclosed to the endoscopists. Data collection included the index colonoscopy report, the pathologic report, and the recommendations given by the physician. We then performed an intervention – we presented the first phase results to the all the physician, giving a personal reports to each physician. We also conducted a study group meeting where post polypectomy surveillance guidelines were reaffirmed and a dedicated form for reporting post-polypectomy surveillance recommendations, created in the patient's electronic medical file was presented. The second phase of the study included a second prospective, post-intervention collection of post-polypectomy recommendations.
Results: Prior to the intervention, only 76% of the post-polypectomy colonoscopies included a clear written recommendation for surveillance, of which 57% received a recommendation consistent with societal guidelines. After the intervention, 85% of the post-polypectomy colonoscopies had clear written recommendation for surveillance, of which 72% received a recommendation consistent with the guidelines ($p = 0.044$ and $p = 0.004$ respectively). Before intervention, various methods were used by the physicians for recommendations regarding surveillance

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	Recommendations		Recommendations		Recommendations non-adherent to guidelines	
	Had recommendation	Didn't have recommendations	Adherent	Non-adherent	Too late recommendations	Too early recommendations
Prior to Intervention	130	41	72	58	15	41
After intervention	153	28	110	43	5	38
Total	283	69	182	101	20	79
P-value	0.044		0.004		0.063	

[Table 1; Documentation and consistency of post-polypectomy surveillance recommendations before and after intervention.]

colonoscopy (as part of the endoscopic report, or added to the pathologic report, or handwritten on the pathologic report, or in a follow-up clinic visit report). After intervention, 62% of recommendations were written in the new electronic form, of which 79% were consistent with guidelines. When the electronic form wasn't used, only 59% were consistent with the guidelines ($p = 0.009$).
Conclusion: Intervention, by guideline re-affirmation, and creation of a dedicated reporting form, significantly increases the number of well documented follow-up recommendations after polypectomy, and their consistency with societal guidelines.
Disclosure: Nothing to disclose

P0793 FACTORS INFLUENCING ACHIEVEMENT OF ADEQUATE BOWEL PREPARATION: ANALYSIS OF THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION GROUP (ECQI) PROCEDURE QUESTIONNAIRE

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Introduction: Assessment and rate of adequate bowel preparation are important quality measures for colonoscopy according to European Society of Gastrointestinal Endoscopy (ESGE) guidelines.[1] We aimed to assess factors influencing the likelihood of adequate bowel preparation for colonoscopy.
Aims and Methods: The development of the European Colonoscopy Quality Investigation Group (ECQI) online questionnaire has been previously described.[2,3] We analysed data collected between 2/6/16 and 31/1/18. A univariate logistic regression analysis was performed to assess which factors influence achievement of adequate bowel preparation, defined as a Boston Bowel Preparation Scale (BBPS) score ≥ 6.
Results: Data from 4447 completed questionnaires were analysed. 126 procedures were excluded due to insufficient information to establish adequacy of bowel cleanliness; of the remainder, 3726 (86%) procedures scored BBPS ≥ 6 and 595 (14%) BBPS < 6.
The achievement of adequate bowel cleansing was significantly affected by age (< 50 vs. ≥ 50 odds ratio (OR) 2.05, $p < 0.001$), gender (male vs. female OR 0.77, $p = 0.004$), inpatient status (inpatient vs. outpatient OR 0.42, $p < 0.001$), total quantity of fluid consumed ($p < 0.001$), dosing regimen ($p < 0.001$), the quantity of bowel preparation consumed ($p < 0.001$), and the duration between procedure and the last intake of bowel preparation ($p < 0.001$) (table 1). Reason for procedure also had a significant affect ($p < 0.001$), with screening due to familial risk increasing the likelihood of BBPS ≥ 6 (vs. clinical signs and symptoms OR 2.02, $p = 0.004$). Whether the patient followed instructions has a large influence on bowel clearance (yes vs. no OR 7.07, $p < 0.001$). Body mass index and the time of procedure (am vs. pm) had no significant impact.
Conclusion: Adequacy of bowel preparation can be affected by age, gender and in/outpatient status. Indication can also influence adequacy of bowel clearance, along with both the total quantity of fluid and the quantity of bowel preparation consumed. In addition, using a split-dosing regimen with the last dose taken within 5 hours of the procedure appears to increase the likelihood of a BBPS ≥ 6. Ensuring good explanation of how to take the bowel preparation and stressing the importance of following instructions to the patient could also improve bowel clearance. Further information can be found at www.ecqigroup.eu

Variable	Proportion achieving BBPS ≥ 6	Odds ratio (95% CI)	p value	p value for variable
How much fluid was consumed in total, including additional products?				**<0.001**
Less than 1 litre	70/96 (72.9%)	Reference		
1–3 litres	888/1067 (83.2%)	1.84 (1.14, 2.97)	0.012	
3–6 litres	2643/3011 (87.8%)	2.67 (1.68, 4.24)	<0.001	
>6 litres	61/69 (88.4%)	2.83 (1.19, 6.72)	0.018	
Dosing regimen				**<0.001**
Evening	598/805 (74.3%)	Reference		
Same day	647/754 (85.8%)	2.09 (1.62, 2.71)	<0.001	
Split	2428/2694 (90.1%)	3.16 (2.58, 3.87)	<0.001	
How much bowel preparation was consumed?				**<0.001**
0–50%	7/27 (25.9%)	Reference		
50–75%	53/116 (45.7%)	2.40 (0.94, 6.12)	0.066	
75–99%	430/549 (78.3%)	10.32 (4.26, 24.99)	<0.001	
100%	3174/3548 (89.5%)	24.24 (10.18, 57.71)	<0.001	
Time period between last intake of bowel preparation and procedure				**<0.001**
Less than 5 hours	1903/2095 (90.8%)	Reference		
5–10 hours	897/1048 (85.6%)	0.60 (0.48, 0.75)	<0.001	
10–15 hours	786/985 (79.8%)	0.40 (0.32, 0.49)	<0.001	
Over 15 hours	49/84 (58.3%)	0.14 (0.09, 0.22)	<0.001	

[Table 1. Influence of individual variables on achieving adequate bowel preparation]

Disclosure: Amaro A, Agrawal A, Brink L, Hünger M, Jover R, Ono A, Petruzziello L, Toth E; Consultancy and Advisory Board participant to Norgine: Spada C; Consultant fee from Norgine: Fischbach W; Consultancy and Advisory Board participant to Norgine; Speaking – Abbott, Bio Merieux, Falk, Merck Serono, Novartis, Nycomed, Sanofi Aventis, Shire; Advisory speaking – Aptalis, Fresenius Biotech, Pfizer; Advisory – Boehringer Ingelheim, med update: Riemann JF in terms of ECQI, consultant to Norgine, otherwise no conflict of interest: Koulaouzidis A; no relevant conflict of interest: Kinnunen U; No conflict of interest: Patai Á; No conflict of interest: Curran V; Employee of Norgine.

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P0794 CLINICAL OUTCOME AFTER COLONOSCOPIC POLYPECTOMY OF PATIENTS TAKING DIRECT ORAL ANTICOAGULANTS: COMPARISON WITH CLOPIDOGREL

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Introduction: Direct oral anticoagulants (DOACs) are increasingly used for the prevention of stroke in patients with atrial fibrillation and prevention and treatment of deep vein thrombosis or pulmonary embolism. However, little is known about the outcome after polypectomy of patients under DOACs medication.
Aims and Methods: We performed a retrospective study of patients who had colonoscopy polypectomy at Asan Medical Center from November 2010 to December 2017. We compared the frequency of delayed post-polypectomy bleeding (PPB) for the patients taking DOACs (DOAC group) with patients taking clopidogrel (clopidogrel group).

Results: A total of 405 patients underwent polypectomy during the study period; 320 were on DOACs and 685 were on clopidogrel. The duration of drug discontinuation before colonoscopy was mean 2.9 ± 1.7 days in DOAC group and 5.9 ± 2.5 days in clopidogrel group, respectively. Patients in each group resumed taking DOACs on mean 1.9 ± 2.9 days and clopidogrel on mean 2.0 ± 1.5 days after polypectomy, respectively. Logistic regression analysis revealed no significant difference in frequency of PPB between DOACs users and clopidogrel users. (1.6% vs 1.6%, p = 0.968, unadjusted OR = 0.977, 95% CI 0.312–3.058).
Conclusion: The risk of post-polypectomy bleeding in patients taking DOACs seems not to be higher than the one of post-polypectomy bleeding in patients taking clopidogrel. Further studies are necessary to evaluate the risk of post-polypectomy bleeding related to DOACs.

	DOACs user	Clopidogrel user	P value
Patients characteristics (n = 405)			
M:F	100:31	214:60	0.690
Age, mean ± SD years	71.7 ± 9.0	67.5 ± 9.3	0.000
Polyp characteristics (n = 1005)	320	685	
Right colonic polyps:left colonic polyps	94:37	192:82	0.728
Polyp size, mean ± SD mm	7.53 ± 4.0	7.63 ± 4.5	0.749
Histopathology, n (%)			0.863
Tubular or tubulovillous adenoma			
Low-grade dysplasia	231 (72.1)	503 (73.4)	
High-grade dysplasia	3 (0.9)	10 (1.5)	
Sessile serrated adenoma/polyp	18 (5.6)	37 (5.4)	
Hyperplastic polyp	20 (6.3)	37 (5.4)	
Adenocarcinoma	10 (3.1)	14 (2.0)	
Others	38 (11.9)	84 (12.3)	
Procedure characteristics (n = 1005)			
Types of endoscopic resection, n (%)			0.091
Cold snare polypectomy	86 (26.9)	207 (30.2)	
EMR	225 (70.3)	451 (65.8)	
Precut EMR	0 (0)	12 (1.8)	
Piecemeal EMR	3 (0.9)	7 (1.0)	
ESD	6 (1.9)	8 (1.2)	
Prophylactic hemostasis	96 (30)	151 (22.0)	0.006
Immediate post-polypectomy bleeding, n (%)	17 (5.3)	44 (6.4)	0.492
Delayed post-polypectomy bleeding, n (%)	5 (1.6)	11 (1.6)	0.959

[Characteristics of the patients, polyps, and procedures]
Disclosure: Nothing to disclose

P0795 EFFECTIVENESS OF LIDOCAINE AS ANTISPASMODIC DRUGS DURING COLONOSCOPY: A MULTICENTER DOUBLE-BLIND, RANDOMIZED CONTROLLED TRIAL

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Introduction: Colonic spasm can interfere with colonoscopy, but the number of antispasmodic agents is limited, and they can cause complications. Topical administration of lidocaine may inhibit intestinal spasm induced by colonoscopic movement. In this study, we aimed to assess the inhibitory effect of topical lidocaine compared with a placebo control.
Aims and Methods: In five tertiary-care hospitals in Japan, 128 patients requiring endoscopic resection of a colorectal lesion were enrolled and randomly and double-blindly allocated to colonoscopy with topical administration of 2% lidocaine solution 20mL (LID, n = 64) or normal saline 20mL (control, n = 64). During colonoscopy, the assigned solution was applied with a spray catheter near the lesion and the area was observed for three minutes. The primary endpoint was the inhibitory effect at three time-points (1, 2 and 3 minutes after dispersion), using a three point scale (excellent, fair, poor). The secondary endpoints were rebound spasm and adverse events. Serum lidocaine levels were measured in 32 patients (LID 16, control 16). The study was approved by the Institutional Review Board of all five participating institutions and registered with the UMIN Clinical Trials Registry (UMIN000024733).
Results: There were no significant differences in patient demographics between groups. The proportion of patients with "excellent" scores was greater in the LID group than the control group, with significant differences observed at 2 minutes (p = 0.02) and 3 minutes (p = 0.02). In LID group, the rate of "excellent" scores increased by 12.5% at 2 minutes and was maintained at 3 minutes. Rebound spasm did not occur in the LID group, compared with 15.6% of the control group (p = 0.001). There were no adverse events. All serum lidocaine levels were below detectable levels.
Conclusion: Topical lidocaine is an effective and safe method for suppressing colorectal spasm during colonoscopy.
Disclosure: Nothing to disclose

P0796 DEEP LEARNING FOR REAL-TIME AUTOMATED POLYP LOCALISATION IN COLONOSCOPY VIDEOS

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Introduction: Colonoscopic polypectomy can prevent colorectal cancer. Polyp detection rates vary considerably due to human error and missed adenomas may contribute to interval colorectal cancers. Automated polyp localisation using deep learning may avoid these problems. Previous work focused on detecting the presence of polyps in individual frames captured from videos. Our aims in this pilot study were to extend this to polyp localisation within video sequences and to explore future-proofing by using algorithms trained on old image processors to locate polyps found using newer endoscopic technologies.
Aims and Methods: We trained and validated a Convolutional Neuronal Network (CNN) on 18517 frames created by merging research colonoscopy datasets from the Medical Image Computing & Computer Assisted Intervention Society challenges. 75% of frames contained polyps in both standard and high definition (HD) from older processors including Olympus Exera II (160/165 series) and Pentax EPKi 7000 (90i series). Our test set consisted of 11 HD videos featuring polyps in white light collected using the latest Olympus 290 endoscopes. Estimated median polyp size was 4mm (range 2–15) and morphology included (Paris Classification IIa = 4, Is = 6 and IIa+IIs LST-G = 1). Images were manually annotated by drawing bounding boxes around polyps and quality controlled by removing uninformative frames (e.g. blurred). A total of 2,611 polyp-containing frames were analysed in the test set. A true positive was scored if the computer-generated segmentation mask prediction overlapped with the bounding box. A false positive indicated a non-overlapping location (more than one can occur per frame).
Results: Our network operated at real-time video rate. F1 score accuracy was 92.5%. Sensitivity for polyp localisation was 98.5% and per-frame specificity 75.4%. Positive predictive value was 90.1%. Incorrect segmentation mask locations were predominantly limited to 3 videos and were generated by artefacts not represented during training.
Conclusion: We demonstrate through analysis of video frames that a CNN can locate polyps with high accuracy in real-time. The algorithm was trained using multiple endoscopy processors and worked with HD images from a new processor. Crucially the algorithm had not previously viewed or trained with any of the images from the new processor. This suggests that the CNN could remain useful as new endoscopic technologies are introduced. Further work will train our model on larger datasets including complete colonoscopy procedures. This should improve accuracy further. Such a system could be used as a red-flag technique to reduce missed adenomas during colonoscopy.
Disclosure: Nothing to disclose

P0797 USEFULNESS OF NBI MAGNIFYING ENDOSCOPY FOR DIAGNOSIS OF ADVANCED NEOPLASIA AMONG COLORECTAL LESIONS < 10MM

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Introduction: Endoscopic resection of all colonic adenomas improves the mortality caused by colon cancer. Cold polypectomy has been widely accepted for removal of small colorectal polyps on the basis of safety and technical ease. However, careful endoscopic diagnosis for identifying advanced neoplasia is essential at cold polypectomy because of its relative risk of incompete resection and inappropriate histological evaluation.
Aims and Methods: Our aim is to investigate clinicopathological characteristics of colon polyps < 10mm and assess the usefulness of Narrow-band imaging (NBI) magnifying endoscopy for diagnosis of advanced neoplasia. We retrospectively analyzed all colorectal lesions < 10mm which were diagnosed by NBI magnifying endoscopy and resected endoscopically from March 2014 to February 2018. Various clinicopathological characteristics were analyzed. The diagnosis by NBI magnifying endoscopy was performed according to The Japan Narrow-band imaging Expert Team (JNET) classification, which is a consensus

criteria Japanese working group has recently established for the evaluation of colorectal lesions. We assessed the efficacy of JNET classification for diagnosis of advanced neoplasia.
Results: 1374 lesions in 644 patients (64% men, with a mean age of 67.8 years +/- 9.9years) were analyzed. The mean size of lesions was 4.65 +/- 1.68mm. Of the 1374 lesions, 843 (61.4%) were located in the right side of the colon (the cecum, ascending colon, and transverse colon), 458 (33.3%) in the left side of the colon (the descending colon and sigmoid colon), and the other 73 (5.3%) in the rectum. Macroscopically, 562 (40.9%) were polypoid type and 812(59.1%) were flat or depressed type. Pathologically, 1227 lesions (89.3%) were confirmed as adenomas (LGA or HGA). 15 lesions (1.1%) and 5 lesions (0.4%) were determined to be Tis and T1 cancer, respectively, counting 1.5% cancer-carrying rate. 62 lesions diagnosed as JNET1 included no neoplasia and 1279 lesions diagnosed as JNET Type2A harbored only 6 neoplasia (0.5%). In sharp contrast, 32 lesions diagnosed as JNET Type2B comprised 13 neoplasia (40.6%) and one lesion diagnosed as JNET3 was neoplasia (100%). Moreover, all T1 cancers were diagnosed as Type2B or 3.
Conclusion: We detected non-negligible number of advanced neoplasia even among small colorectal polyps < 10mm. JNET classifications Type2 and Type3 are useful diagnosis criteria to pick up neoplasic lesions making it possible to select an appropriate treatment method for achieving complete resection.
Disclosure: Nothing to disclose

P0798 THE DIAGNOSTIC ARTIFICIAL INTELLIGENCE (AI) SYSTEM FOR DETECTION OF COLON POLYPS WITH HIGH EFFICIENCY OF DEEP LEARNING

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Introduction: In the gastrointestinal endoscopic survey, the small neoplastic lesions are reported to be overlooked. Recently, artificial intelligence (AI) has been shown the remarkable progress in image recognition. The application of AI system for the endoscopic images are expected to be the favorable assistance. The recent AI progressions are primarily due to the availability of large-scale annotated datasets. But the high-quality images of gastrointestinal endoscopy are limited, especially with annotated and segmented datasets. The efficient machine learning system with lower-scale datasets of endoscopic images are needed.
Aims and Methods: The aim of this study is to develop the novel diagnostic AI model for colon polyp detection with efficient learning system. We indicated the single deep convolutional neural network (CNN) named single shot multibox detector (SSD) [1] and the pre-trained mode by the 4952 natural images of PASCAL-VOC 2007 for developing the AI diagnostic model. Learning for fine tuning with the small number of non-magnified still images with annotation and segmentation data of protruded small colon polyps (≦10mm) with White Light Imaging, and additional learning by images of normal colon were conducted. The diagnostic model was validated at each points of learning with additional images for learning as follows: (the number of colon polyps: 50, 100, 200, and 300 images, colon polyps and normal colon: 300+300 and 400+400 images) and diagnostic ability was obtained. The validation were conducted by using 200 number of still images of small colon polyps (≦10mm) and 200 number of normal colon which were not used for learning. Additionally, the recognition test for video images by the diagnostic model learned 400 images of polyps and 400 images of normal colon are conducted.
Results: The sensitivity, specificity, accuracy for detecting the small colon polyps were improved as learned images of colon polyps was adding (60.0%, 94.3%, 82.3% by the 50 images learning, 85.0%, 91.8%, 89.5% by the 100 images learning, 90.5%, 93.5%, 92.5% by the 200 images learning, 93.0%, 92.8%, 92.8% by 300 images learning). Additional learning model with normal colon images show improvement of specificity, and the diagnostic model learned by 400 images of colon polyps and 400 images of normal colon show the sufficient diagnostic ability (95.0%, 98.5%, 97.3% by the 300 each images learning, 96.5%, 98.5%, 97.8% by the 400 each images learning). The pilot test by the video endoscopic images show the high frame ratio detection for small colon polyps (frame rate > 25/sec).
Conclusion: This AI diagnostic model suggested that the machine learning by latest deep CNN with fine-tuning enables high efficiency of learning for detecting small colon polyps with limited number of teaching image datasets.
Disclosure: Nothing to disclose

Reference

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P0799 A RANDOMISED CONTROLLED STUDY OF THE PREDICTION OF DIMINUTIVE/SMALL POLYP HISTOLOGY USING DIDACTIC VS. COMPUTER-BASED SELF-LEARNING MODULE IN GASTROENTEROLOGY TRAINEES

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Introduction: Using novel endoscopic optical diagnosis techniques, expert endoscopists are able to predict and differentiate between neoplastic and non-neoplastic colonic polyps with high accuracy and are able to meet the PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) thresholds recommended by the American Society for Gastrointestinal Endoscopy. However, this performance has not been replicated in non-expert endoscopists and thus cannot be currently recommended in clinical practice.
Aims and Methods: The aim of this randomised trial was to establish the optimum method of training, self-training vs. didactic training, to increase the diagnostic accuracy of diminutive/small colonic polyp histological prediction by trainee gastroenterologists.
Gastroenterology trainees from several institutes across the West Midlands, UK, reviewed 78 videos (48 i-Scan-OE and 30 NBI) of diminutive/small in the pre-training assessment. Participants were randomised to receive computer-based learning or didactic training (teaching materials and videos were identical). The same 78 videos, in a different randomised order, were assessed following training. The NICE (NBI International Colorectal Endoscopic) classification and SIMPLE (Simplified Identification Method for Polyp Labelling during Endoscopy) classification systems were used to classify diminutive/small polyps (Figure 1).
Results: 16 trainees (12 gastroenterology trainees and 4 naïve endoscopists-non-GI trainees whom have no prior experience of endoscopy) were randomised to receive either self-training (n = 8) or didactic training (n = 8). A higher proportion of high confidence predictions of polyps were made by the self-training group vs. didactic group both using the SIMPLE classification 77.1% [95% CI 73.4–80.3] vs 69.9% [95% CI 66.1–73.5%] ($p < 0.005$) and using the NICE classification 77% [73.2%−80.4%] vs 69.8% [95% CI 66–73.4%] (p = 0.006). When using NICE classification, the sensitivity of the self-training group compared with the didactic group was 72% vs 83% $p < 0.0005$, and the accuracy 66.1% vs 69.1%. When using SIMPLE classification the sensitivity was 78% vs 83% (p = NS) and accuracy 65.7% vs 69% (Table 1).
Conclusion: Self-learning for the prediction of diminutive/small polyp histology is a method of training that can achieve results similar to the more labour intensive and expensive didactic training. The availability of adequate self-learning teaching modules that teach how to differentiate neoplastic vs. non-neoplastic colonic polyps with high accuracy could enable more widespread implementation of optical diagnosis in clinical practice.
Disclosure: Nothing to disclose

P0800 ENDOSCOPIC SUBMUCOSAL RESECTION (ESR) – INNOVATIVE METHOD AND INSTRUMENTS FOR RESECTION OF BIG LESIONS IN THE GIT

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Introduction: ESD being the preferred method for big and complex lesions in the GIT, but some disadvantages of ESD are obvious:
1. Long and flat learning curve
2. Long-lasting and complex procedure
3. Relatively high rate of complications, bleeding and especially perforations
4. Uneven plane of resection
5. Hence, ESD is confined to expert endoscopists.

Thus, a new method, called "Endoscopic Submucosa Resection (ESR)" incl. innovative instruments, called "Flat Adenoma Resection Instruments (FARIn)", have been developed to overcome these drawbacks.
ESR consists like ESD of different steps. First a primary circumferential incision, but then followed by application of and resection with an innovative snare-like resection effector of a FARIn allowing vertically deep end even plan RF-surgical cutting close the muscularis propria without danger of perforation.

Aims and Methods: First systematic clinical study in 22 patients with 15 big lesions in the rectum, 6 in the colon and one in the stomach. The lesions were bigger than 2 cm or had a high risk of perforation (e.g. submucosal lesion, because of location).
To evaluate safety and efficacy of ESR with FARIn especially the intended pressing of the instrument against the wall of the GIT during RF-application to remove the specimen close at the muscularis propria.
In a step-up approach these first patients have been treated without circumferential incision as the first step.
Results: In all 22 patients the lesions were removed successfully without relevant complications and without perforation. The rate of en-bloc resection or resection of one large piece with few small pieces was 15 of 22.
Optimal cutting quality, no delay of cutting even in very big lesions, a completely even cutting plane close to the muscularis propria and very low thermal artifacts allowed a representative, high-quality histopathology. A pure resection time less than 30 seconds could be achieved in all cases.
The new method of ESR using FARIn proved to be promising, especially the possibility of vertically deep resection without risk of perforation, the high quality of cutting and specimen showed clear advantages compared to conventional snare-resection or to ESD.
These findings and a short learning curve due to high ergonomics of the instrument justify further studies including circumcision of the lesion as a first step before application of the snare-like effector of a FARIn to evaluate, if ESR may become a superior alternative to EMR and ESD in therefore suitable cases.
Conclusion: ESR, a new method with innovative instruments for resection of big and complex lesions in the GIT showed in a first clinical assessment remarkably reasonable results in term of efficacy, safety ergonomy and procedure time.
Disclosure: Nothing to disclose

P0801 MELANOSIS COLI: A HELPFUL CONTRAST EFFECT OR A HARMFUL PIGMENTATION?

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Introduction: Melanosis coli is a black or brownish discoloration of the colonic mucosa that results from accumulation of lipofuscin pigment in macrophages within the lamina propria. This condition has long been considered as a harmless pigmentation associated with, but not confined to, a long-term use of anthraquinone laxatives. Several clinical and experimental studies, however, have provided some evidence of a possible relationship between long-term laxative use or melanosis coli and colorectal cancer risk. Other and more recent studies have shown no association with colorectal cancer. Essentially, the majority of these studies did not include matched controls and may be widely affected by confounders.
MC is usually reported to spare hyperplastic and adenomatous polyps. This enables enhanced visibility and improved observation of polyps in the dark background mucosa, probably linking melanosis coli with an increased polyp detection rate. Wither this association signifies also a causal relationship due to an oncogenic or toxic effect of melanosis on colonic mucosa is still unknown.
There is a common impression among endoscopists that melanosis coli is associated with difficult endoscopy and inadequate preparation. This may offset the advantage suggested by the contrast effect and raise the concern of increased cancer miss rate or decreased polyps' detection.
Aims and Methods: We performed a retrospective, large cohort, single-center study, aimed to compare the polyp detection rate and colorectal cancer diagnosis in melanosis patients against matched controls without melanosis. Patients diagnosed with melanosis coli on colonoscopy at our institution over a 15-year period were included. Each melanosis patient was matched with 3 controls by age, gender, setting (inpatient/outpatient) and procedure's indication. We determined the adequacy of bowel preparation in both groups. Cecal intubation rate, polyp detection rate and diagnosis of colorectal cancer were recorded and compared between the 2 matched groups before and after adjustment for bowel preparation. Multivariate analysis was performed to determine the effect of independent parameters associated with polyp detection rate.
Results: A cohort of 718 patients with endoscopic finding of melanosis (melanosis group) and 2154 controls (control group) were included. The polyp detection rates were 33.4% and 21.8% of melanosis and control groups respectively ($p<0.001$). Melanosis however was associated with less diagnosis of colorectal cancer than controls (0.3% vs. 3.9%; $p<0.001$). To eliminate the effect of first colonoscopy, we excluded repeated colonoscopies and performed a subgroup analysis on 596 patients (83%) who underwent first-time colonoscopy. This subpopulation revealed no change in polyp detection rate (32%) or colorectal cancer diagnosis (0.33%). In addition to the recognized positive impact of age and sex on polyp detection, multivariate analysis showed that inpatient setting (OR 1.487, 95% CI, 1.099–2.012), positive fecal occult blood test or personal polyp history as indication for colonoscopy (OR 1.825, 95% CI, 1.276–2.611; $p=0.01$ and OR 5.464, 95% CI 3.865–7.723; $p<0.01$ respectively) and melanosis diagnosis on endoscopy (OR 1.986, 95% CI, 1.626–2.425; $p<0.01$) were significantly associated with polyp detection rate. Melanosis patients tend to be less adequately prepared compared to controls (58.5% vs. 65.7%; $p<0.001$).
Conclusion: Melanosis coli is not associated with a greater risk for CRC. Rather, there is an increase in polyp detection rate, apparently due to chromo-endoscopy-like effect of melanosis.
Disclosure: Nothing to disclose

P0802 THE PRESENCE OF A GASTROENTEROLOGY TRAINEE DURING COLORECTAL CANCER SCREENING COLONOSCOPY IMPROVES ADHERENCE TO QUALITY INDICATORS

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Introduction: The effectiveness of colorectal cancer screening colonoscopy (CRCSC) in decreasing colorectal cancer incidence depends on the detection of polyps and the quality of the procedure. Several key quality measures have been proposed to improve the effectiveness of screening colonoscopies [1].
Aims and Methods: We aimed at evaluating quality indicators of CRCSC in a tertiary teaching hospital with gastroenterology trainees in endoscopy and determine if the presence of trainees influences the quality of CRCSCs. A total of 2118 consecutive CRCSC reports were retrospectively evaluated over a 5 year period. The adherence to currently utilized quality indicators was assessed. Statistical analysis was performed with SPSSv23; A p value <0.05 was considered statistically significant.
Results: The mean age of the patients was 65.5 ± 10.7 years and 56.9% (1205) were women. Sedation was performed in 77.1% (1634) CRCSCs. In 516 (24.4%) of the exams a gastroenterology trainee was present. Cecal intubation rate (CIR) was 86.5% (1833). Most common reasons for an incomplete CRCSC were: patient intolerance 46.3% (132); inadequate bowel preparation 20.4% (58) and technical difficulties with colonic loop formation and adherences in 15.1% (43). Photodocumentation of cecal landmarks (PCL) was performed in 97.3% (1783) of the cases. Polyp detection rate (PDR) was 34.3% (726), out of which 13.4% (97) of the polyps were $\geq$1cm in diameter. The Boston Long-lastingBowel Preparation Score (BBPS) for bowel preparation was used in 25% (530) of CRCSCs. Bowel preparation was considered good in 64.6% (1369) of the cases and fair in 19.7%(417) cases. In multivariate analysis (including gender, age, BBPS, PCL, CIR, PDR and sedation), the presence of a gastroenterology trainee was an independent predictor of compliance to CRCSCs quality indicators: use of BBPS score (OR 7.9, 95% CI 5.7–9.0, $p < 0.001$), PCL (OR 2.8, 95% CI 1.1–6.9, $p=0.025$) and PDR (OR 1.5, 95% CI 1.2–1.8, $p=0.001$). The presence of a gastroenterology trainee during CRCSCs was the only independent predictor of a higher PDR (OR 1.6, 95% CI 1.3–2.0, $p < 0.001$).
Conclusion: A suboptimal CIR were mostly due to intolerance and inadequate bowel preparation. The presence of a gastroenterology trainee improved adherence to quality indicators in CRCSCs, namely an adequate description of bowel preparation, the PCL and the PDR.
Disclosure: Nothing to disclose

Reference

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P0803 COMPARISON OF NEWER COLONOSCOPY DEVICES WITH STANDARD FORWARD VIEWING (SFV) HIGH-DEFINITION COLONOSCOPES IN DAILY PRACTICE

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Introduction: For years efforts have been made to improve the quality of colonoscopy. Cap-assisted colonoscopy has been shown in some studies to increase the adenoma detection rate (ADR). Full-spectrum colonoscopes (FUSE) with 330°angle of view showed by initial studies a significantly lower adenoma miss-rate and higher ADR. Subsequent FUSE studies with already high ADR with SFV were unable to confirm these results. Our practice-based, randomized study compares the efficiency, i.e. ADR, of the relatively inexpensive cap assisted, the FUSE or SFV colonoscopy.
Aims and Methods: From March 2015 through February 2018 patients referred for ambulant colonoscopy were randomly allocated to either colonoscopy with high definition SFV Pentax i10 ($n=958$) or FUSE instruments ($n=1552$). The group of patients assigned to SFV endoscopy was since March 2017 examined with the additional use of Endocuff ®, making up another 339 patients. All procedures were performed by one experienced endoscopist.
Results: Baseline characteristics of the 2849 patients were similar within the three groups. Mean age was 64 (CI 63–66), half were male, BBPS (Boston Bowel Preparation Scale) score was 7.23 (CI 7.2–7.3). 30% were screening, 60% surveillance, the remaining diagnostic colonoscopies. Ileum intubation rate was 99% in all three groups. Patients were sedated with Propofol (mean dose overall 195; CI 190–200), significantly less with Endocuff (172; CI 165–180), $p=0.0007$. With multivariate analysis male sex, diabetes and age were significant risk factors for more adenomas. Better bowel cleansing was also significantly associated with

higher adenoma detection. ADR was 50% for FUSE, 54% for SFV and 47% for Endocuff (ns = not significant). Adenoma per colonoscopy (APC) were 1.1 in FUSE vs 1.2 in SFV vs 1 with Endocuff (ns). All polyps per colonoscopy (PPC) were 1.8, 1.9 and 1.5 respectively. 4% of all polyps in all groups were pedunculated the others sessile. 1.2 to 1.8% of polyps could not be examined histologically. 80% of the polyps were below 5 mm of size, 15% were between 5–9 mm and 5% bigger than 1 cm. One-third were right sided, one-quarter located in the tansverse colon. 76% (FUSE), 80% (SFV) and 67% (Endocuff) were tubular adenomas. For villous adenomas it was 2% for FUSE, 2% for SFV and 1.5% for Pentax with Endocuff. In the SFV group 38% serrated adenomas (SSA) were found, for FUSE 28% and for Endocuff 31%. Hyperplastic polyps were 24% in de FUSE group, in SFV 20% and in Endocuff 14% (p 0.04). 0.7% were carcinomas. Time to ileum was with FUSE 5.4 min, with SFV 5.5 min, with Endocuff 6.3 min. Intervention time was for all groups 3.3 min (showing no difference in the handling of interventions). Withdrawal time was 16.3 min with FUSE, 18.1 min for SFV and 14.1 min for Endocuff ($p = 0.04$).

Conclusion: In a collective of 2849 patients randomly assigned to 3 different types of colonoscopies neither FUSE nor Endocuff could increase the ADR in a significant way. At present if ADR reaches around 50% no further benefit can be expected from new technology. Key factor for a high ADR seems to be long withdrawal times (e.g. 14 up to 18 min in SFV). FUSE and Endocuff show significant shorter endoscopy times (FUSE little faster in ascent, Endocuff and FUSE faster in withdrawal), Endocuff even significantly less medication for sedation.

Disclosure: Nothing to disclose

P0804 THE OBJECTIVE EVALUATION USING EYE TRACKING FOR VISIBILITY OF COLORECTAL LESIONS

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Introduction: Recently, image-enhanced endoscopy (IEE) such as blue laser imaging (BLI-bright) and linked-color imaging (LCI) has been reported to improve detection and the miss rate of colorectal lesions. Improvements in visibility due to IEE have been assessed by according to endoscopists' visibility scores in many studies. However, such assessments are subjective, and objective assessments, such as quantifying the time required for endoscopists to detect lesions, are lacking. We have considered that one method of objectively measuring endoscopists' attention in real time, and thus determining the time they need to detect lesions, is eye tracking. Eye tracking uses a sensor to detect exactly where a participant's eyes are focused.

Aims and Methods: We aimed to objectively assess the detectability of BLI-bright, LCI and WLI in the colorectal lesions using eye tracking.

We recruited 11 endoscopists, 2 experts and 9 trainees, who were required to evaluate a total of 90 images of 30 colorectal lesions (28 flat lesions of less than 5 mm, one depressed lesion of 5 mm, one SSA/P of 10 mm) was used. The 3 images of each lesion comprised white light imaging (WLI), BLI-bright, and LCI at the same position in the image using the EC-L590ZP, EC-L600ZP, and EC-L600ZP7 colonoscopes (Fuji film Co, Tokyo, Japan). The lesions were not located central in the image to avoid too easily detecting. Eye movements were tracked with the Tobii X2-60 eye tracking device (Tobii AB, Danderyd, Sweden). Images were shown on a screen in random order for 5 s per image; between each image, the screen went dark for 3 s. Participants stopped eye movement upon detecting the lesion. The detection time was defined as the time between the image being displayed and the time at which the evaluator's eyes stopped. Detection time for undetected lesions was considered to be 5 s for analytic purposes. We assessed the number of missed lesions and the lesion detection time between the 3 image modalities, the difference between experts and trainees.

Results: One expert whose eye movements could not be tracked was excluded. Of the total of 300 assessed images per modality, 38 (12.6%) lesions were missed with WLI, 18 (6.0%) with BLI-bright, and 13 (4.3%) with LCI; the miss rate of the latter two groups was significantly lower than that of the WLI ($p < 0.01$), but was not significantly different between them ($p = 0.54$). The mean (± standard deviation) detection times were 1.58 ± 1.60 s for WLI, 1.01 ± 1.21 s for BLI-bright, and 1.10 ± 1.16 s for LCI. The detection times for both BLI-bright and LCI were significantly shorter than that for the WLI ($p < 0.0001$), but were not significantly different between each other ($p = 0.34$). In the miss rate and the detection time between expert and trainees, there was a significant difference in WLI, but there was no significant difference in BLI-bright and LCI.

Conclusion: Both BLI-bright and LCI improved the detection rate and speed of colorectal lesions by endoscopists, especially trainees compared to WLI when objectively assessed using eye tracking.

Disclosure: Nothing to disclose

P0805 AN INTERNATIONAL SURVEY OF COLORECTAL POLYPECTOMY PRACTICE DEMONSTRATES ENCOURAGING ADHERENCE TO PUBLISHED GUIDANCE AND HIGHLIGHTS SPECIFIC AREAS FOR IMPROVEMENT

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Introduction: Multiple evidence-based guidelines have been produced recently to address the question of how best to perform colonoscopic polypectomy.

Aims and Methods: We aimed to assess the adherence to these guidelines in 7 countries using an online survey, comparing responses to the standards presented in the 2017 ESGE Colorectal 1 polypectomy guideline. An institutional review board approved online survey was distributed to the members the gastroenterological and surgical societies of 7 countries via email during July 2017. The survey presented images of colorectal polyps and their colonic location and asked for the polypectomy technique respondents would use in their daily practice. A reminder email was sent after two weeks and the survey closed after 4 weeks.

Results: 19,467 endoscopic practitioners in 7 countries received the survey. Of 772 (4.0%) who responded, 707 (91.6%) fully completed the survey and their data was analysed. 162, 155, 131, 102, 60, 53 and 45 respondents were from Australia, USA, UK, Belgium, Canada, Israel and New Zealand respectively. 625/707 (88.8%) were physicians, 9.9% were surgeons and 1.3% were nurse endoscopists. Respondents had a median endoscopy practice duration of 18 years (IQR 10–27). Of two images of < 10 mm right sided colonic polyps presented, 51.1% of respondents suggested they would perform cold snare polypectomy in line with guidance. 11.2%, however, suggested cold biopsy forceps and 37.7% suggested endoscopic mucosal resection (EMR) / hot snare polypectomy. Of two large 20 and 45mm transverse colon LSLs with no endoscopic evidence of SMIC, 80.9% suggested EMR, undertaken themselves (48.3%) or referred (32.6%) to another practitioner in line with guidance. 13% would have biopsied the 45mm lesion prior to referral. 9% suggested they would refer these lesions directly to a surgeon. Regarding an image of a large 80mm sigmoid lesion with an endoscopically visible demarcated area consistent with deep submucosal invasive cancer, 51.6% said they would refer to a surgeon in line with guidance whereas 27% suggested they would attempt EMR, 1.4% ESD and the remainder refer the case to another endoscopic practitioner.

Comparing the adherence to guidelines throughout all questions, surgeons (50%) were less adherent than physicians (65%), $p = < 0.001$, consultants (63%) similar to trainees (67%), $p = 0.122$ and those who had undertaken an interventional endoscopy fellowship (63%) similar those who had not (64%), $p = 0.450$.

Conclusion: These data demonstrate encouraging adherence to international guidelines. The work of international endoscopy societies should focus on encouraging the use of and promoting training in cold snare polypectomy for diminutive polypectomy and techniques for endoscopic imaging of large colorectal polyps.

Disclosure: Nothing to disclose

Reference

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P0806 DETERMINING THE MOST EFFECTIVE SURVEILLANCE SYSTEM AFTER AN ENDOSCOPIC POLYPECTOMY: A STUDY BASED ON THE LONG-TERM SURVEILLANCE OF 3,038 PATIENTS

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Introduction: No guidelines have yet been established in Japan for the surveillance after endoscopic removal of colorectal polyps. However, Takano hospital has developed a periodical endoscopic follow up system which has been in place since 1983 to observe patients who have undergone an endoscopic polypectomy. Moreover, this system has been carried out according to the current surveillance system since 2006. The results of 3,038 patients have been retrospectively analised to determine the most effective surveillance method after an endoscopic polypectomy.

Aims and Methods: [The Takano Hospital surveillance colonoscopy programme] All colorectal polyps of any size that were adenomas or suspected to be adenomas were endoscopically removed and the patients were then enrolled in our surveillance programme. The subjects were basically in a clean colon condition. The programme is as follows: one year after the endoscopic removal of the polyp (s) the patients are notified by mail to voluntarily undergo a colonoscopy; polyps are endoscopically removed if detected; patients are notified again by mail the following year to undergo another colonoscopy; and if no polyps are detected the patients are then recommended to undergo a colonoscopy every two years for a set period of time. Mails to the patients are discontinued if they fail to respond after three notification attempts.

Patients (n = 3,038) who adhered to this surveillance programme were enrolled in this study. There were 1,866 males (61%) and 1,172 females (39%). The mean age was 61.2 ± 10.9 years and the observation period was 3.1 years (maximum 11 years) on average.
The detection rate of cumulative adenoma and the cumulative detection rate of advanced neoplasia (AN) that includes carcinomas, high-grade adenomas, adenomas 10mm or more in size, and adenomas with villous components were analised using the Kaplan-Meier method. All 3,038 patients were initially analised and then divided into the AN group (n = 1,180) and the non-AN group (n = 1,858) for further analysis.
Results: The overall cumulative detection rates of adenomas were 16.4% at 1 year, 40.8% at 2 years, and 58.9% at 10 years. The cumulative detection rates in the AN group were significantly higher ($p < 0.01$) than the non-AN group. They were 18.5% at 1 year, 45.5% at 2 years, and 51.9% at 9 years, compared with 15.5% at 1 year, 38.1% at 2 years, and 58.9% at 10 years in the non-AN group. Moreover, AN was detected in 104 patients (57 in the AN group and 47 in the non-AN group). The overall cumulative detection rates of AN were 0.3%, 5.1%, and 8.4% at 1, 5, and 10 years, respectively. The cumulative detection rates of AN in the AN group were significantly higher ($p < 0.001$) than the non-AN group. They were 0.4% at 1 year, 7.4% at 5 years, and 9.9% at 9 years, compared with 0.3% at 1 year, 3.8% at 2 years, and 7.1% at 10 years in the non-AN group.
Conclusion: The cumulative detection rate of AN is significantly higher than that of non-AN when the primary lesion is AN and surveillance every 2 years is effective. However, further analysis is needed to determine whether the interval can be extended to 3 or more years. The findings of this study suggest that surveillance after 1 year is unnecessary.
Disclosure: Nothing to disclose

P0807 A NEW MODIFIED SIZE, MORPHOLOGY, SITE, ACCESS (SMSA) SCORE FOR IS A NOVEL RISK ASSESSMENT TOOL PREDICTING CRITICAL OUTCOMES OF ENDOSCOPIC MUCOSAL RESECTION (EMR)

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Introduction: Endoscopic mucosal resection (EMR) is now the standard of care for treatment of colorectal laterally spreading lesions (LSLs). The SMSA score is an effective tool in grading the difficulty of polypectomy but does not recognize EMR specific risk factors[1]. EMR specific risk assessment tools to predict procedural outcomes are currently lacking.
Aims and Methods: To develop and validate a new EMR specific endoscopic risk score (SMSA-EMR score) to predict technical success, adverse events and recurrence after EMR.
Prospective multicenter data on consecutive large LSLs (≥ 20mm) referred for EMR was included (from 9/2008–5/2017). Independent risk factors associated with difficulty of resection at EMR were identified from literature review and the existing well validated SMSA score. A binary logistic regression model was then generated from a random half of the cohort to derive the SMSA-EMR score. This new score assesses large LSLs in four domains with information gained from the EMR procedure. This score was then applied to the remainder of the cohort.
Results: 2675 lesions in 2675 patients (52.6% M, 65.2% right colon) underwent EMR. The new score was validated on 1157 lesions with a median lesion size of 35mm (IQR 25–45mm). Each lesion was scored on four variables and based on the total SMSA-EMR score divided into two groups, low-risk and high-risk (See Table 1), comprising 54.8% and 45.2% of the cohort respectively. Failed single session EMR occurred in 46 (3.9%) LSLs and was predicted by the SMSA-EMR score ($p < 0.001$), see Table 2. Adverse outcomes were observed with significantly less frequency in the low-risk group, which included intra-procedural bleeding [Odds ratio (OR) – 0.42, 95% Confidence Interval – (0.30–0.57), $p < 0.001$], post-EMR bleeding [OR – 0.54 95% CI (0.33–0.89), $p = 0.002$] and surgical referral at 2 weeks [OR – 0.53 95% CI (0.31–0.93), $p = 0.03$]. Recurrence at first surveillance colonoscopy (SC1) was significantly less likely for the low-risk group [OR 0.34 95% CI (0.23–0.51), $p < 0.001$].
Conclusion: SMSA-EMR is a novel, readily applicable endoscopic risk assessment score which identifies a subset of patients undergoing EMR who are at increased of a failed procedure, adverse events and recurrence. This score has important implications for the post-procedure care of high-risk patients such as planning for overnight hospital admission and ensuring patient adherence to attending follow up examinations. On a broader scale this score may also serve as a benchmark for assessment of trainee competency in advanced tissue resection. It may also lay the foundation to allow for assessment of EMR quality across different endoscopy units, similar to the scoring systems used in surgical audits. Further large multicenter prospective trials are however required to validate this new score for EMR.
Disclosure: Nothing to disclose

Reference

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P0808 THE THERAPEUTIC OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL LARGE PROTRUDING TUMORS

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Introduction: Colorectal endoscopic submucosal dissection (ESD) is widespread as a minimally invasive treatment for colorectal lesions. The procedure is associated with greater technical difficulty than gastric or oesophageal ESD due to poor maneuverability and structural characteristics. Amongst such cases, those involving fibrosis are extremely difficult. Large, protruding lesions are typical examples of such cases. These lesions are not only difficult to diagnose preoperatively, the muscular layer appears to be drawn by the lesion even in the case of intramucosal lesions (muscular-retracting sign), making separation both difficult and dangerous in some cases. We investigated the safety and validity of this procedure based on ESD treatment outcomes for cases of large, protruding lesions of at least 3 cm treated at Keio university hospital.
Aims and Methods: The subjects comprised 30 patients who underwent colorectal ESD at Keio university hospital between 2012 and June 2017 for large, protruding lesions of at least 3 cm in size. We investigated (1) lesion characteristics (location, macroscopic type, tumour diameter) and treatment outcomes (procedure time, endoscopic en bloc resection rate, pathological complete resection rate, procedure-related adverse events, presence/absence of fibrosis), and then compared (2) clinicopathological factors in cases with muscular-retracting sign (positive group) with cases without such findings (negative group).

Abstract No: P0807

	Low-Risk	High-Risk	Total	p	Low risk vs high risk OR (CI)	p
Total count, n (%)	634 (54.8)	523 (45.2)	1157			
Technical success of EMR, n (%)	624 (98.4)	487 (93.1)	1111 (96.0)	<0.001	4.61 (2.3–9.4)	<0.001
CSPEB, n (%)	27 (4.3)	40 (7.6)	67 (5.8)	0.01	0.54 (0.33–0.89)	0.02
IPB, n (%)	87 (13.7)	143 (27.3)	230 (19.9)	<0.001	0.42 (0.3–0.57)	<0.001
Surgical referral at 2 weeks, n (%)	22 (3.5)	33 (6.3)	55 (4.8)	0.02	0.53 (0.31–0.93)	0.03
EDR SC1, n (%)*	44 (9.4)	89 (23.1)	133 (15.6)	<0.001	0.34 (0.23–0.51)	<0.001
EDR SC2, n (%)*	13 (5.5)	22 (10.4)	35 (7.8)	0.05	0.50 (0.25–1.02)	0.06
SMSA-EMR Score						
Size: <40mm-0 ≥40mm-3	Lesion lift: Y-0 N-2	Morphology: Sessile-0 Flat-3	Granularity: Granular-0 Nongranular-1	Total score: Low-risk≤2 High-risk>2		

*[SMSA – EMR Score and **Outcomes:** CSPEB (clinically significant post endoscopic bleeding), IPB (intra-procedural bleeding), *total no. underwent SC1/2]*

Results: (1) The location was the right colon in 15 cases, the left colon in 4 cases and the rectum in 11 cases. The macroscopic type was Is in 16 cases and Isp in 14 cases. The mean tumour diameter was 39.8 mm (30–67). The mean procedure time was 55.9 minutes (15–120), the endoscopic en bloc resection rate was 96.7%, the pathological complete resection rate was 86.7% and fibrosis was noted in 12 cases (40%). In terms of procedure-related adverse events, perforation was noted in 1 case and treatment had to be suspended in 1 case. (2) Findings positive for muscular-retracting sign were noted in 7 cases (23.3%). Amongst these cases, the invasion depth was adenoma in 2 cases, intramucosal carcinoma in 3 cases and submucosal invasive carcinoma in 2 cases. The endoscopic en bloc resection rate was 85.7%, the pathological total resection rate was 57.1% and procedure-related adverse events (perforation) was noted in 1 case. Although no significant difference was observed between the positive and negative cases in terms of lesion location or macroscopic type, mean tumour diameter and mean procedure time were significantly larger/longer in the positive group.
Conclusion: Our results suggested that treatment outcomes for ESD performed on large, protruding lesions of 3 cm or larger were favourable. It also appears that ESD could be used to resect even lesions accompanied by muscular-retracting sign. Some cases of adenomas also exhibit muscular-retracting sign and, if possible, endoscopic resection is optimal. However, as procedures in this investigation were performed by an experienced endoscopists, it is currently unclear as to whether ESD is unconditionally safe for such cases. It appears necessary to keep surgical resection in mind, and to judge one's own skill level as well as the level of difficulty posed by the lesion preoperatively.
Disclosure: Nothing to disclose

P0809 THE TRACTION METHOD "RUBBER-CLIP-METHOD" CONTRIBUTES TO EFFECTIVE SUBMUCOSAL DISSECTION IN COLORECTAL ESD

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Introduction: In colorectal ESD, it is important to obtain sufficient traction for effective submucosal dissection. However, with gravity alone, it is often difficult to obtain sufficient traction for effective submucosal dissection. On the other hand, several traction methods have been developed and their usefulness have been reported. Although they are useful, some points remain in terms of complexity or cost, and so on. Here, we introduce another traction method using clip with rubber band, "rubber-clip-method (RCM)". The advantages of RCM are simplicity, cost effectiveness and capability to change direction of traction.
Aims and Methods: We aimed to investigate the usefulness of RCM in colorectal ESD. A retrospective, single-center, observation study. Out of 145 consecutive patients of superficial colorectal neoplasms experienced in January 2014 – August 2017, 118 patients were included. 6 cases of NET-G1, 7 cases discontinued ESD due to severe fibrosis, 2 cases performed ESD with surgical treatment, and 12 cases used traction methods other than RCM were excluded. Of the included 118 cases, 51 cases were not used traction method (non-traction group), and 67 cases were used RCM (RCM group). Study 1: The comparison of the results of the ESD of the non-traction group and the RCM group. Study 2: We divided cases into 2 groups according by operation time, 88 cases of less than 120 minutes and 30 cases of 120 minutes or more. And we investigated the influence of using RCM or differences of background factors for long operation time of ESD with univariate and multivariate analysis.
Results: Study 1: Background factors such as age, male-female ratio, tumor location, macroscopic type, specimen diameter, pathological type, depth of invasion, degree of fibrosis and operability of endoscopic maneuver showed no remarkable differences between two groups. Both the rate of en bloc resection of RCM group and non-traction group (97% vs 88%, respectively) and the perforation rate (0% vs 4%, respectively) showed better tendency with RCM. The operation time of RCM group was significantly shorter than non-traction group (63 minutes vs 114 minutes (median), respectively). Study 2: In the univariate analysis, four factors such as the specimen diameter (40 mm or more), the severity of fibrosis (moderate or more), operability of endoscopic maneuver (poor) and without traction method showed a significant relationship with long operation time of ESD. In the multivariate analysis, the above four factors independently showed a significant effect for long operation time of ESD. Therefore, the use of RCM was a factor that independently affected the operation time.
Conclusion: The traction method "clip with rubber band method" contributes to effective submucosal dissection in colorectal ESD.
Disclosure: Nothing to disclose

P0810 EFFECTIVENESS OF DIGITAL QUALITY ASSURANCE SYSTEM IN COLONOSCOPY SCREENING FOR COLORECTAL CANCER – A RANDOMIZED HEALTH SERVICES STUDY

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Introduction: The European Society of Gastrointestinal Endoscopy guidelines (1) recommend measuring patient experience and 30-day complication rate after colonoscopy. We aimed to compare effectiveness of digital and paper-based feedback of patients experience and 30-day complications after screening colonoscopy.
Aims and Methods: We included all primary screening colonoscopies performed in two centres from September 2015 to December 2016. Consecutive patients were randomized in a 1:1 ratio either to intervention arm (choice of feedback method) or control arm (routine paper-based feedback). Participants in the intervention arm were asked on their preferred method of feedback (paper-based, automated telephone or online survey) and additionally were informed about the planned automated telephone contact 30 days after the procedure to assess complications. Participants in control group were not contacted, instead they could self-report complications in routine way. The primary endpoint was participant's response rate to feedback questionnaire. Secondary endpoint was participant's response to complications questionnaire. The study was registered as a randomized health services study (RHS_008_2015_june).
Results: We included a total of 2,541 participants, median age: 59.9 years, males:females ratio 1.05 (1,281 in intervention arm, 1,260 participants in control arm).
The response rate to feedback questionnaire for total study population was 63.16%. In the intervention arm, 155 (12.1%) participants chose online survey, 287 (22.4%) – automated telephone survey and 839 (65.5%) – paper-based survey. There was no significant difference in response rate between study groups (64.8% vs 61.5%; $p = 0.08$). Overall response rate was lower in participants aged less than 60 years (57.8% vs 68.1%, $p < 0.001$), males (61.3% vs 65.1%, $p = 0.05$), and participants in small, non-public centre as compared to large, public centre (49.1% vs 64.5%, $p < 0.001$). Free choice of feedback method significantly improved response rate among participants with baseline lower response rate: younger than 60 years (60.8% vs 54.7%; $p = 0.031$), male (64.0% vs 58.6%; $p = 0.045$) and in small non-public centre (56.2% vs 42.5%; $p = 0.043$).
In the intervention arm, 1,168 participants (91.2%) answered the phone call concerning complications. Of them, 776 (66.4%) completed the automated questionnaire. A total of 79 participants (6.2%) reported complications. When verified, 46 reported complications (58.2%) were administrative errors. Another 25 (2.1%) reported complications were not clinically relevant. Finally, only 2 participants (0.2%) reported clinically relevant complications – one post-polypectomy bleeding requiring hospital admission and one appendicitis with appendectomy one day after screening colonoscopy. No complications were self-reported in the control group.
Conclusion: The overall response rate was not significantly improved with digital feedback, yet it yielded significant improvement in participants with baseline low response rate. Our study demonstrated feasibility and efficacy of digital patient feedback on complications after colonoscopy.
Disclosure: Nothing to disclose

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P0811 THE ROLE OF PAIN CATASTROPHIZING IN PAIN EXPERIENCE DURING ENDOSCOPIC PROCEDURES

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Introduction: Endoscopic procedures are unpleasant and in most cases painful. Identifying the factors that may contribute to their acceptance might be beneficial for the patient and helpful for the phyisician. Pain Catastrophizing (PC) has been associated with a number of pain-related outcomes, including chronic pain in IBD and experimentally induced pain but its role in the experience of pain during medical procedures has not yet being investigated.

Aims and Methods: We investigated the role of PC and its relation to patient reported and clinician rated pain during endoscopic procedures.
143 consecutive outpatients undergoing endoscopy from September to May 2017 were enroled. Gender (57% females), age (M = 57.83; SD = 17.17), body mass index (M = 25.28; SD = 4.22) and previous endoscopic experiences (56%). During endoscopy, operators evaluated the patient using the Pain Assessment in Advanced Dementia (PAINAD) Scale. The Ramsay Sedation Scale (RSS) was used to assess patient's level of consciousness and sedation effectiveness. After endoscopy and before discharge patients reported about pain and discomfort during the procedure. A total score for self-reported pain was derived through principal component analysis of visual-analogue, verbal, numerical and face scales. The Pain Catastrophizing Scale (PCS) was also administered to retrospectively assess patient's aptitude for catastrophic pain. We carried out regression and mediation analyses to test study's main hypotheses.
Results: Age, gender, BMI and previous endoscopic experiences were uncorrelated with clinician reported pain. As it regards self reported pain, the analysis revealed marginally significant differences by gender ($p < 0.05$) and age ($p < 0.05$) with women and younger people reporting more pain. PC was significantly larger for women ($p < 0.01$). Clinician rated pain during the procedure predicted patient self reported pain (Beta = +0.646; $p < 0.001$; $R2 = 0.41$). PCS was also associated with self-reported pain (Beta = +0.584; $p < 0.001$; $R2 = 0.34$). Mediation analyses revealed that the relationship between clinician rated pain and self reported pain was accounted for by PCS (Indirect Effect of clinician rated pain on self reported pain through PCS = +0.191; [+0.142; +0.258]). Nevertheless, clinician-rated pain (Beta = +0.264; $p < 0.001$; $R2 = 0.41$) still was predictive of self-reported pain controlling for PCS. Mediation analyses results were robust controlling for gender, age and body mass index as well as for previous endoscopic experiences and types of endoscopic procedure.
Conclusion: PC was found to play a central role in the experience of pain during both upper and lower endoscopy in fact PC explains the association of clinician rated pain with patient reported pain. While similar findings have been reported in the context of chronic pain studies, this is the first study showing that catastrophizing is also important in the experience of pain during medical procedures. In order to make endoscopic procedures more acceptable and to facilitate the medical examination by the operator, non pharmacological interventions to reduce PC by a cognitive-behavioral therapy might disclose an avenue for future research and clinical practice.
Disclosure: Nothing to disclose

P0812 SAFETY AND EFFICACY OF THE FULL-THICKNESS RESECTION DEVICE (FTRD) IN THE COLORECTUM: A POOLED ANALYSIS OF PUBLISHED RESULTS

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Introduction: The full-thickness resection device (FTRD) is approved for the resection of difficult adenoma and subepithelial tumors in the colorectum.
Aims and Methods: The aim of this study was to analyse the safety and efficacy of the FTRD in the colorectum. A pooled analysis of data from published studies was performed. All studies that reported on the use of the FTRD in the colon and rectum were eligible for inclusion. A literature search was done to identify published studies and relevant congress abstract databases were searched.
Results: A total of 18 studies were included, 9 of them published as full-text and 9 as congress abstracts, which comprised a total of 532 patients from 7 countries. The target lesion was reached with the FTRD mounted on top of the endoscope in 522 (98.1%) patients and technical success was achieved in 486 (91.4%). The full-thickness resection was histological confirmed in 326 of 401 (81.3%) patients, in the remaining 131 no data on this endpoint was reported. The R0 resection rate was 77.5% and achieved in 383 of 494 patients for which data on resection margings were reported. Technical problems were mostly related to the resection snare, which occurred in 34 cases. In most of these cases a successful resection however was achieved by use of a conventional resection snare following clip application with the FTRD. Complications included minor bleeding and postpolypectomy syndrome in 14 (2.6%) patients each. Severe bleeding was rare and occurred in 2 (0.4%) patients and perforations were reported in 13 (2.4%) patients. A surgical intervention due to a FTRD related complication was necessary in 9 (1.7%) patients.
Conclusion: The FTRD system provides high efficacy in the colorectum. The complication rate is low and most complications can be managed conservatively or endoscopically.
Disclosure: Nothing to disclose

P0813 DOES POLYP DETECTION RATE CORRELATE WITH MEAN ADENOMA PER COLONOSCOPY?

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Introduction: Adenoma detection rate (ADR) is the primary quality indicator for colonoscopy. Mean adenoma per colonoscopy (APC) reflects colon inspection better than ADR and is more appropriate to illustrate differences between individual endoscopists. Both these factors are rather difficult to obtain in terms of time and personnel. Polyp detection rate (PDR) is a user friendly alternative of ADR that can be easily evaluated from administrative data.
Aims and Methods: The aim of our study was to assess whether PDR and APC are correlated and to determine conversion factor to predict APC from PDR in preventive (faecal occult blood test positive (FOBT+) and screening) colonoscopies.
Retrospective study included asymptomatic individuals aged 45–75 who underwent preventive colonoscopy in 2012–2016 as part of Czech prospective multicenter study monitoring metabolic risk factors of colorectal cancer. Individuals with incomplete colonoscopy and endoscopists with less than 30 colonoscopies and/or no detected adenoma in the observed group were excluded from the study. Spearman's correlation coefficient was used to assess the relation between individual PDR and APC. The resulting conversion factor to predict APC from PDR was obtained by linear regression.
Results: In total, the study included 1,614 preventive colonoscopies performed by 16 endoscopists. Correlation between PDR and APC in all preventive colonoscopies was high and statistically significant (Rs 0.70; $p = 0.0027$). There is a stronger correlation between PDR and APC in men (Rs 0.73; $p = 0.0029$) than in women. Conversion factor to convert APC from PDR is 0.0123 and 0.0108 for all preventive and screening colonoscopies respectively. In FOBT+ colonoscopies linear regression did not reflect the actual variability observed in data.
Conclusion: There is a strong correlation between PDR and APC. Because of better availability, PDR may replace ADR and APC in colonoscopy quality assessment. With some limitations, APC may be estimated from PDR using a conversion factor that varies based on colonoscopy indication and patient gender. With respect to the minimum ADR requested, i.e. 25% recommended by both ASGE and ESGE, all preventive colonoscopies should reach APC $\geq$ 0,4.
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Disclosure: Nothing to disclose

P0814 IMPROVED COLORECTAL ADENOMA DETECTION RATE WITH LINKED COLOR IMAGING (LCI) TECHNOLOGY COMPARED TO WHITE-LIGHT HIGH-DEFINITION COLONOSCOPY: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: LCI (Linked Color Imaging) is a new endoscopic visualization technique which may increase colorectal adenoma detection rate by the improved endoscopic image enhancement combined with virtual chromoendoscopy. However only limited data available in the literature on the effectiveness of this new technology.
Aims and Methods: We aimed to evaluate the effectiveness in the adenoma detection rate of LCI in patients referred to colonoscopy and compared to the results of the white-light colonoscopy technique.
We enrolled outpatients consecutively, between October 2016 and December 2017, who were met the study inclusion criteria. Patients with previous CRC history or incomplete colonoscopy were excluded. All of the colonoscopic procedures were made under deep propofol sedation guided by an anesthesiologist team. Eligible patients were randomly selected to undergo colonoscopy with high-definition white-light colonoscopy (HD-WLC) technology or LCI Eluxeo technology during instrument withdrawal, by Fujinon 7000 processor and with EC590Z, EC760, EC760Z colonoscopes. Each colonoscopic procedure was performed by three expert endoscopists with a minimum 6-minutes-withdrawal time.
Results: A total of 1100 patients were randomized. 552 patients were enrolled in the LCI group and 548 patients into the WLC group. Adenoma detection rate (patients having at least one colorectal adenoma) was significantly higher in the LCI group as compared to the control WLC group: 34.4% vs. 26.8%, respectively ($p = 0.007$). No significant differences were observed in the patient demographic characteristics, quality of colonoscopy preparation and withdrawal time between the two groups.
Conclusion: Based on our randomized controlled trial the LCI electronic chromoendoscopic enhancement of the Fujinon Eluxeo colonoscopy system was superior compared to the conventional HD-WLC in detecting of colorectal adenomas. This difference mainly explained by the more sensitive detection of minute colonic adenomas.
Disclosure: Study was supported by ECT grant GINOP 2.1.1.-15- 2015-00128

P0815 ENDOSCOPIC AND MOLECULAR CHARACTERISTICS DURING THE DEVELOPMENT OF TRADITIONAL SERRATED ADENOMA

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Introduction: Colorectal serrated lesions (SLs) include hyperplastic polyp (HP), traditional serrated adenoma (TSA) and sessile serrated adenoma/polyp (SSA/P). Our previous study shows that Type II-O pit pattern is highly specific to SSA/Ps, and additional changes in the pit patterns (III, IV or V) are associated with malignant progression to SSA/P with cytological dysplasia (CD) or high-grade dysplasia (HGD) (1). However, endoscopic features in TSAs are not fully understood.

Aims and Methods: To establish accurate colonoscopic diagnosis and treatment of TSAs, we aimed to clarify the associations among the morphological, pathological and molecular characteristics of SLs. A total of 401 premalignant and malignant colorectal lesions were enrolled in this study. Using magnifying colonoscopy, microsurface structures were assessed based on Kudo's pit pattern classification system, and the Type II pit pattern was subcategorized into classical Type-II, Type II-Open (Type II-O) and Type II-Long (Type II-L). Biopsy specimens were obtained from all lesions for genomic DNA extraction, after which lesions were treated by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). *BRAF*/*KRAS* mutations and DNA methylation of *SMOC1*, which is specifically methylated in TSAs (2) and CpG island methylator phenotype (CIMP) markers (*MINT1, -2, -12, -31, p16 and MLH1*) were analyzed through pyrosequencing.

Results: Pit patterns of the 383 colorectal lesions were as follows: Type II (n = 40), Type II-L (n = 9), Type II-O (n = 100), Type II plus III/IV (n = 21), Type II-L plus III/IV (n = 17), Type II-O plus III/IV (n = 40), Type II-L plus V (n = 4), Type II-O plus V (n = 12) and Type III/IV (n = 140). Type II-O was tightly associated with sessile serrated adenoma/polyps (SSA/Ps) with *BRAF* mutation and CIMP-high. Most lesions with simple Type II or Type II-L were hyperplastic polyps (HPs), while mixtures of Type II or Type II-L plus more advanced pit patterns (III/IV) were characteristic of traditional serrated adenomas (TSAs) (sensitivity, 73.7%; specificity, 92.1%). Type II-positive TSAs frequently exhibited *BRAF* mutation and CIMP-low, while Type II-L-positive TSAs were tightly associated with *KRAS* mutation, *SMOC1* methylation and CIMP-low.

We next assessed the association between pit patterns, molecular features and HP subtypes. We found that Type II-L was more frequent in goblet cell rich type (GCHP) (33.3%) than in microvesicular type (MVHP) (9.3%). GCHP with Type II-L frequently exhibited *KRAS* mutation, while majority of MVHP with Type II-O exhibited *BRAF* mutation. *SMOC1* methylation was less frequent in HP. These results suggest HPs with a Type II-L pit pattern and *KRAS* mutation may overlap with GCHPs and develop into TSAs with *KRAS* mutation. Finally, we analyzed a series of SLs with HGD. The Type II-L-derived cancers were strongly associated with TSA histology in the premalignant components, *KRAS* mutation, *SMOC1* methylation, CIMP-low and lack of *MLH1* methylation.

Conclusion: Our results suggest that Type II subtypes may reflect distinct molecular subclasses in the serrated neoplasia pathway, and that Type II-L plus more advanced pit patterns could be useful hallmarks for identifying TSAs at high risk of developing into CRC.

Disclosure: Nothing to disclose

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P0816 PREDICTIVE FACTORS FOR REPEATING COLONOSCOPY IN OUTPATIENTS WITH INADEQUATE BOWEL PREPARATION

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Introduction: Inadequate bowel cleansing has been observed in 10–25% of all colonoscopies. US Taskforce's recommendation is to repeat colonoscopy in individuals with poor bowel preparation within 1 year post index colonoscopy. However, in most cases this time interval is defined on an individual basis and is at the discretion of the performing endoscopist.

Aims and Methods: Our aim is to identify predictive factors for repeating colonoscopy in individuals with inadequate bowel preparation on the first diagnostic examination. Over a 22-month period (01/2013 to 10/2014), all patients who underwent colonoscopy in our center and had inadequate bowel preparation, were identified. Endoscopic records over at least a 3-year period after index colonoscopy were reviewed as per the quality of bowel preparation, the limit of the examination, the timing between index and repeat colonoscopy as well as the identification of polyps (size, type, number) and cancer. The quality of bowel preparation was categorized as adequate or inadequate according to each endoscopist's subjective impression. Multivariate analysis was performed in order to identify factors independently associated with repeat colonoscopy among patients with inadequate bowel cleansing.

Results: Of the 12,948 colonoscopies performed at 2 different sites, the quality of the bowel preparation was suboptimal (inadequate or poor) in 990 outpatients. Among these 990 individuals, colonoscopy was repeated within a 3-year period in 261 (26.3%).

The mean time (standard deviation) interval between the index and the repeat colonoscopy was 2.78 (4.51) months. Despite the suboptimal preparation, caecum was intubated in 69.7% of the index. Adenomas were identified in 130 cases while there were 113 cases of advanced neoplasia (65 advanced adenomas and 48 cancers).

Among the 261 repeated colonoscopies, the bowel preparation was adequate in 71.2% of the cases with 74 adenomas and 8 colorectal cancers seen only on the second examination, corresponding to an adenoma and cancer miss rate of 59.7% and 61.1% respectively.

Predictive factors for repeating colonoscopy were the "very poor" bowel preparation, the detection of polyps and of advanced adenomas on index coloscopy as well as the positivity of the faecal occult blood screening test. Reaching the caecum during index colonoscopy was negatively associated with repeating colonoscopy in the reference period.

			95% C.I.for EXP (B)	
	Sig	Exp (B)	Lower	Upper
Very Poor Preparation	.000	2.267	1.584	3.244
Polyp-1st colonoscopy	.000	2.484	1.490	4.142
Adenoma-1stcolonoscopy	.995	.998	.553	1.801
Advanced Adenoma-1st colonoscopy	.001	2.820	1.518	5.237
Polyethylene-glycol based preparation	.164	.584	.274	1.245
Positive Fecal Occult Blood Test	.000	2.910	1.642	5.160
Complete colonoscopy (up to caecum)	.000	.273	.195	.381

[Table 1]

Conclusion: Only 1 out of 4 outpatients with suboptimal preparation repeated the examination within 3 years. Miss rates for adenomas and cancer remain high for colonoscopies with poor bowel preparation. Caecal intubation on index colonoscopy with poor bowel preparation is an independent predictor for not repeating coloscopy in the subsequent 3-year period. However endoscopists are urged to reach the caecum in each colonoscopy, as otherwise their caecal intubation rate would be penalized. Guidelines are needed to define how to proceed in cases with inadequate bowel preparation, in order to guarantee that a repeat colonoscopy will be undertaken, and with adequate bowel preparation.

Disclosure: Nothing to disclose

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P0817 ENDOSCOPIC MUCOSAL RESECTION WITH ANCHORING OF THE SNARE TIP: MULTICENTER RETROSPECTIVE EVALUATION OF THE EFFECTIVENESS AND SAFETY

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Introduction: Endoscopic mucosal resection (EMR) is the reference to resect colorectal neoplasia between 10 and 30 mm. Main objective of EMR is to resect completely the neoplastic tissue (complete resection) and if possible in only one piece (En Bloc) with safe margins on histological assessment (R0). In case of R0 resection, the risk of local recurrence is 0% and control for local recurrence detection can be avoided. Conventional EMR lead to 65% of En Bloc resection for lesions under 20 mm. Anchoring the tip of the snare is a technical

trick allowing to fix the snare tip into the submucosa in order to reduce snare sliding to the lesion edges. The aim of the present study was to evaluate the effectiveness and the safety of this anchoring-EMR (A-EMR).
Aims and Methods: We performed a retrospective analysis of A-EMR procedures performed consecutively in 4 French centers between May 2017 and January 2018. In those 4 centers, anchoring was systematically attempted for all EMR using Olympus® conventional snares (10 or 25 mm). All specimens were stretched on cork for pathology.
Results: 141 A-EMR were performed in 125 patients by 9 operators during the study period. Mean lesion size was 19.8 mm (range 8–40 mm). Anchoring was technically successful in 96.5% of cases. En bloc and R0 resection proportions were respectively 81.6% and 70.0%. R0 proportion significantly reduced with lesion size with respectively 82.6% in lesions < 20 mm, 55.3% between 20 and 30 mm and 50.0% over 30 mm ($p = 0.002$). Complete perforations closed endoscopically occurred in 2.1% of cases and partial ones with target sign in 1.4% of cases.
Conclusion: Anchoring-EMR is effective to remove with margins (R0) the lesions between under 30 mm and safe with 2.1% of perforation closed endoscopically. This technique could improve R0 resection rate compared to conventional EMR but prospective randomized comparison is requested.
Disclosure: Nothing to disclose

P0818 EFFICACY, SAFETY AND LONG-TERM OUTCOMES OF PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION FOR THE TREATMENT OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS IN AN ENDOSCOPY REFERRAL CENTER

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Introduction: Endoscopic mucosal resection (EMR) has been demonstrated to be safe and efficient for the treatment of large non-pedunculated colorectal polyps (LNPCPs). Moreover, it is cost-effective compared to endoscopic submucosal dissection and surgery. However, most of studies include both en bloc and piecemeal EMR (pEMR).
Aims and Methods: We aimed to assess the safety, efficacy and long-term outcomes of pEMR for the treatment of LNPCPs. Medical records of consecutive patients who underwent pEMR for LNPCPs ≥20 mm in size between 2010 and 2016 were extracted from endoscopic data base of our Division and reviewed. Patients with inflammatory bowel diseases, familiar polyposis, circumferential lesions, endoscopic findings of submucosal invasive cancer or invasive cancer at the histopathological evaluation post-pEMR were excluded.
Results: 271 lesions in 245 patients were included in the study (122 males, mean age 66 years, range 35–88). Mean lesion size was 32.6 mm (20–100), median 30 mm. 257 (94.8%) were naïf lesions, 14 were remnants after incomplete EMR. 190 (70.1%) lesions were located in the right colon, 47 (17.3%) in the left colon, 34 (12.5%) in the rectum. Lateral Spreading Tumors (LSTs) granular homogeneous were 56 (20.7%), LSTs granular nodular mixed 62 (22.9%), LSTs non granular 84 (31%), sessile polyps 69 (25.4%).
pEMR was complete in 269 (99.3%) lesions. In two (0.7%) naïf LNPCPs pEMR was not completed. In one case because of intra-procedural perforation, in the second because of submucosal fibrosis. Histology revealed 218 (80.4%) adenomas (68 tubular, 123 tubulovillous, 27 villous), 49 (18.1%) sessile serrated adenomas, 4 (1.5%) hyperplastic polyps. High-grade dysplasia was observed in 159 (58.6%) lesions. Complications occurred in 47 (17.3%) LNPCPs: 14 (5.2%) intra-procedural and 28 (10.3%) post-procedural bleedings, 2 (0.7%) burning syndromes, 3 (1.1%) intra-procedural perforations. One intra-procedural bleeding and the 3 perforations needed surgical management (8.5% of complications). 234/269 (87%) completely resected LNPCPs had 1–4 surveillance colonoscopies (SCs) within a period of 3–48 months. Recurrent lesions were 48 (20.5%) at the first SC, 62 (26.5%) at any SC. 20 lesions recurred twice, 5 three times. 56 (90.3%) recurrences had further curative endoscopic resection. 6 (9.7%) recurrences underwent surgery, 3 of them (1.3% of lesions in follow up) due to of the presence of cancer in bioptic specimens.
Conclusion: Our data confirm that pEMR is a safe and effective technique for the treatment of LNPCPs. However, considering the high recurrence rate post-pEMR and the risk of cancer, a careful and prolonged endoscopic follow-up is mandatory.
Disclosure: Nothing to disclose

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P0819 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL TUMORS ACCOMPANIED BY FIBROSIS IN THE SUBMUCOSAL LAYER

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Introduction: The possibility of complete curative en bloc resection is sometimes related to the presence and degree of fibrosis in the submucosal layer (SM), rather than tumor size and location. In this study, clinical outcomes of ESD for colorectal neoplasms accompanied by fibrosis were analyzed, to achieve exact diagnosis and safe treatment of such lesions.
Aims and Methods: The aim of this study was thus to establish a safe and curative ESD procedure for colorectal neoplasms showing fibrosis in the SM layer. ESD was performed for 1,512 colorectal neoplasms in 1,473 patients (male 839, female 6334, average 66.1 years old) from January 2003 to June 2017, and was completed for 1,497 lesions. Of these cases, 315 showed SM fibrosis. These cases were divided into three groups: absence of fibrosis (A), fibrosis due to benign causes (B), and fibrosis due to cancer invasion (C). Furthermore, cases were classified as mild (grade 1), moderate (grade 2), or severe (grade 3). Clinical outcomes and pathological findings of the above-mentioned ESD cases were analyzed according to these endoscopic classifications to facilitate the safe achievement of ESD. In addition, histological validation of endoscopic diagnosis was examined for the 240 of the 315 cases with fibrosis, to clarify for differential diagnosis between Type B and Type C.
Results: Of the 315 cases with fibrosis, 210 cases involved benign causes (Type B), and 115 cases were considered related to cancer invasion (Type C). As the results of the validation study ($n = 240$) for differential diagnosis between Types B and C as follows; sensitivity: 88.7%, specificity: 90.5%, accuracy: 89.2%, PPV: 96.3%, NPV: 74.0%. En bloc resection rates ($n = 315$) were as follows: A, 97.8%; B-1: 96.9%; B-2: 88.5%; B-3: 63.5%; Type C-1: 100%; C-2: 96.3%; C-3: 61.1%. The en bloc resection rates for types B-3 and C-3 were significantly lower ($p < 0.05$) than that for Type A. There were no significant differences between Type A and Types B-1, B-2, C-1, and C-2 lesions. There were 8 cases (0.5%) of perforation, 4 of which (Type B) required emergency surgery. From these results, tumors accompanied by mild to moderate fibrosis become the standard indication for ESD. The tumors accompanied by severe fibrosis should be indicated as relative indications for ESD and required high quality of ESD technique to avoid perforation.
Conclusion: Accurate diagnosis of fibrosis based on the perioperative endoscopic findings appears feasible and contributes to completing the ESD procedure safely and curatively.
Disclosure: Nothing to disclose

P0820 ENDOSCOPIC FEATURES OF RESPONSE TO NEOADJUVANT (CHEMO)RADIOTHERAPY FOR RECTAL CANCER: PRELIMINARY RESULTS

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Introduction: Rectal cancer patients with a clinical complete response (CR) to neoadjuvant (chemo) radiotherapy can be treated with a watch-and-wait (W&W) approach.
Aims and Methods: The aim of this study was to assess the diagnostic performance of restaging endoscopy for the selection of luminal CR after (chemo) radiotherapy. This study was performed in a single center where restaging endoscopy was routinely performed after neoadjuvant treatment for rectal cancer to assess the luminal response. All patients underwent flexible sigmoidoscopy 6–12 weeks after the end of (chemo) radiotherapy, followed by rectal surgery or a W&W approach with a follow-up of ≥2 years. All white light endoscopic images were retrospectively re-evaluated by two experienced endoscopists (one surgeon and one gastroenterologist). The presence of a white scar, flat ulcer, irregular ulcer, adenomatous tissue or tumour mass were evaluated and the likelihood for a CR was scored at a 5-point scale (1 = definite CR, 5 = definite residual tumour). Histology after surgery represented the reference standard (ypT0 = CR). In patients undergoing W&W, a regrowth free period of ≥2 years was also considered a CR. Area under the ROC-curve (AUC), sensitivity and specificity were calculated, considering a likelihood score 1 or 2 as complete response. In addition, the interobserver agreement was calculated.
Results: Sixty-five consecutive patients were included (71% male, mean age: 65 years). Forty-two patients had surgery (ypT0: 12/42) and 23 patients underwent W&W (2 year regrowth free: 20/23). Median time to restaging endoscopy was 9 weeks (IQR 8–12). Median time from endoscopy to surgery was 22 days (IQR 15–45). The positive predictive value (PPV) for a CR was 81/87% when a white

scar was present. PPV for CR were 43/75% and 35/41% when adenomatous tissue or a flat ulcer were present. PPV for CR were 0/20% and 21/30% when an ulcer with irregular border or tumour mass were present. AUC, sensitivity and specificity for the prediction of a CR with endoscopy were 0.74 (95% CI 0.66–0.89), 69% and 79% for reader 1 and 0.81 (95% CI 0.71–0.92), 66% and 91% for reader 2. The interobserver agreement was substantial (quadratic weighted k = 0.68). In 30 patients, a biopsy was taken. The addition of biopsy results to endoscopic images did not improve the diagnostic performance for the selection of CR for both readers.
Conclusion: Endoscopy predicts complete response after a median time of 9 weeks with a sensitivity of 66–69% and specificity of 79–91%. The above mentioned endoscopic features can be used to select patients for an extended observation period to select for organ-saving treatment. Endoscopy should be used in combination with MRI to provide more detailed information on the response in the deeper layers of the bowel wall and the mesorectum.
Disclosure: Nothing to disclose

P0821 GASTRIC ADENOMA OR EARLY GASTRIC CANCER IS AN IMPORTANT RISK FACTOR FOR COLORECTAL ADENOMA

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Introduction: Patients diagnosed with gastric cancer have a higher prevalence and increased risk of colorectal cancer. But a few studies reflecting colonic endoscopy quality have investigated the risk of colorectal cancer or adenoma in patients with early gastric cancer or gastric adenoma.
Aims and Methods: The purpose of this study is to investigate the prevalence of colorectal adenoma or cancer in patient with gastric adenoma and early gastric cancer. We performed a prospective single center study. From January 2015 to December 2016, 307 patients who had treated stomach ESD due to early gastric cancer or adenoma of 110 patients were enrolled. Healthy age- and sex-matched controls were enrolled from general screening population. Demographic factors and colonoscopic findings of the cases and the controls were collected and prevalence and risk factor of colorectal adenoma and cancer of both groups are analyzed.
Results: Data from 110 patient in the gastric neoplasm group (93 with gastric adenoma, 17 early gastric cancer) and 110 healthy control group participants were included in the statisti-cal analysis. The presence of gastric adenoma or early gastric cancer was an independent risk factor for colorectal adenoma (OR = 3.4771, 95% CI = 1.9727–6.1289). The presence of gastric adenoma or early gastric cancer was an independent risk factor for colorectal high risk adenoma (OR = 5.0980, 95% CI = 1.9995–12.9986). There was no statistical relation between gastric adenoma or early gastric cancer and colorectal cancer. (p = 0.0948)
Conclusion: The risk of colorectal adenoma and advanced colorectal adenoma increased significantly in patients with gastric adenoma and early gastric cancer. Therefore, we suggest that colonoscopic surveillance should be strictly considered in patient with gastric adenoma and early gastric cancer.
Disclosure: Nothing to disclose

P0822 WHICH FACTORS ARE RELATED TO A RISK OF DEVELOPING A PERFORATION AFTER A COLONOSCOPY IN AN ORGANISED POPULATION-BASED COLORECTAL CANCER SCREENING PROGRAMME? A NESTED CASE-CONTROL STUDY

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Introduction: In the Basque Country (one of the 17 autonomous regions of Spain), with an average population of 1,422.369 inhabitants, colorectal cancer (CRC) screening was introduced in 2009 for persons within 50–69 ages, by Immunochemical test (FIT) and colonoscopy under sedation as a diagnostic procedure. Colonoscopy is an invasive procedure and is not without risk. Overall pooled colonoscopy complication prevalence for post-colonoscopy perforation, bleeding and mortality is 0.5/1000 (95% confidence interval (CI) 0.4–0.7), 2.6/1000 (95% CI 1.7–3.7) and 2.9/100,000 (95% CI 1.1–5.5) colonoscopies.
Aims and Methods: To determine which independent risk factors are related with a perforation after a screening colonoscopy, with the future ambition of decreasing the post-colonoscopy complications. All screening colonoscopies after a positive FIT were analysed related to 2009–2016 invitations. All medical records were assessed by experts. 160 perforations were identified by the discharged of the Colorectal Cancer Screening Programme database. Perforation was considered either surgical or medical treatment. A multivariate model was performed and the perforations Independent Predictors were identified through a logistic regression.
Results: After 54,675 colonoscopies, perforation complication rate was 0.3%. The risk of perforation after a colonoscopy was 2.9/1,000 and the risk of post-polypectomy perforation was 2.4/1,000. The 15.6% and the 18.9% of the cases had cardiopathy and neumopathy history respectively. On the other hand the 3.8% of the patient were treated with anticoagulant therapy, the 18.2% with antiagregants and the 10% with corticoids. The 36.9% of cases had a history of abdominal surgery and the 37.4% presented diverticulosis during the colonoscopy procedure. Firstly we made an univariate analysis taking into account the following variables that may be related with a perforation during a colonoscopy: sex, age, body mass index, history of abdominal surgery, cardiopathy and neumopathy history, antiagregant or anticoagulant therapy, chronicity index, diverticulosis, polyp size ≥20 mm, polypectomy, pT1 or advanced adenoma in the diagnosis, location of major size of polyp and highest number of polyps, adenoma and polyp detection rates and bowel preparation. The variables with a significant result in the univariate analysis were; history of neumopathy, history of abdominal surgery, diverticulosis, polyp size ≥20 mm, pT1 in the diagnosis and location of the polyps.
After a multivariate analysis the perforation independent predictors were: history of abdominal surgery (OR:4.3; 95% CI:2.0–9.3), polyp size ≥20 mm (OR:4.3; 95% CI:1.9–9.7), pT1 in the diagnosis (OR:16.9; 95% CI:2.0–139.1) and right location of the polyps (OR:5.3; 95% CI:1.9–15.0). The logistic model explained 77% of the complications (95% CI 0.71–0.84, $p < 0.001$).
Conclusion: The colonoscopy is an invasive procedure with a small but not insignificant risk of perforation. That is why, it is crucial to know which factors predict the risk of perforation in order to implement countermeasures. The study that we present show that abdominal surgery, polyp size ≥20 mm, pT1 in the diagnosis and right location of the polyp are independent factors to consider while performing the colonoscopies.
Disclosure: Nothing to disclose

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P0823 ROLE OF FAECAL IMMUNOCHEMICAL TESTING IN THE DIAGNOSTIC WORKUP OF PATIENTS WITH IRON DEFICIENCY ANAEMIA

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Introduction: Gastroscopy and colonoscopy are frequently included in the routine diagnostic workup of patients with iron deficiency anaemia (IDA). However, a high percentage of these examinations do not show any significant lesion. Faecal immunochemical testing (FIT) could be used to increase the efficiency of the IDA diagnostic workup due to its ability to detect intact globin from colorectal lesions.
Aims and Methods: We aimed to assess whether FIT may discriminate between significant colorectal or upper gastrointestinal lesions, saving unnecessary explorations in patients with IDA.
Methods: consecutive naive patients with moderate-severe IDA defined as Hb < 11.9 g/dL in men and Hb < 10.9 g/dL in women, and ferritin ≤ 30 g/dL, were enrolled from April 2016 to December 2017 in a prospective, observational study. Inpatients, patients under 18 years-old, with personal history of inflammatory bowel disease, gastrointestinal cancer, gastrointestinal surgery, evidence of bleeding, gastroscopy and/or colonoscopy in the past 5 years, pregnancy or refusal to participate were excluded. Demographic data, comorbidity (Charlson's Index), concomitant medication (corticosteroids, NSAID, anticoagulants) and laboratory variables were collected. Faecal haemoglobin was measured using 1-kit OC-Sensor^{TM}, (FIT positive ≥10 mg/g), previously to endoscopic procedures. Gastroscopy with gastric and duodenum biopsies and colonoscopy were performed in the same day. Significant upper gastrointestinal lesion (SUGIL) included: cancer, angiodysplasia, polyp ≥10 mm, erosions, celiac disease, erosive esophagitis, *H. pylori gastritis or peptic* ulcer. Significant colorectal lesions (SCL) comprised: colorectal cancer (CRC), angiodysplasia, advanced polyp, colitis or erosions. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), the area under the curve (AUC) of FIT for SCL and CRC were calculated.
Results: 245 patients were included (66.1% female, mean age 71 ± 12 years, mean Hb 9.7 ± 3.5 g/dl). A significant gastrointestinal lesion was detected in 154 (62.8%) patients whereas the diagnosis was uncertain in the remaining 91 (37.2%) patients. The most frequent SUGIL were *Helicobacter pylori* gastritis (n = 31) and angiodysplasia (n = 11), whereas the most frequent SCL were

advanced polyp (n = 30), CRC (n = 28) and angiodysplasia (n = 19). Of 119 (48.8%) patients with a positive FIT result, 65 (54.6%) had SCL (PPV 54.6%) and 37 (31.0%) had SUGIL (PPV 31.3%). Conversely, among 126 patients with a negative FIT result, 48 (38.1%) had SUGIL and 20 (15.9%) SCL. Overall, 106 patients with a negative FIT result did not have any SCL at colonoscopy (NPV 84.1%). FIT detected 26 out 28 CRC (Sensitivity 92.8%). Only 9 (3.7%) patients had SUGIL and SCL simultaneously, having all of them a positive FIT result. The AUC of a positive FIT result for SCL and CCR was 0.78 and 0.87, respectively. In the multiple regression analysis, only non-use of NSAIDs and positive FIT were independently associated with SCL. If we had started the diagnostic workup performing colonoscopy in patients with a positive FIT result, gastroscopy in patients with negative FIT result or both explorations when the initial examination did not show any significant lesion, we would have saved 104 (21%) examinations without loss of diagnostic efficacy.
Conclusion: In patients with IDA, FIT may guide the sequence of endoscopic procedures, saving unnecessary explorations.
Disclosure: Nothing to disclose

P0824 ENDOSCOPIC TREATMENT OF BILE DUCT STONES IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Nowadays Endoscopic treatment of Bile duct stones in patients with surgically altered anatomy have become popular with enteroscopy-ERCP and EUS-hepaticogastorostomy (EUS-HGS) technique. We have retrospectively investigated surgically altered patients with bile duct stones which ware treated by enteroscopy-ERCP or EUS-BD technique or PTBD or surgery.
Aims and Methods: We have reviewed medical records from 2009 to 2017 and finally found consecutive 188 cases (284 sessions) of bile duct stones with surgically altered anatomy. Averaged age is 74.3y/o and male: female is 141(75%): 47(25%). The group of Roux-en-Y(R-Y) with gastrectomy were 95 cases (128 sessions) which included gastric cancer 87cases and 8 others, R-Y without gastrectomy were 29 cases (70 sessions) which included biliary cancer 12 cases, maljunction 8 cases, and 9 others, PD were 35 cases (53 sessions) which included pancreas cancer 20 cases, biliary casncer 7 cases and 8 others, and Billroth-2 were 29 cases (33 sessions) which included gastric cancer 11 cases, duodenal cancer 9 cases and 9 others. Generally we started to treat these patients with enteroscopy-ERCP which were mainly short-type single-balloon enteroscopy (SBE), and EUS-HGS thechnique and PTBD were employed, if failed. In case of large stone, we dilate the papilla by 15–20mm CRE balloon, then directly insert SBE into bile duct and crash the stones by EHL under endoscopic guidance.
Results: The rate of blind reach end and success rate were 88/95 cases (92.6%) and 79/81 cases (97.6%) in the Roux-en-Y(R-Y) with gastrectomy group, 28/29 cases (96.6%) and 28/28 cases (100%) in R-Y without gastrectomy, 34/35 cases (94.3%) and 33/33 cases (100%) in pancreato-duodenectomy, and 27/29 cases (93%) and 24/24 cases (100%) in Billroth-2, respectively. Totally 164/188 cases (87%) were treated by SBE which included 13 cases of EHL treatment by directly inserted SBE and remained 2 cases by EUS-HGS, 5 cases by PTBD, 6 cases by surgery, and conservative 11 cases. The adverse events were 3.1% in pancreatitis, 0.7% in bile leakage, 1.7% in perforation, and 1.1% in bleeding.
Conclusion: We concluded that 87% of bile duct stones were treated by enteroscopy-ERCP in surgically altered anatomy cases, and EUS-HGS was seemed to be new second option.
Disclosure: Nothing to disclose

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P0825 APPLICABILITY OF ASGE CRITERIA FOR ERCP IN CHOLECYSTECTOMIZED PATIENTS

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Introduction: ASGE guidelines suggest that cholangiopancreateography (ERCP) should be performed in patients at high risk of choledocolithiasis after biochemical tests and abdominal ultrasound. In cholecystectomized patients the diagnostic considerations could be different since the cut-off of 6mm for dilatation of the common bile duct (CBD) may be inappropriate.
Aims and Methods: Patients with high-risk criteria for choledocholithiasis (CBD stone on ultrasound, ascending cholangitis, total bilirubin (TB)> 4mg/dL or dilatation of CBP> 6mm associated with TB between 1.8–4mg/dL) who underwent ERCP from 2014–2017 were included. The aim of this study was to evaluate the applicability of ASGE criteria for ERCP in cholecystectomized patients
Results: Included 328 patients – 259 with prior cholecystectomy (79%) and 69 without prior cholecystectomy (21%). The presence of CBD stones and the size of the stone on ultrasound were predictors of coledocolithiasis in ERCP in both groups ($p < 0.05$). Dilatation of CBD was predictive only in the group of patients without previous cholecystectomy ($p = 0.01$ vs $p = 0.199$). Ascending cholangitis and bilirubin levels were not statistically significant predictors in both groups ($p > 0.05$).
The overall positive predictive value (PPV) of ASGE criteria was 71% (29% false positives), and the PPV in the group of cholecystectomized patients was 71% vs 70% in the group of non-cholecystectomized patients.
Conclusion: Although dilatation of CBD is not a predictive factor for choledocholithiasis in cholecystectomized patients, the ASGE criteria have a positive predictive value similar to that of non-cholecystectomized patients.
Disclosure: Nothing to disclose

P0826 EFFICACY OF ETOMIDATE- VERSUS PROPOFOL-BASED SEDATION FOR ADVANCED ENDOSCOPIC PROCEDURE : A PROSPECTIVE, RANDOMIZIED NON-INFERIORITY TRIAL

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Introduction: Propofol is widely used for endoscopic sedation in advanced therapeutic endoscopy, but concerns regarding cardiopulmonary adverse events remain. Etomidate has known to have little effect on the cardiovascular or respiratory systems. We aimed to compare the efficacy and safety of balanced etomidate and balanced propofol sedation in therapeutic endoscopic procedure.
Aims and Methods: This study was a prospective, randomized non-inferiority trial that included patients who had been scheduled for advanced therapeutic endoscopy. All endoscopic sedation was based on midazolam and fentanyl, and then patients randomly received either propofol or etomidate as an add-on drug. The main outcomes were sedation efficacy measured on a 10-point visual analog scale (VAS),and sedation safety.
Results: A total of 186 patients (propofol group: n = 94, etomidate group: n = 92) was evaluated. Etomidate group failed to prove the non-inferiority for overall satisfaction of patients measured by VAS score, with a difference of −0.35 (95% confidence interval [CI] = −1.03 to 0.34, $p = 0.030$). Among endoscopists and nurses, etomidate showed non-inferiority to propofol with differences of 0.06 and 0.08, respectively (endoscopists: 95% CI = −0.55 to 0.66, $p < 0.001$; nurses: 95% CI = −0.57 to 0.73, $p = 0.001$) for a non-inferiority margin of −1. In terms of safety, overall cardiopulmonary adverse events occurred less commonly in etomidate group (27.7% vs. 14.1%, $p = 0.023$). Hypoxia occurred in 5.3% of cases in the propofol group and in 1.1% of cases in the etomidate group ($p = 0.211$). Cardiovascular adverse events tended to be more common in propofol group, but the difference was not statistically significant (23.4% vs. 13.0%, $p = 0.068$). Myoclonus occurred in 12.1% (11/92) of cases in the etomidate group only. Balanced etomidate sedation had a lower risk of overall cardiopulmonary adverse events by multiple logistic regression analysis (odds ratio 0.401, $p = 0.018$).
Conclusion: Etomidate-based sedation during advanced endoscopic procedures was fail to prove the non-inferiority to propofol based sedation in satisfaction of patients. However, etomidate-based sedation showed better safety in terms of cardiopulmonary adverse events and may be an alternative option for advanced endoscopic procedure, especially in patients with cardiopulmonary diseases.
Disclosure: Nothing to disclose

P0827 THE PERIAMPULLARY DIVERTICULUM: BOON OR BANE FOR THE ERCP ENDOSCOPIST?

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Introduction: The prevalence of periampullary diverticulum (PAD) is relatively high (9% to 33%) in patients who undergo an endoscopic retrograde cholangiopancreaticography (ERCP). It is currently unclear if the presence of PAD impacts the success, difficulty and complication rates of ERCP.
Aims and Methods: The aim of the study is to investigate the success rate, procedure difficulty (ERCP grade, cannulation difficulty, procedure time) and complication rate between patients with and without PAD. In addition, we sought to determine whether there is a difference in ERCP indication and size of choledocholithiasis between the groups. Patients with PAD were further analysed according to ampulla location (within PAD, at the edge of PAD, near PAD) and size of PAD (small: < 1.5cm, large: > 1.5cm). A single-centre cross-sectional study was conducted. A total of 548 ERCP procedures were performed at our endoscopy centre from January 2015 to December 2016. Patients with

previous ERCP (sphincterotomy, stent insertion), inability to locate the ampulla or abandoned procedure were excluded. 357 procedures in 351 patients were analysed.
Results: Of the 357 procedures, 116 (32.5%) were found to have PAD. The ampulla was located within the diverticulum in 10 (8.9%), on the edge of the diverticulum in 44 (38.9%) and near the diverticulum in 59 (52.2%). There were 72 (64.3%) large and 40 (35.7%) small PAD. Patients with PAD were older (69 vs. 60 years, $p < 0.001$) and more likely to undergo ERCP for choledocholithiasis (93.9% vs. 83.8%, $p = 0.007$). Comparing the 2 groups (with PAD vs without PAD), there was no statistically significant difference in success rate (93.8% vs. 91.4%), the median procedure time (34mins vs 30.5mins), and complication rate (6.6% vs 3.5%). There was also no statistically significant difference between the 2 groups in terms of cannulation difficulty, categorized in ascending order of difficulty—level 1 (62.7% vs 63.8%), level 2 (23.6% vs 22.4%), level 3 (7.5% vs 4.3%), and level 4 (6.2% vs 9.5%). Similarly, there was no statistically significant difference in terms of ERCP grading, grouped in ascending order of difficulty—grade 1 (78.8% vs 78.5%), grade 2 (17.8% vs 19.8%), and grade 3 (3.3% vs 1.7%). Multivariate logistic regression showed that younger age was an independent predictor of cannulation success ($p = 0.023$), while older age ($p = 0.010$) and indication other than choledocholithiasis ($p = 0.038$) were independent predictors of cannulation difficulty. Patients with PAD had a 3.3 times higher odds of having choledocholithiasis compared to those without ($p = 0.006$).
Conclusion: ERCP in the presence of PAD is as successful, easy and safe as for patients without PAD. Older age and procedure indication other than choledocholithiasis may increase the difficulty of the procedure.
Disclosure: Nothing to disclose

P0828 UTILITY OF SPYGLASS® DS PERORAL CHOLANGIOSCOPY IN INDETERMINATE BILIARY LESIONS

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Introduction: Accurate diagnosis of indeterminate biliary lesions is necessary for proper treatment plan. We aim to assess the diagnostic accuracy of SpyGlass visual assessment and Spybite biopsy in patients with indeterminate biliary lesions.
Aims and Methods: Between August 2016 and August 2017, we review a retrospective analysis of the patients with indeterminate biliary stricture who had an inconclusive results on the cross-sectional imaging or endoscopic retrograde cholangiopancreatography (ERCP) guided tissue sampling.
Results: A forty-eight patients (28 men, mean age 72.3 years) with indeterminate biliary lesions underwent SpyGlass® DS peroral cholangioscopy (SDPC). The SDPC was technically success in all of the case. The final diagnosed in 48 patients were malignant tumor in 17 patients, and benign lesions in 32 patients. The sensitivity, specificity, and overall accuracy of SpygGlass visual assessment and Spybite biopsy for the diagnosis of malignancy were 94.1% (16/17), 93.5% (29/31), 93.7% (45/48), 47% (8/17), 100% (31/31), 83.8% (40/48), respectively. There was no procedure related complication.
Conclusion: The SDPC demonstrated relative accurate rate of diagnosis for indeterminate biliary lesions with excellent safety profile and high technical success rate.
Disclosure: Nothing to disclose

P0829 COMPARISON OF ENDOSCOPIC SPHINCTEROTOMY, ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION AND ENDOSCOPIC SPHINCTEROTOMY PLUS ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION TREATMENT FOR REMOVAL OF LARGE BILE DUCT STONE

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Introduction: Large bile duct stones (> 15 mm in transverse diameter) appear to be more difficult to be remove with conventional methods such as endoscopic sphincterotomy (EST) and endoscopic papillary balloon dilation (EPBD). However, EPBD is limited to small stones of < 10 mm in diameter because it dose not enlarge the bile duct orifice to the same extent as EST. Therefore, extraction of a large bile duct stone may require mechanical lithotripsy (ML) in addition to EST or EPBD. The main complication during ML is basket and stone impaction that could occur even during a routine stone extraction, and it could increase the risk of pancretaitis and cholangitis. We used EST, endoscopic papillary large balloon (12–20 mm) dilation (EPLBD) and limited EST plus EPLBD to remove large bile duct stone in our patients.
Aims and Methods: We aimed to compare and evaluate the therapeutic outcome and complications of EST, EPLBD and limited EST plus EPLBD for large bile duct stone extraction.
Methods: A total of 185 patients with large bile duct stones (> 15 mm in transverse diameter), who received EST, EPLBD and limited EST plus EPLBD treatment between 1, January 2010 and 28, February 2018 at Kaohsiung Chang Gung Memorial Hospital, Taiwan, were recruited in this retrospective study. Patients will be divided into three groups: EST group (31), EPLBD group (96) and limited EST plus EPLBD group (58). The primary outcome variables are the success rate of complete stone removal and presence of complications after three endoscopic treatment.
Results: Limited EST plus EPLBD group resulted in similar outcomes in overall successful stone removal (98.3%) compared to EST group (93.5%) and EPLBD group (92.7%). Limited EST plus EPLBD group had higher success rate of the first session treatment (98.3%) compared to EST group (83.9%) and EPLBD group (86.5%) ($p = 0.032$). ML was required in 4(12.9%) EST group, 10(10.4%) EPLBD group and 2(3.4%) limited EST plus EPLBD group, but they were no significant difference ($p = 0.215$). Post-procedure bleeding occurred in EST group (9.7%) was higher than limited EST plus EPLBD group (0%) ($p = 0.038$). Post-procedure pancreatitis and cholangitis were no significant difference in three groups. No perforation was found in three groups. Procedural time of the first session treatment in limited EST plus EPLBD group was longer (32(12–26) min) than EST group (23.5(17–68) min) and EPLBD group (25.0(14–60) min) ($p = 0.001$). Recurrent bile duct stone occurred in 4 (4.2%) EPLBD group and 5 (8.6%) limited EST plus EPLBD group. Multivariate analysis revealed that dilated bile duct with the largest common hepatic duct (CHD) or common bile duct (CBD) diameter was the only risk factor for bile duct stone recurrence in limited EST plus EPLBD group ($p = 0.022$).
Conclusion: Limited EST plus EPLBD is equally effective as EST and EPLBD for the removal of large bile duct stone. Limited EST plus EPLBD had higher success rate and longer procedural time of the first session treatment. EST group occurred post-procedure bleeding was higher than limited EST plus EPLBD group. Multivariate analysis revealed that dilated bile duct with the largest CHD or CBD diameter was the only risk factor for bile duct stone recurrence in limited EST plus EPLBD group.
Disclosure: Nothing to disclose

P0830 EVALUATION OF THE SAFETY AND EFFICACY OF ENDOSCOPIC SPHINCTEROTOMY FOLLOWING ADDITIONAL BALLOON DILATION FOR THE MANAGEMENT OF COMMON BILE DUCT STONES

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) has high risk of complications such as acute pancreatitis, perforation, acute and delayed bleeding. Endoscopic sphincterotomy (EST) is common technique as a papillary manipulation for endoscopic removal of common bile duct (CBD) stones. However, skill of the operator is necessary to obtain enough incision and EST includes the risks of bleeding and perforation. Endoscopic papillary balloon dilation (EPBD) was simple and easy procedure on the papilla, however, EPBD was reported higher incidence of post-ERCP pancreatitis (PEP) than EST and difficulty in CBD stone removal procedure. To minimize any complications and make procedures easy, we perform EPBD (balloon diameter: 8 or 10mm) with very small incision (EPBD+EST) for the management of CBD stones from 2012. In this study, we evaluated the safety and efficacy of this new technique retrospectively.
Aims and Methods: This study is retrospective chart review analysis in single academic center. In 778 cases with naive papilla who were received endoscopic treatment with papillary manipulation from January 2009 to March 2018. There are 466 cases with common bile duct stones, EST alone was performed until 2012 and EPBD+EST was performed from 2012 through 2018, basically. The cases needed with more than 12 mm papillary dilatation were excluded. We compared the incidence of complications including PEP, acute and delayed bleeding, perforation between two groups.
Results: The EPBD+EST group had 340 cases and the EST alone group had 126 cases. There were no significant differences in the patient characteristics (age, gender, the size and number of the stones). Procedure time was not significantly different between the EPBD+EST group and the EST alone group. The EPBD+EST group had 2.1% (7 cases) of PEP and the EST alone group 2.4% (3 cases), respectively. However, there were no significant difference between them. On the other hand, bleeding rate in the EPBD+EST group was 1.8% (acute: 5 cases, after: 1 case) and significantly lower than 6.3% (acute: 7 cases, after: 1 case) in the EST alone group ($p = 0.01$). Any bleedings were mild by the severity classification of ASGE. For a hemostasis, 5 cases of balloon pressure and one case of clipping were performed in the EPBD+EST group, and 7 cases of balloon pressure and 1 case of HSE injection were performed in the EST alone group. A perforation was not occurred in the EPBD+EST group, but 1.6% (2 cases) in the EST alone group, respectively. The rate of perforation was not significantly different between the 2 groups. In the EPBD+EST group, one case had bile leakage as a major complication. It was considered that bile leakage was caused by the expanding with pinching stones between balloon and bile duct wall at the time of EPBD. There was also no significant difference in the rate of complete stone extraction. Recurrence of the CBD stones were analyzed in the cases observed over 1 year (mean observation al time: 49.4 months), and there was no significant difference.
Conclusion: EPBD with very small EST technique for removing bile duct stones was considered as a safer procedure than EST alone. An incidence of bleeding was significantly lower than EST alone without increasing of PEP. Similar procedure time despite of performing additional balloon dilation may suggest the removing procedure of stones was easier than EST alone. It was single-center

retrospective analysis with relatively small number of cases, further prospective evaluation was required to confirm the usefulness.
Disclosure: Nothing to disclose

P0831 SAFETY AND EFFICACY OF NEEDLE KNIFE PAPILLOTOMY AND NEEDLE KNIFE FISTULOTOMY IN PATIENTS 90 YEARS OF AGE AND OLDER

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Introduction: Needle knife papillotomy (NKP) and needle knife fistulotomy (NKF) are two major rescue techniques for facilitating biliary cannulation and are associated with post-ERCP complications. However, there are limited data, especially in the extreme elderly.
Aims and Methods: The aim of the current study was to evaluate the safety and efficacy of NKP and NKF in nonagenarians. Medical records of 184 patients with difficult biliary cannulation who underwent NKP and NKF from September 2000 and March 2018 were analyzed. Patients were divided into two groups: 90 years age and older (Group A: n = 26) and less than 90 years old (Group B: n = 158). Patient characteristics, indications for ERCP, technical success and complications were retrospectively evaluated. Success was defined as deep placement of a catheter into the common bile duct. A diagnosis and severity of ERCP complications was made according to Cotton's classification.
Results: Mean age was 92.6 ± 2.7 (range 90–101) and 75.5 ± 9.9 (range 41–89) years old in Group A and Group B, respectively. Choledocholithiasis (58.1%) was the most frequent indication followed by malignant biliary obstruction (34.8%). Ten patients (38.4%) in Group A and 70 (44.3%) in Group B underwent prior placement of a pancreatic stent ($p = 0.672$). Periampullary diverticulum was found more often in patients of Group A (23.1%) than of Group B (10.8%, $p = 0.105$). The number of patients with American Society of Anesthesiologists (ASA) physical status class ≥ 3 was significantly larger in Group A than in Group B (53.8% vs 29.1%, $p = 0.023$). Threw was no significant difference in the success rates of cannulation in the first session (61.5% vs 65.8%, $p = 0.839$) and in the final session (96.2% vs 96.8%, $p > 0.999$) between Group A and Group B. Mean time to NKP/NKF and mean procedure durations were not significant between the two groups. Three complications (11.5%) occurred in Group A (pancreatitis in 1, perforation in 1, cholecystitis in 1) and 27 (17.1%) in Group B (pancreatitis in 15, bleeding in 4, perforation in 2, cholecystitis in 6). Complication rates was not significantly different. The use of a pancreatic stent was not related to complication rate. Early mortality rate was significantly higher in Group A than in Group B (19.2% vs 2.5%, $p = 0.003$). No ERCP-related deaths occurred in both groups.
Conclusion: With adequate timing and experience, NKP and NKF can be regarded as safe and effective procedures in extreme elderly.
Disclosure: Nothing to disclose

P0832 INITIAL EXPERIENCES WITH TRANSPANCREATIC PRECUT SPHINCTEROTOMY

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Introduction: In certain cases of ERCP with naive papilla biliary access cannot be obtained with standard cannulation. In these cases, advanced techniques, for example precut papillotomy may help. With transpancreatic precut sphincterotomy (TPS) the precut is performed with the sphincterotome in the biliary direction while a guidewire and the tip of the sphincterotome is inserted in the main pancreatic duct.
Aims and Methods: ERCP related procedural data (cannulation technique, cannulation time, success rate, complications, etc.) are collected prospectively in the Hungarian ERCP Registry at our department since the beginning of 2017. All TPS and needle knife precut (NKP) cases were collected from the databases and the outcomes of these advanced biliary cannulation techniques were compared.
Results: TPS was performed in 15, while NKP in 109 cases. Prophylactic pancreas stent (PPS) was inserted after TPS in 14 cases (93.3%), while in 17 (15.9%) cases after NKP. All TPS, 103 (94.4%) NKF patients received 100 mg indomethacin suppository after the procedure. All pateints received appropriate post-ERCP prevention. The success rate (86.6% vs. 85.3%), the post-ERCP pancreatitis rate (2.2% vs. 4.6%) and the perforation rate (0% vs. 4.6%) were more favourable in the TPS group compared to the NKP group. The rate for significant bleeding was better in the NKP group (13.3% vs 7.4%)
Conclusion: Our data suggest that TPS with PPS insertion can be a safe and useful tool in difficult biliary access, when the guidewire can be inserted deeply in the main pancreatic duct.
Disclosure: Nothing to disclose

P0833 IS ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY MORE RISKY AND COMPLICATED FOR THE ELDERLY? A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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Introduction: Life expectancy is continually increasing, which is coming along with an increasing the demand of endoscopic retrograde cholangiopancreatography (ERCP) in patients with advanced age. Few recent prospective studies have addressed the adverse events on the feasibility and safety of ERCP in elderly patient although technical advances and better operator experience in ERCP. In this study, we compare the differences on success rates and adverse events of ERCP in patients older and younger than age 80.
Aims and Methods: From January 2015 to December 2015, we prospectively enrolled patients with naïve papilla who referred for ERCP at 6 centers of Daegu-Gyeongbuk province. Patient and procedure related variables were recorded on data collection sheet at the time of ERCP. Patients were grouped according to age for patients ≥80 years old (group A) and patients < 80 years old (group B). Demographic data, success rate, outcome, complications, risk factors and mortality were compared between the groups.
Results: There were 1191 ERCPs performed (238 patients older than 80 years, 953 procedures in patients younger than 80 years). The median age was 70 years and male:female ratio was 1.38:1. Mean age was 83.7 years in the group A and 63.1 years in the group B. The cannulation success rate was lower in group A (95.0 vs. 97.1%, $p = 0.107$). There was no significant difference in the overall complication rates between group A and B (18.9 vs. 20.9%, $p = 0.500$) and ERCP-related mortality (0.4% vs 0%, $p = 0.200$, respectively). Post-ERCP pancreatitis was found relatively often in patients of group A (9.2%) than of group B (8.0%, $p = 0.524$). All patients of pancreatitis had full recovery with supportive and medical treatment. There was no significant difference in the other complication rate such as bleeding, perforation, cholangitis and others between two groups.
Conclusion: ERCP in the patients aged 80 years or older is safe and has a high degree of success. However, post-ERCP pancreatitis must be carefully attended in older patients because of relatively high risk. The incidence of other adverse events of ERCP is similar in older patients compared with younger ones.
Disclosure: Nothing to disclose

P0834 EFFICACY OF DOUBLE-BALLOON ENDOSCOPY FOR THERAPEUTIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) and associated procedures are difficult to perform in patients with surgically altered anatomy. Some studies have suggested that ERCP using a double-balloon endoscope (DB-ERCP) is useful for removing gallstones or remaining anastomotic constrictions in such patients. This procedure was first covered by the National Health Insurance of Japan in 2016, and it is expected that the demand for DB-ERCP will now increase. This study considered the efficacy and safety of DB-ERCP in patients with surgically altered anatomy.
Aims and Methods: This retrospective study included 29 patients (49 procedures, male/female: 24/5, average age: 76 [63–90] years) with surgically altered anatomy, who underwent DB-ERCP between July 2015 and February 2018 at Kure Medical Center and Chugoku Cancer Center. Procedures were performed by two endoscopists, one experienced in ERCP, another in DBE. DB-ERCP was performed using EI-530BI or 580BT (FUJIFILM systems). The treatment results, adverse events, and clinical outcomes of DB-ERCP were evaluated.
Results: Endoscopic biliary treatment was attempted with the surgical reconstruction technique for 30 procedures in 15 gastrectomy patients (Roux-en-Y reconstruction: 29 procedures in 14 patients, and gastrojejunal bypass: 1 procedure in 1 patient) and for 19 procedures in 14 choledochojejunal anastomosis patients (pancreatectomy: 14 procedures in 11 patients, and cholecystectomy/ bile duct resection: 5 procedures in 3 patients). The success rate of reaching the major papilla or target anastomosis was 91.8% (45/49), and the mean access time was 27 (5–84) min. The biliary cannulation success rate was 72.4% (21/29) on the first attempt. In 2 of the 8 unsuccessful cases, the percutaneous transhepatic cholangiography-drainage (PTCD) rendezvous technique was used, and biliary

intubation was ultimately successful in 79.6% (39/49). In patients in whom the target area could be reached, the biliary cannulation success rate was 86.7% (39/45). By the reconstruction technique, the success rates were 76.7% (23/30) for post-gastrectomy (Roux-en-Y reconstruction: 23/29 procedures, and gastro-jejunal bypass: 0/1 procedure), 92.9% (13/14) for post-pancreatectomy, and 60% (3/5) for post-cholecystectomy/bile duct resection. The procedures included dilatation in 34 procedures (endoscopic sphincterotomy (EST): 1 procedure, endoscopic papillary balloon dilatation (EPBD): 16 procedures, and anastomosis site dilatation: 13 procedures), drainage in 17 procedures (endoscopic nasobiliary drainage (ENBD)/endoscopic retrograde biliary drainage (ERBD): 15 procedures, and metallic stent placement: 2 procedures), and lithotomy in 24 procedures. The mean total procedure time was 95.3 (39–156) min. Procedural adverse events included guidewire-induced perforation in 1 patient and intra-abdominal deviation of the PTCD catheter in 1 patient; both were relieved with conservative therapy.
Conclusion: DB-ERCP for the intestinal tract with surgically altered anatomy is useful and can be performed with relatively minimal invasiveness. However, no standard procedure has yet been established. In some cases, examination duration is prolonged, and in some patients, biliary cannulation could be difficult even if the major papilla or target anastomosis was achieved. Thus, it is desirable to accumulate more cases to lead to further improvements in these endoscopes and devices.
Disclosure: Nothing to disclose

P0835 A NOVEL TECHNIQUE USING A LOOP-DEVICE FOR REPOSITIONING A NASOBILIARY CATHETER FROM MOUTH TO NOSTRIL IN ERCP

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Introduction: Endoscopic nasobiliary drainage (ENBD) has been widely used for biliary decompression in patients with biliary disease. However, it is difficult to reposition a nasobiliary catheter from mouth to nostril. We developed a new device for repositioning of ENBD catheter (Patent pending). The new device has a curved flexible loop and handle bar. The aim of this study was to evaluate the usefulness of new loop-device for helping the repositioning of an ENBD catheter from mouth to nostril.
Aims and Methods: Between January 2016 and December 2017, a prospective observational study was performed to evaluate the time for repositioning a nasobiliary catheter in ERCP. It was compared the result of ENBD procedure between new loop-device technique and conventional technique. In subgroup analysis, we evaluated the occurrence of oral cavity injury and time to ENBD catheter moving from mouth to nostril.
Results: A total of 206 ENBD procedures were performed using these two techniques. The mean time for repositioning a nasobiliary catheter was shorter in loop device technique than conventional technique (39 sec vs. 361 sec, $p < 0.001$). Total success rate of new device technique was achieved in 98.1%. There was no complication such as oral cavity injury.
Conclusion: This technique using our new loop-device was useful for repositioning a nasobiliary catheter from mouth to nostril in ERCP. Outstanding merit of new device is that it does not require the removal of mouthpiece before ENBD positioning. It can help to perform a rapid ENBD procedure and avoid the finger injury of ERCPist.
Disclosure: Nothing to disclose

P0836 APPROPRIATE THERAPEUTIC STRATEGY FOR INITIAL ENDOSCOPIC DRAINAGE IN OBSTRUCTIVE JAUNDICE

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Introduction: The first endoscopic bile duct drainage method used to treat obstructive jaundice differs according to the pathology and institutional policy. Although endoscopic nasal biliary drainage (ENBD) has advantages such as occlusion prevention by washing at bedside after indwelling, endoscopic bile duct drainage (EBD) with a plastic stent (PS) is often used owing to the complexity of ENBD. We investigated the influence of prior indwelling ENBD in obstructive jaundice on the patency of PS after EBD, endoscopic procedure frequency and hospitalisation period.
Aims and Methods: We enrolled 63 subjects with malignant distal bile ducts requiring drainage due to obstructive jaundice (34 with acute cholangitis) and 40 subjects with cholangitis due to common choledocholithiasis. The subjects were classified into prior ENBD (EBD with prior ENBD) and EBD (EBD without prior ENBD) groups.
Results: The median age was 70 (range, 54–93) and 77 (range, 55–92) years in patients with distal bile duct malignant stenosis and in those with cholangitis due to choledocholithiasis, respectively. The median PS survival was 29 ($n = 24$) and 43 ($n = 39$) days in the prior ENBD and EBD groups among patients with distal bile duct malignant stenosis and 29 ($n = 13$) and 37 ($n = 21$) days in the prior ENBD and EBD groups among those with cholangitis due to choledocholithiasis, respectively; the mean PS survival was not significant in either of the groups ($p = 0.59$). In the prior ENBD group, the serum bilirubin level before treatment was significantly higher than that in the EBD group ($p = 0.04$); however, there was no significant difference in the number of endoscopic procedures and hospitalisation period between the groups. No evidence for severe cholangitis exacerbations was observed in the initial EBD group.
Conclusion: Currently, there are few studies that have compared ENBD and EBD as the initial endoscopic drainage procedures to treat obstructive jaundice. In this study, ENBD did not result in a prolonged follow-up period for PS or increased hospitalisation period and number of endoscopic procedures. However, considering the complexity of the procedure and suffering of the patient, EBD alone should be used even in cases of acute cholangitis.
Disclosure: Nothing to disclose

P0837 IMPACT OF PERIAMPULLARY DIVERTICULUM ON ERCP PERFORMANCE: A MATCHED CASE-CONTROL STUDY

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Introduction: Periampullar diverticulum (PAD) is an outpouching within the ampulla that develops with aging and is usually found incidentally during endoscopic retrograde cholangiography (ERCP). PAD can interfere with biliary drainage and has been associated with the development of bile duct stones, gallstones and acute cholangitis. There is conflicting data on whether the presence of a PAD affects therapeutic success rates during ERCP.
Aims and Methods: We aimed to compare ERCP performance in patients with PAD with age and gender-matched controls using a U.S. national database. We reviewed ERCP recorded between 2000 and 2012 in the Clinical Outcome Research Initiative database.
ERCP cases in adults (≥18 years) with a periampullary diverticulum were included if the endoscopist reported a duodenal diverticulum in the CORI software. Patients were included if they had age, gender and description of major papilla visualization (achieved or not) available. Patients with PAD were compared with age and gender-matched controls, selected randomly using a 1:3 fashion from all other ERCPs, regardless of the procedure indication. Demographic variables, procedure time (from scope insertion to withdrawal), endoscopic and fluoroscopic findings, and therapeutic success (e.g. stone extraction, determined by endoscopist) were compared. ERCP complications and medication use are not consistently recorded in CORI, and were not included in our study design.
Univariate regression was performed and a multivariate regression model was elaborated with variables considered significant ($p < 0.05$). Adjusted odds ratio were reported for each variable.
Results: Initial CORI database review revealed 28,271 ERCPs. PAD was reported in 1,325 (4.7%) cases (8.6% in patients ≥70 years old). We identified 1,089 PAD cases with complete information and selected 3,267 matched controls for comparison. Average age was 68.4 ±14.3 years, and 2,400 (55.1%) were male. 42% patients with PAD had their ERCP as outpatients while 52% controls had ERCP done as outpatients. Anesthesia risk score was similar between both groups.
Biliary stones (choledocolithiasis, cholelithiasis or biliary pancreatitis) were twice more common in patients with PAD. Patients with PAD were less likely to have a cancer diagnosis or required stents (placement, replacement or removal). The presence of PAD was associated with shorter procedure time, but similar fluoroscopy time. After removing procedures where therapeutic success could not be established, there was no difference in ERCP therapeutic success between both groups (94.9% in PAD, 96.0% in controls [$p = 0.2$]). The presence of a PAD did not decrease the visualization rates of the minor papilla (endoscopic view), the common bile duct or pancreatic duct (fluoroscopy).
There was no difference in ERCP therapeutic success between both groups in univariate and multivariate analysis (OR 0.63 [95% CI 0.39–1.00]). Patients with PAD required a sphincterotomy more frequently (OR 1.27 [95% CI 1.02–1.58]). Presence of a PAD increased the chance of a procedure being completed in < 30 minutes (OR 1.70 [95% CI 1.38–2.09]).
Conclusion: No significant difference was seen for ERCP performance in patients with PAD adjusting for hospital setting, procedure duration, use of sphincterotomy and two major indications (bile stone disease or stent-related procedures). Our results support literature showing that PAD should not be considered a barrier to ERCP success. This study also substantiates the hypothesis that PAD interferes with adequate biliary drainage and promotes bile stone formation.
Disclosure: Nothing to disclose

P0838 DEXMEDETOMIDINE IS SAFE AND REDUCES THE ADDITIONAL DOSE OF MIDAZOLAM FOR SEDATION DURING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN VERY ELDERLY PATIENTS

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) often requires deep sedation. Dexmedetomidine, a highly selective α2-adrenoceptor agonist with sedative activity and minimal effects on respiration, has recently been widely used among patients in the intensive care unit. However, its use in endoscopic procedures in very elderly patients is unclear. In this study, we retrospectively investigated the safety and efficacy of dexmedetomidine sedation during ERCP.

Aims and Methods: The study included 62 very elderly patients (aged over 80 years) who underwent ERCP from January 2014, with sedation involving dexmedetomidine (i.v. infusion at 3.0 μg/kg/h over 10 min followed by continuous infusion at 0.4 μg/kg/h) along with midazolam. For comparison, the study included 78 patients who underwent ERCP before January 2014, with midazolam alone. We considered additional administration of midazolam as needed to maintain a sedation level of 4, according to the Ramsay sedation scale. The outcome measures were amount of midazolam, adverse events associated with sedatiohemodynamic.

Results: The study included 62 very elderly patients (aged over 80 years) who underwent ERCP from January 2014, with sedation involving dexmedetomidine (i.v. infusion at 3.0 μg/kg/h over 10 min followed by continuous infusion at 0.4 μg/kg/h) along with midazolam. For comparison, the study included 78 patients who underwent ERCP before January 2014, with midazolam alone. We considered additional administration of midazolam as needed to maintain a sedation level of 4, according to the Ramsay sedation scale. The outcome measures were amount of midazolam, adverse events associated with sedation, and hemodynamics.

Conclusion: Dexmedetomidine can decrease the incidence of respiratory complications and the total dose of other sedative agents. It can be used as an alternative to conventional methods with midazolam for adequate sedation during ERCP in very elderly patients.

Disclosure: Nothing to disclose

P0839 TOTALLY-ENDOSCOPIC ENTERAL ANASTOMOSES: A NEW EFFECTIVE WAY TO CHANGE THE TREATMENT OF POSTSURGICAL LATE COMPLICATIONS OF HEPATICO-JEJUNOSTOMY

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Introduction: Bilio-digestive anastomoses are common in many operations.
The management of biliary diseases in bilio-digestive anastomosis is complex and still represents a challenging topic, especially in case of biliary anastomotic strictures. The critical points about the endotherapy are the availability to reach the anastomotic site and the capability to perform an effective endoscopic retrograde cholagiography (ERC). To improve the results of endotherapy, we propose a new type of endoscopic strategy to reach the biliary anastomosis.

Aims and Methods: To reach the anastomotic site, we perform a totally-endoscopic enteral by-pass between the duodenal or the gastric wall and the biliary jejunal loop both with fluoroscopic and endoscopic ultrasound's guide. We present our 32-case series of consecutive patients treated by endoscopic enteral-enteral anastomosis and subsequent ERC.

Results: Biliary anastomotic reach was obtained in 93.75% of cases and therapeutical ERC's rate was 93.75% (100% if biliary anastomosis was reached). Clinical success rate was 100%. Morbidity and mortality were respectively 6.25% and 0%.
Short-term complications (before 48 hours) occured 3.12% (1 self-limited bleeding).
We did not report any long-term complication (after 48 hours).
Overall recurrence rate was 6% (1 case of biliary lithiasis and 1 case of biliary strictures' recurrence). Mean follow-up lasted 2.5 (3months-5 years).
The main advantages of the new endoscopic method are hereafter resumed. The first one is to let unreachable anastomoses endoscopically-reachable again. The second one is to obtain a stable endoscopic position to use endoscopes with large operative channel. This leads to a longer and increasing dilation of the biliary stenosis, also in case of complex strictures and multiple-ducts biliary anastomosis. The third point is the availability of a stable new pathway to check the results and eventually re-treat the patient, especially in case of complex biliary anastomotic strictures.

Conclusion: This new technique seems to be safe and effective to treat the complications of the bilio-digestive anastomosis, in expert hands.

Disclosure: Nothing to disclose

P0840 NEEDLE-KNIFE FISTULOTOMY VERSUS STANDARD BILIARY SPHINCTEROTOMY FOR CHOLEDOCHOLITHIASIS: RECURRENCE OF COMMON BILE DUCT STONES

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Introduction: In Common Bile Duct (CBD) stones the access to CBD can be achieved through the papilla orifice followed by endoscopic sphincterotomy (ES), or through a precut fistulotomy (PF) in case of difficult cannulation;the two methods alter papilla anatomy differently, therefore intuitively leading to a different rate of stone recurrence. No data on stones recurrence in patients with CBD stones after PF has been published.

Aims and Methods: The aim was to evaluate CBD stone recurrence,re-intervention rate after PF versus ES.
We performed a retrospective single-center cohort study including patients undergoing for the first time ERCP for CBD stones with PF in case of failed repeated cannulation attempts, matched for sex and age to ES patients randomly extracted from our database. T-test and Fisher's tests were used for continuous and categorical variable comparison. Recurrence probability was calculated with Kaplan-Meier curve, and Cox analysis was employed to calculate hazard ratios (HR).

Results: 85 PF patients were included, with 85 matched controls (mean age 68.7 years, 45.9% males). PF patients had the same overall reintervention rate of ES (14.1% vs 12.9%) with a HR of 1.11 (95% CI 0.49–2.50; $p = 0.81$), but mean time to reintervention was significantly lower (74.9 ± 74.6 vs 765.6 ± 961.3 days; $p < 0.0001$). HR of ERCP repetition raised to 2.52 (95% CI 1.02–6.24; $p = 0.03$) if the analysis was therefore limited to the first 1000 days. The only factor associated to ERCP repetition risk was incomplete clearing.

Conclusion: Risk of reintervention was significantly higher in the short-term after PF. Therefore, patients undergoing PF should undergo closer follow-up in the first years after ERCP.

Disclosure: Nothing to disclose

P0841 BILIARY METAL STENTS IN PATIENTS WITH MALIGNANT JAUNDICE AND CBD STRICTURE: A RETROSPECTIVE COHORT STUDY COMPARING UNCOVERED, PARTIALLY COVERED AND FULLY COVERED STENTS

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Introduction: Endoscopic transpapillary biliary drainage is the treatment of choice for obstructive jaundice caused by malignant strictures. Different types of self-expanding metal stents (SEMS) are available: fully covered (FC), partially covered (PC) and uncovered (UC). The advantage of metal compared to plastic prostheses is the reduced risk of rehospitalization and complications expecially in patients expected to survive for more than 3 months. However what is the most effective type of metal prosthesis is still debated.

Aims and Methods: The aim was to evaluate the reintervention rate after positioning of metal stents, comparing FC versus PC versus UC SEMS.
We performed a retrospective single-center cohort study including patients undergoing ERCP with positioning of SEMS for the first time for CBD malignant stenosis. A repeated ERCP was indicated in case of jaundice and/or cholangitis. T-test and Fisher's test was used for comparison of continuous and categorical variables. Reintervention probability was calculated with Kaplan-Meier curve, Cox analysis was employed to calculate hazard ratios (HR).

Results: 321 patients (63 FC, 55 PC, 203 UC) were included in this preliminary analysis, (mean age 69.2 ± 11.8years, 52.6% males); 90.3% had pancreatic cancer, 3.7% cholangiocarcinoma, 6% had ampullary tumors or pancreatic neuroendocrine tumors. 29.3% patients were metastatic, 47% locally advanced, 23.7% were surgically resectable. Overall reintervention rate for FC vs PC vs

UC SEMS was respectively 31.7% vs 12.7% vs 30%. Main reason for ERCP repetition was occlusion due to sludge and ingrowth in UC stents and occlusion due to sludge and displacement in FC. Patients with partially covered SEMS vs fully covered or uncovered SEMS had a HR of 0.49 (95% CI 0.27–0.88 p = 0.058) for repetition of ERCP.
Conclusion: To our knowledge, this is the first study comparing all three different types of SEMS to each other in terms of reintervention rate in patients with malignant jaundice. The 51% reduced risk of reintervention after PC SEMS positioning should encourage controlled studies to verify their higher benefit of this stent compared to FC and UC SEMS.
Disclosure: Nothing to disclose

P0842 CLINICAL OUTCOME OF THE RESECTION MARGIN POSITIVE OR UNCERTAIN CASES AFTER ENDOSCOPIC PAPILLECTOMY FOR AMPULLARY NEOPLASMS

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Introduction: Endoscopic papillectomy (EP) can be the first-line less-invasive treatment in patients with ampullary adenoma without intraductal extension. However, the evaluation of resected margin was often difficult because of the burning effect caused by EP. This study investigated the clinical course of resection margin positive or uncertain cases after EP.
Aims and Methods: Between January 2007 and October 2017, 38 patients who performed EP for ampullary tumor were included in this study. Indication for EP was adenoma as determined by preoperative biopsy, without tumor spread into the bile/pancreatic duct by endoscopic ultrasound (EUS) or intraductal ultrasound (IDUS). EP was carried out with a standard polypectomy snare using the blended electrosurgical current, and we tried to place both bile duct and pancreatic duct stent after EP.A pathologist examined the resected specimen. The clinical outcomes after EP were retrospectively investigated. This study was approved by the institutional review board of Kobe University Graduate School of Medicine.
Results: 23 patients were men, 15 were women. The mean age of the patients was 65 years old. 34 patients (89.5%) were carried out en block resection, and 4 patients (10.5%) were piecemeal resection. Early complications occurred in 32% of all the patients (hemorrhage occurred in seven and pancreatitis occurred in eleven). 28 were diagnosed as adenoma, 10 were diagnosed as adenocarcinoma histopathologically. The resection margin was negative in 21 patients (55.3%), and positive or uncertain in 17 patients (44.7%). The resection margin at the vertical end was positive or uncertain in 13 patients (Group A), and at the horizontal end was positive or uncertain in 4 patients (Group B). In Group A, 1 patient was diagnosed as T2 (Du1) histopathologically, and received additional surgery. 6 patients were adenocarcinoma in adenoma, and 3 were received additional surgery, the other 3 were selected follow-up observation (no recurrence occurred in this investigation). In patients received additional surgery, 2 were not found residual tumor, and 1 was found residual adenoma in resected specimens. Remaining 6 patients in group Awere adenoma, and local recurrence after EP were found in 2 patients. 2 recurrent cases were successfully treated with argon plasma coagulation (APC). In Group B, 1 patient was adenocarcinoma in adenoma, and the patient received additional surgery with no residual tumor in the resected specimen. 3 patients were adenoma with no recurrence. Ampullary tumor-related death was not observed in these cases. The mean follow-up period was 1651 days.
Conclusion: Resection margin positive or uncertain cases after EP could be managed by endoscopic treatment including APC rather than surgical treatment even in the carcinoma in adenoma cases. EP would be an effective less-invasive treatment for ampullary tumors.
Disclosure: Nothing to disclose

P0843 LOW NEGATIVE PRESSURE SUCTION YIELDS BETTER QUALITY SMEARS – PROSPECTIVE COMPARISON OF SLOW-PULL AND STANDARD SUCTION TECHNIQUES OF ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION

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Introduction: Standard suction (SS) technique using a 10mL syringe is the recommended sampling technique of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in the diagnosis of pancreatic cancer, but it often leads to elevated number of smears with increased bloodiness with no improvement in diagnostic accuracy. However, mainly retrospective studies are available about the detailed sampling methods of cancers of other organs, and in these cases, there are no evidence-based recommendations. Aim of our prospective study is to compare the diagnostic yield and quality of cytological and/or histological samples obtained by slow-pull (SP) and SS techniques of EUS-FNA.
Aims and Methods: 378 EUS-FNAs were performed between January 2014 and December 2016 at the University of Szeged, 1st Department of Medicine. Histological and cytological samples were obtained from a total of 462 organs. In the prospective study we assessed the data of EUS-FNA samplings in which 22G needle and both techniques were applied. Patients with cystic lesions and EUS-FNA examinations with undocumented sampling technique were excluded from the study. We separately assessed and compared the efficiency of the two sampling techniques in soft, vascularized (liver, lymph nodes, adrenal gland, etc.) and hard, fibrotic neoplasia (pancreatic cancer, submucosal neoplasia, etc.). The quality of EUS-FNA samples was assessed based on the number of obtained and diagnostic smears, bloodiness, cellularity and diagnostic yield.
Results: 56 soft (39 lymph nodes, 9 primary or metastatic liver, 2 Klatskin, 2 pararectal and 3 mediastinal lesions) and 147 fibrotic (145 pancreatic and 2 abdominal) tumors were enrolled. In cases of hard, fibrotic tumors the diagnostic yield of the sampling (67.35% vs. 68.02%) and the cellularity of smears did not differ significantly between SP and SS groups (1.44 vs. 1.27), however it was substantially higher in case of soft tumors using SP technique of EUS-FNA (60.71% vs. 46.43% and 1.34 vs. 0.77; $p < 0.001$). The SS techniques resulted in significantly higher number of smear pairs both in soft, vascularized (1.74 vs. 3.19; $p < 0.001$) and fibrotic tumors (1.62 vs. 3.28; $p < 0.001$), but at the same time the proportion of diagnostic samples decreased (46.51% vs. 36.52% and 49.17% vs. 30.67%; $p = 0.003$). The SS technique substantially increases the bloodiness of smears independently from tumor (in soft tumors: 1.50 vs. 2.06 and in fibrotic tumors: 1.48 vs. 2.05). Histological samples were obtained in almost the same proportion of soft and fibrotic cancers (76.87% vs. 82.17%), and their diagnostic yield did not differ between subgroups (69.01% and 71.74%).
Conclusion: Independently from tumor consistency, the low negative pressure suction generated by SP technique yields better quality smears. The lower bloodiness and decreased number of slides could make the pathological diagnosis faster and more cost-effective. In case of vascularized tumors, the higher negative pressure suction resulted lower diagnostic yield, therefore we recommend the SP technique as the first method in the EUS-FNA sampling of soft tissues, such as lymph nodes and liver cancers.
Disclosure: Nothing to disclose

P0844 CLINICAL UTILITY AND YIELD OF EUS IN PATIENTS WITH A PRIOR NON-DIAGNOSTIC MRCP; A TERTIARY CARE CENTRE EXPERIENCE

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Introduction: The most effective investigation for suspected gallstones between MRCP and EUS is unclear. A 2015 Cochrane systematic review of their performance in common bile duct (CBD) stones concluded that the tests were of comparable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to better accuracy in detecting small stones. MRCP is routinely favoured as the 2nd line test following a non-diagnostic abdominal ultrasound and EUS subsequently performed as the 3rd line test when suspicion remains after a non-diagnostic MRCP. The yield and clinical utility of EUS in this setting is unclear. The aim was to identify the yield of EUS in patients with prior non-diagnostic MRCP undergoing EUS in our tertiary service.
Aims and Methods: All EUS reports from 2017 were reviewed along with the electronic patient records to identify cases with prior MRCP. Indication for the procedure, symptoms, liver blood tests and interval between MRCP and EUS were recorded. Findings of sludge, microlithiasis (stones < 2mm) and discrete stones were categorised together as stones. Subsequent ERCP or cholecystectomy was identified. Yield was defined as a finding that would lead to a change in management.
Results: A total of 1058 diagnostic EUS were screened of whom 253 (24%) had prior MRCP and formed the study group. Median age was 58 (16–88) years, 179 (71%) were female and 91 (36%) had a cholecystectomy. Median interval between EUS and MRCP was 5.2 (0.1–37) months. Indications for EUS were: n = 76 (30%) dilated CBD, n = 65 (26%) query CBD stones, n = 54 (21%) unexplained acute pancreatitis (AP), n = 23 (9%) right upper quadrant pain, n = 17 (6.7%) abnormal LFTs, n = 16 (6.3%) double duct sign and n = 2 (1%) dilated PD. There was a yield from EUS in 30 (12%) patients with no significant difference between those with (n = 11) or without cholecystectomy (n = 19). Stones were identified in 24 cases with median size of 4 mm (range 2–8) in: CBD (n = 16), cystic duct (n = 1) and GB (n = 7). Three had abnormal CBD without stones (calcification CBD wall, thick walled CBD, polyp), 1 patient with possible stone on MRCP had no stone seen on EUS, 1 had a pancreatic mass, and 1 had chronic pancreatitis. All patients in whom EUS findings indicated an intervention (26/30) have been referred: ERCP in 13, cholecystectomy in 9, ERCP & cholecystectomy in 3 and chemotherapy in 1.
Conclusion: EUS following non-diagnostic MRCP is a sizeable workload accounting for 24% of diagnostic activity in our unit with a clinically significant yield in 12% of predominantly small stones. Further prospective studies are required to ascertain the most cost-effective way to incorporate EUS into the investigation of suspected gallstone disease.
Disclosure: Nothing to disclose

P0845 PREDICTING MALIGNANCY RISK IN GASTROINTESTINAL SUBEPITHELIAL TUMORS WITH CONTRAST-ENHANCED HARMONIC ENDOSCOPIC ULTRASOUND USING A PERFUSION ANALYSIS SOFTWARE

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Introduction: Contrast-enhanced harmonic endoscopic ultrasound (CEH-EUS) is a promising imaging modality that can identify subepithelial tumors (SETs) by detecting the degree of enhancement. However, whether CEH-EUS alone can predict the malignancy risk of gastrointestinal stromal tumors (GISTs) remains unclear. This study aimed to evaluate the feasibility of CEH-EUS using a perfusion analysis software for distinguishing among SETs and for predicting the malignancy risk of GISTs.

Aims and Methods: We retrospectively included patients with subepithelial lesions who underwent preoperative CEH-EUS. In total, 44 patients with histologically proven GISTs and benign SETs were enrolled in the study. Perfusion analysis was performed using a perfusion quantification software. Area under time intensity curve (AUC), peak enhancement (PE), wash-in rate (WiR), and wash-in perfusion index (WiPI) were calculated and compared between GISTs and SETs.

Results: When we allocated the enrolled patients into high- and low-grade malignancy, and benign groups, significant statistical differences of AUC ($p < 0.001$), PE ($p < 0.001$), WiR ($p = 0.009$), and WiPI ($p < 0.001$) were identified in the high-grade malignancy groups compared to benign groups.

Conclusion: CEH-EUS with a perfusion analysis using a perfusion analysis software could be a quantitative and independent method for predicting malignancy risk in gastrointestinal SETs.

Disclosure: Nothing to disclose

P0846 USEFULNESS OF PROCORE 20G NEEDLE FOR DIAGNOSIS OF PANCREATIC SOLID TUMOR

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Introduction: For pathological diagnosis of the pancreatic solid tumor, EUS-FNAB is known as a standard method that is minimally invasive and accurate. Many kinds of needles have been developed to improve diagnostic yield. EchoTip ProCore has the core trap at the side of needle for receiving core sample, the shape of the core trap is forward bevel in ProCore 20G (PC20) and reverse bevel in ProCore 22G (PC22). We compared the usefulness and safety with PC20 and PC22.

Aims and Methods: We conducted a retrospective study of EUS-FNAB with a PC20 or a PC22 for pancreatic solid tumor performed between April 2013 and March 2018 at Kyorin University hospital. The main outcome was to compare the usefulness by histological as well as cytological yield. The secondary outcome was the number of passes to obtain a diagnosis, the necessity of needle change and ratio of complications. First, we collected specimens by suction method, with two passes of puncturing. In cases with a lot of bleeding and cases with the small amount of specimens which was insufficient to exam, and cases when the needle was broken, we added more passes, changed to slow-pull method and other needles. Group 4,5 in histology and Class IV,V in cytology were diagnosed as malignant tumor.

Results: A total of 110 patients were enrolled this study. PC20 was used in 50 patients and PC22 was used in 60 patients. The final diagnosis were pancreatic ductal carcinoma in 94, metastasis pancreatic carcinoma in 3, neuroendocrine tumor in 2, autoimmune pancreatitis in 7, chronic pancreatitis in 3 and solid pseudopapillary neoplasm in 1. Maximum diameter of tumor, location of the pancreatic tumor, puncturing line, mean number of passes, and final diagnosis were not significant difference. Sensitivity, specificity and accuracy combining pathology and cytology were 97.4%, 100% and 97.6% in PC20, and 76.6%, 100% and 79.2% in PC22, there was significant difference at sensitivity and accuracy ($p = 0.006$ and 0.01). Even when comparing the pathological diagnosis of PC20 with the cytological diagnosis of PC22, sensitivity and accuracy were significant difference (sensitivity 97.9% vs 68.6% $p = 0.0001$, accuracy 98.0% vs 73.3% $p = 0.0004$). The histological accuracy was achieved by the 1st, 2nd and after 3rd pass in 90.0%, 96.0% and 98.0% at using PC20, and 45.0%, 58.3% and 65.0% at using PC22 ($p = 0.0001$, 0.0001, 0.0001 respectively). The necessity of needle change was not significantly different between two needles. Mild pancreatitis occurred 1 patient in PC20, and hemorrhage occurred 1 patient in PC22, complication rate was not significant difference.

Conclusion: Our results showed that PC20 is more useful for diagnosis of pancreatic solid tumor with higher sensitivity and accuracy than those of PC22. In addition, it was suggested that the diagnosis could be obtained with fewer punctures on the PC20. As a limitation, we could not evaluate the involvement of needle shape and thickness.

Disclosure: Nothing to disclose

P0847 ENDOMETRIOSIS NODULE THICKNESS ON PRE-OPERATIVE RECTO-SIGMOID ENDOSCOPIC ULTRASONOGRAPHY PREDICTS THE NEED FOR BOWEL RESECTION VERSUS SHAVING TECHNIQUE

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Introduction: Recto-sigmoid endometriosis is an underdiagnosed disease responsible for non-specific digestive symptoms. Two surgical approach, recto-sigmoid bowel resection (segmental or patch) and shaving technique (intra-muscular layer dissection) are available. The aim of this study was to assess if pre-operative recto-sigmoid endoscopic ultrasonography (RS-EUS) findings might predict the need for bowel resection

Aims and Methods: This retrospective study was conducted between January 2012 and March 2018 on patients with recto-sigmoid endometriosis evaluated by RS-EUS who underwent a curative surgical procedure in our tertiary center. Logistic multivariate regression was used after univariate statistical analysis on nodules' RS-EUS features (thickness, width, infiltration of the sub-mucosae, presence of a bump into the digestive lumen and presence of multiple recto-sigmoid localizations).

Results: 73/362 patients with recto-sigmoid endometriosis were evaluated by RS-EUS and underwent a recto-sigmoid surgery. After univariate analysis, thickness, width and infiltration of the submucosae were identified as potential predictive factors for bowel resection. In a multivariate logistic regression model, only thickness appeared to be a significant predictive factor for bowel resection ($OR = 1.49$, IC95% [1.04–2.12], $p = 0.028$. ROC analysis showed that a thickness over 5.20 mm might be used as cut-off value with a sensitivity of 76%, a specificity of 82%, and an $AUC = 0.82$. Cut-off values for 100% sensitivity and 100% specificity were 0.90 mm and 10,00 mm respectively.

Conclusion: Presence of a recto-sigmoid nodule of endometriosis with more than 5.20 mm of thickness on RS-EUS predicts the need for recto-sigmoid bowel resection versus shaving technique. Prospective studies are needed to confirm these results.

Disclosure: Nothing to disclose

P0848 ROLE OF CONTRAST- ENHANCED ENDOSCOPIC ULTRASOUND IN DIFFERENTIATION OF PANCREATIC CYSTS

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Introduction: It is a great challenge to differentiate between the type and the malignant potential of a newly diagnosed pancreatic cyst. Our aim was to assess the role of contrast-enhanced endoscopic ultrasonography (EUS) for increasing diagnostic accuracy.

Aims and Methods: The prospective study included 49 patients with pancreatic cysts. Inclusion criteria were: age over 18, presence of an undetermined pancreatic cyst >10mm (CT, MRI), informed consent. Exclusion criteria were: severe chronic pancreatitis, cyst<10mm, platelet count<50,000/cm3, refuse of the patient to participate. We analyzed the cyst wall, the septae and the solid components of the pancreatic cyst with and without contrast enhancer (CE)(2,4ml SonoVue-Bracco,Italy). The examinations were performed using an Olympus echoendoscope and Aloka ultrasound machine. The final diagnosis was based on fine needle aspiration result, surgery or follow-up.

Results: There were 49 patients (33 females, 16 males) included. Cyst size was between 10–90mm. The pancreatic location of the lesions were the head ($n = 13$), the uncinate process ($n = 6$), the neck ($n = 11$), the body ($n = 11$), and the tail ($n = 8$). The types of cysts were serous cystadenoma ($n = 8$); mucinous cystadenoma ($n = 10$); Intraductal Papillary Mucinous Neoplasm (IPMN) ($n = 26$); pseudocyst ($n = 5$). For the serous cystadenomas, a hyperenhancement of the cyst wall and septae with a slow wash-out and honeycomb aspect was observed in 7 of 8 patients. In case of mucinous cystadenomas hyperenhanced thick walls, septae and fast wash-out was characteristic (8/10). For IPMNs, the hyperenhancement of the cyst wall and fast wash-out was found (24/26). All the pseudocyst presented hypoenhancement or no enhancement of cyst wall (5/5). Trough the enhancement pattern mucinous lesions could be differentiated from nonmucinous lesions.($Se = 88\%$, $Sp = 46\%$; $p = 0.0139$). From 18 pancreatic cysts with solid components in standard EUS, hyperenhanced mural nodules were present in 9 of them and malignancy was confirmed for all this cases (surgery $n = 12$; EUS-FNA $n = 18$).

Conclusion: The enhancing pattern was useful to differentiate malignant nodules from mucus or debris and mucinous from nonmucinous pancreatic cystic lesions.

Disclosure: Nothing to disclose

P0849 ENDOSCOPIC ULTRASOUND GUIDED FINE-NEEDLE ASPIRATION OF RECTAL AND PERIRECTAL LESIONS

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Introduction: Endoscopic ultrasound guided fine-needle aspiration (EUS-FNA) is a well-established diagnostic tool in the upper gastrointestinal tract, but evidence is limited about its use in the rectum.
Aims and Methods: This retrospective analysis of a prospectively collected database aimed to evaluate the indications and diagnostic yield of EUS-FNA of rectal and perirectal lesions. Rectal EUS-FNA examinations performed at the University of Szeged from 2015 were involved.
Results: A total of 15 rectal EUS-FNAs were performed between January 2015 and March 2018 (mean patient age: 53 ± 4 years, 80% female). Indication for rectal FNA were the following: suspicion of endometriosis in 4 cases, lymph node enlargement in 5 cases, tumor recurrence in 5 cases, and undetermined fluid collection in 1 case. Median lesion size was 24.5 mm [6–45 mm]. Technical success was achieved in 14 cases (93%). Smears were obtained with both stylet-capillary technique and vacuum-aspiration in 11 cases, with only the former in 3 cases, and with only the latter in one case. Tissue sampling was possible in 12 cases (3 with stylet, 2 with vacuum, and 7 with both). Sampling was diagnostic in 6 cases (40%): endometriosis was confirmed in 1 case (25%), lymph node metastasis [from malignant melanoma and anal carcinoma] in 2 cases (40%), and tumor recurrence [two rectal and one ovarian] in 3 cases (60%). No adverse events were reported.
Conclusion: EUS-FNA may assist differential diagnosis of rectal and perirectal lesions by providing a safe sampling method of lesions that are often inaccessible for other modalities. It can be especially useful in confirming recurrence of malignancy and might also have additional value in the diagnosis of lymph node metastases and endometriosis that may occur as submucosal lesion endosonographically.
Disclosure: Nothing to disclose

P0850 ENDOSCOPIC ULTRASOUND-GUIDED BIOPSY OF SUBEPITHELIAL GASTROINTESTINAL LESIONS – JUST WET-IT

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Introduction: Endoscopic ultrasound-guided fine-needle aspiration biopsy (EUSFNAB) is the main method for acquisition of tissue from gastrointestinal subepithelial lesions (SELs). Despite the development of new needles, diagnostic yield remains low. The reason may be an ineffective transmission of negative pressure with the dry technique, as these lesions often have high cellular cohesion. A new method of aspiration has been described, where the needle is filled with saline (wet suction technique, WST), with promising results in pancreatic lesions. This method hasn't been tested in SELs.
Aims and Methods: Prospective single-centre study to assess the diagnostic yield of EUSFNAB+WST in the diagnosis of SELs, without the use of rapid on-site evaluation. In mesenchymal tumours, the diagnosis was considered positive only when immunohistochemistry (IHC) could differentiate between gastrointestinal stromal tumour (GIST) and leiomyoma. The diagnostic yield of this prospective cohort between July 2015 and December 2017 was compared with a retrospective cohort using dry technique from the same institution.
Results: Seventy-one patients with SELs were included (49% male, mean age 66 years). Mean SEL size was 32 mm (min 10, max 120 mm), mean number of passages was 3 (±0.7). A 22G needle was used in 58 patients (82%), 19 G in 8 (12%) and 25 G in 5 (7%). We obtained a conclusive cytopathological diagnosis in 60 cases (diagnostic yield of 85%) and IHC was performed in 58 cases (82%). The most frequent diagnoses were GIST (37%), leiomyoma (14%) and metastases (13%). When compared with a retrospective cohort of 56 cases, diagnostic yield was significantly higher (85% versus 25%, $p < 0.0001$).
Conclusion: Wet suction technique allowed an excellent diagnostic yield in the EUS-guided evaluation of SELs. We suggest that, after proper replication of these results, WST may become the first-line method in the management of these lesions.
Disclosure: Nothing to disclose

P0851 EXAMINATION OF THE USEFULNESS OF ENDOSCOPIC ULTRASONOGRAPHY IN EARLY-STAGE STOMACH CANCERS

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Introduction: With the increasingly widespread use of endoscopic submucosal dissection (ESD) for early-stage stomach cancers, pre-surgical depth diagnosis for determining suitable treatment needs to be increasingly accurate. In normal endoscopic diagnosis, even if a diagnosis of intramucosal carcinoma is made, some lesions actually infiltrate the submucosa. Although there are various theories regarding the usefulness of endoscopic ultrasonography (EUS) in depth diagnosis, no fixed opinion has been arrived at. Therefore, the purpose of this study was to clarify the significance of performing EUS when diagnosing the depth of early-stage stomach cancers.
Aims and Methods: Of the cases that underwent ESD at our hospital between November 1, 2012 and October 31, 2017, subjects comprised 454 lesions in 393 cases for which detailed review of medical records was possible. Subjects were divided depending on whether they underwent preoperative EUS into an EUS group and a non-EUS group. We then retrospectively investigated accuracy rates for depth diagnosis (depths M-SM1 and SM2 or deeper) in each group. Results were then compared with accuracy rates for the tumor site (U/M/L regions), histopathological differentiation (differential type/poor differentiation and undifferentiated type), the presence or absence of ulcerous complications, and differences in the degree of experience of the surgeon.
Results: Overall, the accuracy rate of depth diagnosis in pre-operative endoscopies was 90.7%, and between the EUS and non-EUS groups, accuracy was found to be low in the EUS group (79.6% vs. 94.4%; $p < 0.001$). In the EUS group, no differences were observed in diagnostic accuracy regarding different tumor sites (U/M/L 75.7% vs.90.0% vs.77.8%; $p = 0.56$) or different histopathologies (differential type/poor differentiation and undifferentiated type 79.2% vs. 85.7%; $p = 0.56$). In the EUS group, the accuracy rate was significantly lower in cases with ulcerous complications than those without (ulcer presence/absence 72.2% vs. 90.5%; $p = 0.03$). In terms of surgeon experience, no differences were identified in accuracy rates between trainee and expert surgeons in either the EUS or non-EUS group (76.4% vs. 82.8%; $p = 0.40$) (91.3% vs. 92.3%; $p = 0.68$). Further, no difference was identified in the accuracy rates between trainee and expert surgeons in EUS group depending on whether the lesion was endoscopically-treated (depth M-SM1) (85.4% vs. 92.0%; $p = 0.24$) or non-eligible (SM2 or deeper) (14.3% vs. 25.0%; $p = 0.55$).
Conclusion: In cases that were eligible for ESD, the significance of preoperative EUS was unclear. In cases of ulcerous complications in particular, EUS accurate rates were low, with difficulty discriminating between ulcer echo signals and invasive foci cited as the cause. In cases of ulcerous complications, it appears more important to diagnose depth using regular light imaging.
Disclosure: Nothing to disclose

P0852 UTILITY OF LIVER AND SPLEEN EUS-ELASTOGRAPHY AS A DIAGNOSTIC TOOL FOR PREDICTING LIVER CIRRHOSIS AND PORTAL HYPERTENSION: A PROSPECTIVE CASE-CONTROL STUDY

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Introduction: Liver Cirrhosis (LC) includes hepatic and splenic structural and functional changes, with subsequent Portal Hypertension (HP). Abdominal ultrasound, upper endoscopy and Transient Elastography (T-E) constitute LC and PH standard diagnostic workup, delaying it and increasing health care cost. EUS-Elastography (EUS-E) offers all of these workups in a single step. EUS-E has not been evaluated for this purpose, especially in the spleen.
Aims and Methods: We aimed to evaluate the utility of Liver and Spleen Stiffness Measurement (LSM, SSM) by EUS-E to predict LC+PH. Prospective case-control study. Case group: patients with LC based on clinical, imaging and T-E (FibroScan®; EchoSens, Paris, France) findings. Control group: patients with no liver, biliary tract or spleen disease history, who after normal T-E, they underwent to EUS-E due to subepithelial lesions workup. Liver and Spleen EUS-E were performed in each group by 2 gastroenterologists with expertise in EUS-E, using 3.8 mm working channel linear-array echoendoscope (EG 3870UTK, Pentax Germany) with Hitachi AVIUS Ultrasound Console. LSM and SSM Strain Ratio (SR) and Strain Histogram (SH) were measured 10 times per patient. Azigos vein (AzV) diameter (D), mean velocity (MV) and Blood Flow Volume Index (BFVI) were also measured once. The association between LSM and T-E was verified by Spearman's rank correlation coefficient (rho). Then, LSM, SSM and Azygos vein (AzV) feature cut-off values to assess LC+PH were determined through ROC curve [if Area Under the Curve (AUC) ≥80%] to define overall accuracy (a sub-analyses were built for each LC etiology). A p-value < 0.01 was considered statistically significant. Analyses were performed using R v3.4.2.
Results: 61 patients were included: median age 60 (18–82) years, 36/61 (59%) female. 32/61 (52%) had LC (20/32 NASH, 10/32 Alcohol, 2/32 HBV-HCV). Table 1A shows T-E and EUS-E results between both groups. LSM-SR presented a direct association with T-E (rho = 54%, $p < 0.01$), while LSM-SH presented an indirect one (−47%, $p < 0.01$). Only LSM-SR, LSM-SH, SSM-SR, and SSM-SH, reached AUC ≥80%: 82%, 81%, 81% and 80%; with cut-off values of 5.2, 88.8, 7.5 and 39.9, respectively. They showed no difference between LC+PH etiology through sub-analysis, but AzV-D and AzV-BFVI presented higher AUC for LC+PH by alcohol: 96% and 93%; with cut-off values of 9.1 mm and 56.7 mm/s3. Corresponding overall accuracy is showed in table 1B.
Conclusion: Liver and Spleen EUS-E constitute useful diagnostic tools for predicting LC+PH, and could in a single step replace the standard workup for diagnosis of LC+PH. AzV hemodynamic features let to predict better LC+PH or related to alcoholic etiology, especially with high specificity and PPV.
Disclosure: Nothing to disclose

Abstract No: P0852

	A. T-E and EUS-E results between study groups [median (minimum – maximum range)]			*B. EUS-E overall accuracy*			
	Case group (LC+PH) (n = 32)	Control group (n = 29)	p-value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
T-E Fibrosis [Elastography (kPa)]	21.30 (9.00–75.00)	4.48 (1.90–7.50)	< 0.001	–	–	–	–
T-E Fibrosis variability (IQR/E)	0.14 (0.00–0.32)	0.12 (0.04–0.32)	0.528	–	–	–	–
LSM-Strain Ratio (SR)	7.53 (3.10–16.20)	3.97 (2.01–8.85)	< 0.001	84.3 (67.2–94.7)	82.8 (64.2- 94.2)	84.4 (70.6–92.4)	82.8 (67.8–91.6)
LSM-Strain Histogram (SH)	67.38 (30.30–121.10)	101.70 (53.75–156.10)	< 0.001	87.5 (71.0–96.5)	69.0 (49.2–84.7)	75.7 (64.0–84.5)	83.3 (65.9–92.8)
SSM-Strain Ratio (SR)	12.10 (4.92–50.64)	6.50 (2.34–18.40)	< 0.001	87.5 (71.0–96.5)	69.0 (49.2–84.7)	75.7 (64.0–84.5)	83.3 (65.9–92.8)
SSM-Strain Histogram (SH)	39.63 (14.40–91.50)	65.45 (28.45–111.60)	< 0.001	56.3 (37.7–73.5)	89.7 (72.7–97.8)	85.7 (66.3–94.8)	65.0 (55.2–73.7)
Azigos vein (AzV) diameter (mm)	8.30 (2.62–20.70)	5.10 (3.10–9.80)	0.002	43.3 (25.5–62.6)	96.3 (81.0–99.9)	92.9 (64.5–98.9)	60.5 (52.6–67.8)
Azigos vein (AzV) Blood Flow Volume Index (BFVI) (cm3/s)	51.31 (3.93–220.05)	21.03 (0.70–95.16)	0.005	46.4 (27.5–66.1)	88.5 (69.9–97.6)	81.3 (58.2–93.1)	60.5 (51.4–69.0)

[Table 1. Transient Elastography (T-E) and Endoscopic ultrasound Elastography (EUS-E) results between study groups; and EUS-E overall accuracy.]

P0853 HIERARCHICAL ANALYSIS OF FACTORS ASSOCIATED WITH T STAGING OF GASTRIC CANCER BY ENDOSCOPIC ULTRASOUND: DECISION TREE METHOD

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Introduction: Precise prediction of the depth of tumor invasion (T stage) in gastric cancer is important for the decision of treatment modality and endoscopic ultrasonography (EUS) is known to be the most reliable method for it. However, sometimes it can lead to overtreatment when EUS overestimate T stage or undertreatment when underestimates. Therefore, we examined what factors affect the T stage prediction of EUS.

Aims and Methods: We retrospectively analyzed gastric cancer patients who underwent EUS from September 2005 to February 2016. EUS T stage and pathologic T stage were classified as T1a, T1b, T2 or more and the accuracy of EUS T stage and factors affected over/underestimation were examined by using decision tree analysis-CHAID method.

Results: A total of 4818 patients were finally included in the study. The most significant factor affecting the accuracy of the EUS T stage was size. The rate of overestimation was higher in lesions > 3 cm. (37.2% vs 29.8% vs. 17.1%, $p < 0.001$) In the lesions > 3 cm, the rate of overestimation was higher in lesions with ulcer, compared to that without ulcer. (62.1% vs 35.0%, $p < 0.001$) Meanwhile, for the lesions ≤ 3 cm, the accuracy of the EUS T stage was more affected by differentiation, and followed by location than presentation of ulcer. The rate of overestimation was higher in undifferentiated type. (24.5% vs 13.9%, $p < 0.001$, 33.3% vs 25.7%, $p = 0.011$) In the differentiated type, the location affected the accuracy of the EUS T stage and the rate of underestimation was higher in the upper third (24.5% vs 11.5%, $p = 0.001$, 16.2% vs 9.0%, $p = 0.002$) (Figure 1).

Conclusion: In this hierarchical analysis, the most significant factor affecting the accuracy of EUS T stage was tumor size (3cm). For the lesion larger than 3cm, presentation of ulcer was related with overestimation. However, for the lesion smaller than or equal to 3 cm, differentiation and tumor location were important.

Disclosure: Nothing to disclose

P0854 RANDOMIZED TRIAL COMPARING FNA AND FINE-NEEDLE BIOPSY FOR EUS-GUIDED SAMPLING OF SOLID TUMORS

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Introduction: The definitive diagnosis of solid tumors relies on immunohistochemical staining, which depends on enough tissue being submitted to the pathologist. Achieving adequate tissue acquisition from tumors by EUS-FNA remains a limitation. Advancements in needle design, however, have improved tissue acquisition and therefore may improve the definitive diagnosis by EUS-FNA. Endoscopic ultrasound (EUS)-guided fine needles with side fenestrations are used to collected aspirates for cytology analysis and biopsy samples for histologic analysis. We conducted a large, multicenter study to compare the accuracy of diagnosis via specimens collected with fine-needle biopsy (FNB) Vs. fine needle aspiration (FNA) for patients with solid tumors

Aims and Methods: We performed a prospective single-blind study at 5 tertiary care centers in China. The study comprised 408 patients undergoing EUS for a solid mass (larger than 1 cm) in the pancreas, abdomen, mediastinum, or pelvic cavity, from December 2014 through January 2016. Patients were randomly assigned to groups (1:1) for assessment by FNA (n = 190) or FNB (n = 187). After lesions were identified by EUS; samples were collected in a total of 4 passes by each needle. All procedures were performed by experienced endosonographers; cytologists and pathologists were blinded to the sample collection method. Patients were followed for at least 48 weeks, and final diagnoses were obtained after surgery, imaging analysis, or resolution of lesion. The primary objective was to compare EUS-FNA versus EUS-FNB for the cytological for histological diagnostic accuracy of malignancy using 22G EUS-FNA and the 22G EUS-FNB needles. The secondary outcome measures were rates of analysis yield (%) of malignancy on the first pass, technical failure, complications, and quality of histologic specimens.

Results: Accuracy of FNB analysis in malignancy is higher than all FNA cases (94.09% vs 91.53%,) based on final patient diagnoses. Especially the findings from histologic analysis of FNBs were accurate for 93.55% of the cases, compared to 81.75% for FNAs ($p = 0.001$). In cytology analysis of with malignant masses, samples collected by FNB accurately identified 89.78%, whereas samples collected by FNA accurately identified 85.71% ($p = 0.046$). Patients in whom diagnosis was established in first passes were 87.50% versus 79.17%, for FNA and FNB in the study. There was no significant difference in technical failure or complications between FNA and FNB needles.

Conclusion: In the prospective study of patients with solid tumors, we found EUS guided FNB samples to produce more accurate diagnoses than samples collected by EUS-guided FNA samples.

References: Clinical Trials.gov no.: NCT02327065

Disclosure: Nothing to disclose

P0855 NOVEL EUS-GUIDED IRREVERSIBLE ELECTROPORATION ABLATION OF PANCREAS: AN EXPERIMENTAL STUDY

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Introduction: Endoscopic IRE can be performed using a flexible, thin, needle-shaped electrode for an endoscopic ultrasound (EUS)-guided procedure. This study aimed to evaluate the feasibility and efficacy of performing EUS-guided IRE with endoscopic needle-electrode in porcine pancreas.

Aims and Methods: A 19-gauge (1.1 mm) endoscopic IRE electrode consisting of a flexible electrode covered with protective sheath, needle-shaped tip with two exposed electrode band, generator connectors, and electrode push handle. Experimental endoscopic IRE on the pancreas were performed by EUS-guided approach and compared with surgical approach. The animals were sacrificed after 24 h and their pancreases collected.

Results: IRE ablation using endoscopic needle-electrode was successful technically in EUS-guided approaches for the pancreas. Immediately following IRE, the ablated pancreatic tissue showed no gross change except focal hemorrhage. H&E staining presented a well-demarcated ablation site measuring 1.0–1.5 cm in diameter in the pancreas. TUNEL immunohistochemistry showed diffuse cell death along the puncture site 24 h after IRE. No complication was observed in pigs after endoscopic IRE ablation.

Conclusion: EUS-guided IRE ablation was feasible and effective for pancreas using the newly developed device.

Disclosure: Nothing to disclose

P0856 THE VALIDATION OF STRING SIGN IN THE DIFFERENTIAL DIAGNOSIS OF PANCREATIC CYSTS

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Introduction: Pancreatic cystic lesions (PCL) are common. Mucinous PCL are considered to have malignant potential, albeit in a minority. Differentiating mucinous lesions from non-mucinous ones is, sometimes, challanging. We investigated the efficay of string sign (SS), a very simple test, in this respect.

Aims and Methods: We performed a retrospective analysis reviewing the electronic medical records of the patients between October 2011 and March 2018

identifying the patients with PCL in whom string sign test was performed. This test is done by stretching fluid between fingertips or glass slide and fingertip. In case the stretch is equal or more than 3 mm, we consider it positive. A few drops of fluid is suffice. CEA and amylase measurement was done in case enough fluid was obtained. Cytologic examination was also done in most of the patients. Differential diagnosis of PCL was done by surgery or cytological diagnosis. Immunohistochemical staining for MUC subtypes was performed in 10 cases, five from SS positives, five from SS negatives.
Results: A total of 587 patients with PCL were evaluated by EUS and samples were obtained by fine needle aspiration. Final diagnosis was available in 185 cases: 97 pseudocysts, 38 IPMNs, 10 MCNs, 15 IPMN related adenocarcinoma, 12 adenocarcinoma, 3 ductal adenocarcinoma, 4 Serous cystic neoplasia (SCN), 4 neuroendocrine tumor (NET) and 2 Von Hippel Lindau related cystic lesions. SS testing was done in 172 patients. Fifty-six had histologically confirmed final diagnosis: 38 were mucinous (21 IPMNs, 7 MCNs, 10 IPMN related adenocarcinoma), while 18 were nonmucinous (7 pseudocysts, 3 NETs, 2 SCNs, 6 simple cysts). SS was tested in 22 IPMNs and 7 MCNs, while CEA could be measured in 11 IPMNs and 4 MCNs. There was only one patient with negative SS and high CEA value (818,3 ng/mL). Table 1 represents the diagnostic validation of SS and CEA > 192 ng/mL in mucinous PCL.

	Sensitivity	Specificity	PPV	NPV	Accuracy
String Sign	0.78	0.89	0.93	0.68	0.82
CEA >192 ng/mL	0.73	0.80	0.82	0.70	0.76

[Table 1]

In SS positives, MUC 2 staining was positive in 3/5, while in SS negative group no MUC 2 staining observed. MUC4 staining was positive in remaining two from the former and none from the latter group.
Conclusion: String sign is a highly reliable test in the differential diagnosis of PCL in reference to mucinous etiology. It is not inferior to CEA measurement. Furthermore it may be done in cases in whom enough aspirate fluid is not available for CEA measurement. SS positivity seems to be related to the presence of MUC 2.
Disclosure: Nothing to disclose

P0857 ENDOSCOPIC ULTRASOUND CORE TISSUE ACQUISITION: A SIGLE CENTER PROSPECTIVE STUDY

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Introduction: When on-site cytology is unavailable, European guidelines recommends performing two/three needle passes with a fine-needle biopsy (FNB), although the level of evidence is low.
Core tissue acquisition theoretically improves the diagnostic yield and it is optimal for tissue sampling for immunostaining and histologic diagnosis therefore it could potentially eliminate the use of ROSE.
Recently, a new Franseen geometry needle has been developed to obtain a histologic sample for immunohistochemical staining, and histologic diagnosis.
Although few studies are present in literature, previous observations proved that Franseen biopsy needle yielded high-quality histology samples thus high diagnostic yield.
Aims and Methods: Primary aim is to evaluate the diagnostic accuracy of Franseen geometry FNB in pancreatic (PL) and non-pancreatic lesions (NPL). Secondary aim is to assess the rate of core tissue (preserved architecture specimen) obtained.
A single-center prospective cohort of patients who underwent EUS-FNB for solid lesions >10 mm were enrolled (from June 2017 to January 2018) using 22 and 25 Gauge (G) Franseen needles (Acquire, Boston Scientific needles).
For each needle pass, a different vial was use and numbered. At least three passes were required for cell-block evaluation.
The presence of core tissue was define as a sufficient material for adequate histologic interpretation.
Results: A total of 70 patients (mean age 69 years; range 87–40) were enrolled (33 female). Out of the 58 PL, the most common final diagnosis was pancreatic cancer in 50.
A median of 3.6 needle passes were performed (range 2–5), 22 G needle was used for 48 lesions.
The diagnostic accuracy was 74.2% on the first pass (79.3% in PL vs 50% in NPL), 85.7% (93.1% vs 5.8%) at the second pass and reached 90% at 3rd needle pass (94% PL).
A tissue core biopsy was obtained in 56 lesions (79%) on the first pass and 85.7% after two passes (86.2% and 88.3% in PL respectively). Overall diagnostic accuracy was 92% (95.7% of PL) and a core tissue was achieved in 87.4%.
Conclusion: According to recent guidelines, 90% of diagnostic accuracy was obtained after three FNB passes. This accuracy seems to be even higher in the setting of PL (93% after two passes).
Franseen geometry needles achieved a core tissue in 87% of lesions.
Disclosure: Nothing to disclose

P0858 SURVEILLANCE OF ALLOGRAFT REJECTION AFTER INTESTINAL TRANSPLANTATION USING MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING

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Introduction: Acute cellular rejection (ACR), which is associated with graft failure, is one of the most important vexing problems after intestinal transplantation (IT). Whether endoscopic imaging could be used to predict ACR is not well understood.
Aims and Methods: We aimed to investigate the correlation of an endoscopic scoring system using a magnifying endoscopy under narrow-band imaging (ME-NBI) system with ACR after IT.
Methods: Patients older than 7-years-old after IT were enrolled prospectively between June 2016 to March 2018. Endoscopic examinations were performed through chimney ileostomy to anastomosis site with ME-NBI. The observed endoscopic findings were recorded by five components (''V-E-N-C-H''), each was graded in order of increasing severity from 0 to 2: ''V'' (appearance of villi), ''E'' (erythema in crypt area), ''N'' (capillary network), ''C'' (widening of crypt area), and ''H'' (heterogeneity of mucosal change). The severity of histological rejection was graded as indeterminate, mild, moderate to severe. Biopsy samples were taken from endoscopically suspicious rejection areas for histopathological examination. The correlation between VENCH scoring and histological severity of ACR was analyzed.
Results: During study period, ninety endoscopic biopsies in three (two females, one male) eligible patients were enrolled. The mean ± SD age of study subjects were 39.3 ± 16.2 (range 29~58) year-old and the etiology for IT was all short bowel syndrome after intestinal resection (two ischemic bowel disease, and one chronic intestinal pseudo-obstruction). The operation, cold ischemia, and ward ischemic times were 12 ± 6 (hours), 242 ± 47 (minutes) and 25.7 ± 5.9 (minutes), respectively. The sensitivity, specificity and accuracy of V-E-N-C-H score to predict ACR were 0.97, 0.47, 0.68, and 0.95, 0.71, 0.71, and 0.97, 0.49, 0.69, and 1.00, 0.52, 0.72, and 0.97, 0.67, 0.80, respectively. Coefficient value of Pearson's correlation test for V-E-N-C-H to predict ACR were 0.79, 0.66, 0.75, 0.71, 0.74 and 0.73, respectively ($p < 0.001$).
Conclusion: Early identification of ACR, which is associated with graft failure and patient survival, by intensive endoscopic surveillance of graft is very important. The ME-NBI endoscopic 'VENCH' scoring system is a promising tool for ACR prediction and larger scale studies are warranted to validate these results.
Disclosure: Nothing to disclose

P0859 THE NEW INSERTION METHOD OF THE TRANS-NASAL ILEUS TUBE, THE ANTERIOR BALLOON METHOD, WAS APPLICABLE FOR THE SMALL BOWEL OBSTRUCTION: A RETROSPECTIVE CHART REVIEW OF THE 126 PATIENTS

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Introduction: The gastrointestinal decompression is the initial and effective therapeutic approach for the patients with small bowel obstruction. Several recent studies showed that decompression using the long trans-nasal tube achieved favorable clinical outcomes. Our previous pilot trail method using the newly developed trans-nasal ileus tube, the anterior balloon method, achieved effective decompression to the small bowel obstruction.
Aims and Methods: The present study was investigated the effectiveness of the anterior balloon method for small bowel obstruction compared the ordinary insertion method.
The anterior balloon method used the ileus tube (CLINY double-balloon type; Create Medic Co., Ltd, Tokyo, Japan) of 300 cm length with two (anterior and posterior) balloons. After insertion of the tube into the duodenum, the anterior balloon was injected and suctioned repeatedly with 10 mL of air using the 10 mL syringe until the ileus tube reached closely to the obstruction. A total of 126 patients with small bowel obstruction treated from January 2011 to October 2017 in Ureshino Medical center were retrospectively reviewed. The patients were divided into two groups: the patients treated by the anterior balloon method (44 patients: ABM group) and the patients treated by the ordinary insertion method (82 patients: OIM group). The patients' characteristics including the causes of ileus, the treatment outcome, and the adverse events were compared between the two groups.
Results: The patients' characteristics and symptoms on admission including fever, abdominal pain, abdominal distension, vomiting and defecation were not different between the ABM and OIM groups, and the adhesive small bowel obstruction was the main cause of ileus in the both groups. The insertion time was significantly shorter in the ABM group compared to the OIM group (28.0 ± 8.3 min vs.33.5 ± 13.0 min; $p = 0.005$), whereas the length of the inserted ileus tube was significantly longer in the ABM group (220.7 ± 33.3 cm vs. 157.4 ± 31.7 cm; $p < 0.001$). The mean period of the insertion tube was relatively short in the ABM group than the OIM group (4.1 ± 3.8 days vs.

5.9 ± 5.3 days: (p = 0.034) and the meal could be re-started shorter in the ABN group (4.1 ± 3.8 vs. 6.0 ± 5.2 days; p = 0.027), indicating that the relief of the clinical symptoms was achieved faster in the ABM group. The surgery intervention in the patients with the ileus tube insertion was equivalent in the both groups (20.4% in the ABN group vs. 22.0% in the OIM group). The serious adverse events were not complicated in the both group.

Conclusion: The ABM of the ileus tube insertion achieved the insertion of the long enough ileus tube with the short insertion time compared to the OIM, leading to the better clinical outcomes. The anterior balloon method is one of initial therapeutic selections for the patients with small bowel obstruction, and the present results with the retrospective study might be confirmed by the randomized clinical trials.

Disclosure: Nothing to disclose

Reference

1. Yamaguchi D, Morisaki T, Tsunada S. Effective insertion method of transnasal ileus tube for adhesive small bowel obstruction. *Dig Endosc* 2018;30:120–121.

P0860 HYPERAMYLASAEMIA POST ANTEGRADE DOUBLE BALLOON ENTEROSCOPY – DOES INDOMETHACIN MAKE A DIFFERENCE?

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Introduction: High amylase does not always signify acute pancreatitis and it can occur due to focal areas of ischaemia in the pancreas due to mechanical stress during double balloon enteroscopy (DBE). The use of rectal NSAIDs to prevent post DBE pancreatitis has never been explored unlike in ERCP where patients receiving rectal NSAIDs have a lower incidence of pancreatitis.

Aims and Methods: Patients who received rectal indomethacin (100mg) 30 minutes prior to antegrade DBE were compared to a control group who did not receive indomethacin before the above protocol was implemented. Serum amylase and CRP 3 hours before and after DBE were compared.

Results: 240 patients (56 indomethacin, 184 controls; 50% males; mean age 58.5 ± SD14.0) were included.

Indications included: IDA (37.5%), obscure overt gastrointestinal bleeding (17.1%), suspected Crohn's disease and strictures (17.9%), complication of coeliac disease (1.3%), small bowel (SB) tumours / polyps (17.9%), others (8.3%). Patients had a median of 13.0 ± SD13.0 passes, 65.0 ± SD25.0minutes, 170 ± SD52.0cm of SB examined. 36.3% underwent a therapeutic procedure during DBE: APC/adrenaline/clips (27.5%), foreign body removal (0.4%), polypectomy (8.3%).

Only 4 (1.67%; 2 females) patients developed pancreatitis, all prior to implementation of indomethacin into the local protocol. They had a median age of 47.0 ± SD3.20 years, 11 ± SD29.4 passes, 90 ± SD52.0minutes, 150cm ± SD64.2cm of SB examined and median hospital stay of 14 ± SD3.70 days. 3 had polypectomies. 2 episodes occurred in the same patient. All had evidence of pancreatitis on CT scan. None of the patients received indomethacin before DBE.

Mean amylase (51.6 ± SD22.7 vs 143.0 ± SD143.9IU/L p = 0.0001) and CRP (13.0 ± SD46.1 vs 17.3 ± SD81.7mg/L p = 0.0001) after the procedure were significantly higher than before the procedure. Females had a significantly higher amylase than males post procedure (155.2 vs 130.7 IU/L p = 0.017). Mean amylase 3 hours after DBE was significantly lower in patients who received indomethacin (114 vs 152) (p = 0.044). 83.9% had a rise in amylase in the indomethacin group compared to 92.2% controls. (p = 0.064).

Whilst there was no correlation between post-procedure amylase (p = 0.552), CRP (p = 0.058) and duration of the procedure, there was a significant association between amylase post procedure and length of SB examined. (Spearman's rho 0.186; p = 0.005).

Conclusion: This study identifies a role for rectal indomethacin in patients undergoing antegrade DBE. We have demonstrated that rectal indomethacin reduces amylase post DBE and no patients given indomethacin experienced pancreatitis. Larger studies are required to assess if this also transforms into lowering risk or severity of pancreatitis.

Disclosure: Nothing to disclose

P0861 NEED FOR ENTEROSCOPY IN LIVER TRANSPLANTED PATIENTS

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Introduction: The management of liver transplanted (LT) patients is often complex and requires a multidisciplinary approach. Anaemia due to obscure or overt gastrointestinal bleeding and biliary complications can occur in LT patients; thus, the need for enteroscopy (capsule enteroscopy (CE), double-baloon enteroscopy (DBE)) or a double-balloon cholangiopancreatography (DB-ERCP), can be present also in LT subjects. Nowadays few data about the diagnostic success and safety of these procedures in LT patients are present. Use of DBE is increasing for the management of post-transplant biliary strictures while anecdotal case-reports are available about CE after LT.

We aimed to evaluate the need for enteroscopy after LT and to estimate the success rate and the safety of these procedures.

Aims and Methods: We analysed retrospectively 468 patients, underwent orthotopic LT (OLT), followed in our Liver Transplant Unit in the last 5 years (from January 2013 to January 2018), and collected those who performed an enteroscopy including CE, DBE and DBE-ERCP.

We collected data about the clinical and demographic characteristics of the patients (i.e. age, sex, year and reason of OLT, current medical therapy and comorbidity), the diagnostic yield/success rate of the procedures and incidence of complications. We also valued the enteroscopic success (achievement of biliary anastomosis) and the therapeutic success for DBE-ERCP.

Results: 21 patients (4.5%) underwent one or more enteroscopies (26 procedures): we collect 9 CE (one of that followed by anterograde DBE), 14 DBE-ERCP for 10 patients and 2 retrograde DBE.

Medical indications to perform CE were iron deficiency (7/9) and chronic diarrhoea (2/9).

DB-ERCP was performed primarily for stenosis of the biliary anastomosis, with recurrence cholangitis (4/10) or with asymptomatic cholestasis (1/10). Less frequent indications were gallstones (3/10), PSC-related biliary tract stenosis (1/10) and biliary fistula (1/10).

The diagnostics yield for CE was 55% (5/9) and the most frequent cause of bleeding was jejunal angioectasia (4/9), followed by duodenal ulcer and ileal erosions. The enteroscopic success of DBE-ERCP was 50% (7/14), the first cause of failure was the impossibility to find the biliary anastomosis. The diagnostic success was 50% (7/14).

One patient performed an anterograde DBE for treating a jejunal angiodisplasia, previously found on CE. Two retrograde DBE was performed in patients with suspected thickening of distal jejunal, with one diagnosis of intestinal localization of Large B-cell lymphoma and normal findings in the other patient.

No procedural complications in the long and short term were observed with all the procedures.

Conclusion: A significant number of the liver transplanted patients can have the necessity to perform a small bowel endoscopy. All the analysed procedures were safe and with a good diagnostic yield/success. We suggest that Liver Transplantation Units should have the possibility to perform enteroscopy to improve the management of LT patients.

Disclosure: Nothing to disclose

P0862 ADENOMA DETECTION RATES IS ASSOCIATED WITH RESPECTIVE WITHDRAWAL TIME IN DIFFERENT COLON SEGMENTS

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Introduction: Colonoscopy withdrawal time is significantly correlated with adenoma detection rate (ADR). The 6-minute withdrawal time for colonoscopy is widely considered the standard of care. However, there may not be appropriate if the 6-minute is equally divided into various colon segments. Since the adenoma detection in each colon segment is not the same, there may be differences with the withdrawal time in different colon segments.

Aims and Methods: We aimed to evaluate the relationships between ADR and respective withdrawal time in different colon segments. Outpatients, age range from 18 to 75 and complete colonoscopy, were selected from December 2016 to June 2017 in the digestive endoscopy center. The entire colon was divided into four different segments: ascending colon, transverse colon, descending colon and rectosigmoid colon. The respective withdrawal time and ADR in each colon segment were recorded respectively.

Results: A total of 5027 outpatients were enrolled and the general ADR was 25.1%. The positive withdrawal time (adenomas detected) was longer than negative withdrawal time (non-adenomas detected) (299.37 ± 98.19s vs 209.63 ± 69.50s, t = 20.771, p < 0.001). The age was older in patients that adenomas were detected (55.77 ± 11.18 vs 47.00 ± 13.30, t = 15.864, p < 0.001). The ADR in ascending colon, transverse colon, descending colon and

rectosigmoid colon were respectively 6.2%, 5.2%, 6.1% and 17.3%. While all of their positive withdrawal time were longer than negative withdrawal time (67.31 ± 18.62s vs 51.11 ± 17.86, $t = 10.729$; 87.94 ± 29.51s vs 60.86 ± 22.27s, $t = 12.983$; 86.12 ± 28.42s vs 58.77 ± 22.78s, $t = 13.830$; 74.88 ± 25.67s vs 53.62 ± 20.46s, $t = 18.392$; $p < 0.001$ respectively). The positive withdrawal time in ascending colon was respectively shorter than that in transverse colon and descending colon (67.31 ± 18.62s vs 87.94 ± 29.51s, 86.12 ± 28.42s, $p < 0.001$). However, there were no statistical differences between them in ADR (6.2% vs 5.2%, 6.1%, $p > 0.05$). The positive withdrawal time in transverse colon and descending colon were all longer than that in rectosigmoid colon (87.94 ± 29.51s, 86.12 ± 28.42s vs 74.88 ± 25.67s, $p < 0.001$). While the ADR in rectosigmoid colon was obviously higher than that in other three segments of colon (17.3% vs 6.2%, 5.2%, 6.1%, $p < 0.001$).

Conclusion: ADR and withdrawal time are all various in different colon segments. During the operation of colonoscopy, withdrawal time in ascending colon may be shortened appropriately. The adenomas in rectosigmoid colon are more likely to be detected and do not take longer withdrawal times.

Disclosure: Nothing to disclose

P0863 YIELD OF CAPSULE ENDOSCOPY IN OBSCURE GI BLEEDING – A COMPARATIVE STUDY BETWEEN PREMENOPAUSAL AND MENOPAUSAL WOMEN

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Introduction: Premenopausal women (PMW) often have a complete study of the gastrointestinal tract without findings justifying anemia/blood loss often motivating investigation of other causes.

Aims and Methods: The present study aimed to evaluate differences in capsule endoscopy (CE) performed in the setting of obscure gastrointestinal bleeding (OGIB) among PMW and menopausal women (MW).

Retrospective, single-center study, including female patients submitted to CE in the setting of OGIB between May 2011 and December 2016. Patients were divided into 2 groups according to age, considering fertile age as ≤ 55 years and postmenopausal age as > 55 years. The diagnostic yield (DY), the rebleeding rate and the time to rebleed were evaluated and compared between groups. Rebleeding was defined as drop of $Hb > 2$g/dL or need for transfusional support or presence of melena/hematochezia.

Results: A hundred and eighty three female patients underwent CE for OGIB, of whom 30.6% ($n = 56$) were PMW and 69.4% ($n = 127$) were MW. DY was 35.4% in PMW and 12.5% in MW. The most common findings were angiodysplasias in both groups (PMW-38.8%, MW-62.7%). In PMW, only 1.8% required therapeutic endoscopy. In 18.1% of MW, CE findings led to additional endoscopic treatment. Rebleeding at 1, 3 and 5 years in PMW was 4.6%, 10.2% and 10.2% and in MW it was 22.0%, 32.3% and 34.2% ($p = 0.001$). Postmenopausal status was significantly associated with higher DY ($p = 0.002$), need for endoscopic treatment ($p = 0.003$), rebleeding ($p = 0.001$), and hospitalization ($p < 0.001$).

Conclusion: PMW with suspected OGIB are less likely to have significant findings in CE. In MW DY, need for endoscopic treatment, rebleeding and hospitalization were significantly higher.

Disclosure: Nothing to disclose

P0864 IS PAN-ENTERIC VIDEO CAPSULE ENDOSCOPY A COST-EFFECTIVE OPTION FOR OPTIMIZATION OF CROHN'S DISEASE THERAPY IN ENGLAND?

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Introduction: The treatment paradigm for Crohn's disease (CD) is changing with greater emphasis on treat to target strategies. Video Capsule Endoscopy (VCE) has potential to improve monitoring of CD activity.

Aims and Methods: This study aims to identify whether standard use of VCE in the CD care pathway would be cost effective in England.

A patient-level, care pathway model specific to CD management in England was developed. Specifically, NICE guidance for CD management was supplemented by the consensus opinion of a sample of physicians with CD and VCE expertise. The model included local pricing, NHS tariffs, incidence rates, step-up treatment, and the use of faecal calprotectin testing (FCT) to inform the need for endoscopic monitoring practices: colonoscopy or VCE, respectively. Provision of drug therapy influenced the onset, progression, or remission of CD flares, fistulae, and abscesses. Data for VCE were derived from a pan-intestinal small bowel and colon capsule, which provides pan-enteric assessment VCE (pVCE). Outcomes for 4,000 simulated patients over 20 years were assessed. Cost of care and patient quality of life (QoL) were compared between monitoring options (pVCE or colonoscopy). The willingness to pay threshold was taken as a conservative £10,000 per quality-adjusted life year (QALY) gained. Significance of results at the 95% level was calculated using probabilistic sensitivity analysis.

Results: All experts agreed that the CD care pathway had to be individualised to patient needs. However, consensus was sufficient to develop a protocolised pathway to model. Step-up treatment started with glucocorticosteroid and progressed to biologics (± azathioprine). High-risk patients (≥ 3 risk factors present) could initiate treatment with biologics directly. Need for endoscopy was informed by FCT, that is performed at least once per year.

The 20-year care costs were £69,745 (£3,487 per year) with colonoscopy and £67,806 (£3,390 per year) with pVCE. pVCE was associated with increased patient QoL, with patients accruing a mean of 7.8 QALYs compared with 7.3 QALYs with colonoscopy. The analysis suggested that the use of pVCE for monitoring is beneficial in England, saving £1,941 per QALY gained. Tests showed that pVCE would be considered cost-effective in 96.9% of 2,000 bootstrapped simulations. The 95% credible interval extended to £10,913 per QALY gained.

Key outcome drivers in the simulation were the need for surgical procedures (25% of costs) and the use of biologic therapies (24%). Use of pVCE resulted in earlier detection of inflammation and initiation of biologics, which increased care costs in the short term. In some patients, earlier treatment resulted in optimized outcomes with earlier abscess drainage preventing subsequent resection. As lower-cost biosimilars become available, the cost-effectiveness of pVCE increases.

Conclusion: Use of pVCE for monitoring of CD activity is likely to be cost-effective in England over 20 years. Improved patient outcomes, including reduced need for bowel resection, are additional benefits.

Disclosure: RS is the owner and RTT and MB are employees of Coreva Scientific, which received consultancy fees for this work. NVL and CL are employees of Medtronic. AL and MM have previously provided medical advice to Medtronic for which they received honorarium in line with fair market value.

P0865 SURFACE MAPPING IN PLASTIC GASTRIC MODEL ASSISTED BY A ROBOTIC AUTOSCAN PROGRAM WITH A NEW MAGNETICALLY CONTROLLED GASTRIC CAPSULE ENDOSCOPY SYSTEM COMPARED TO MANUAL CONTROLLING

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Introduction: Capsule endoscopy is a non-invasive method to exam the mucosal surface of the gastrointestinal tract. In the diagnosis of small bowel disease, it is the gold standard in various indications, since 2001. The examination of the stomach with small bowel capsule endoscopy system is not possible because we could not navigate the capsule through the entire lumen. Since 2013, there is a new magnetically controlled capsule endoscopy system (Navicam) which allows precise intraluminal navigation and positioning therefore, ensures a complete examination of the stomach.

Aims and Methods: We tested the new Navicam magnetic capsule endoscopy system in a plastic gastric model to compare the robotically controlled autoscan program modules and the free hand examination. Our study aimed to analyze whether the autoscan modules or the free-hand capsule controlling method is superior in the inner surface mapping of the plastic stomach model. We put in 12 different colored rings externally on the model (one-one on the anterior-posterior wall of the fundus, corpus and antrum, one around the cardia and pylorus, one on the angulus and three on the greater curvature) with different numbers in each quarter on the surface of the model. We make five tests in small and medium-sized stomach and five in medium and large stomach module with the autoscan function and five tests with free-hand controlling done by five trained GI fellows. We analyzed the effectivity of the surface visualization with the total sum of the numbers on the colored rings on the capsules video.

Results: The complete 100% visualization of the inner surface of the plastic stomach model with the medium and large stomach autoscan program module and with the free-hand controlling method could successfully achieved in all tests. With the small and medium stomach mode we could observe only the 97.5% of the inner surface, because of the incomplete visualization of the prepyloric region. With free hand method we needed nearly twice as much average time (749 seconds) to make complete examination as compared to the robotic maneuvering with auto scan program (390 seconds).

Conclusion: Magnetically controlled gastric capsule endoscopy system and autoscan program module are promising tools to visualize the entire mucosal surface of the stomach non-invasively. The NaviCam magnetically controlled capsule examination of the stomach without discomfort and sedation can provide a new dimension of upper gastrointestinal screening programs and can help to lower the mortality of gastric cancer.

Disclosure: Nothing to disclose

P0866 SMALL BOWEL CAPSULE ENDOSCOPY (SBCE) IN THE ELDERLY. A MULTICENTRE PROSPECTIVE STUDY IN LOMBARDY REGION

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Introduction: Data on SBCE performance and yield in the elderly are scant and conflicting. Our aim was to compare SBCE performance and yield in old and very old patients with their younger, adult counterpart in a large, prospective, multicentre study.

Aims and Methods: From October 2011 to December 2013, data of 2294 consecutive patients undergoing SBCE in 30 Centres of Lombardy Region, were prospectively collected in a dedicated database. For the purpose of this study, we included 2260 adult patients (≥18 years old). Patients were stratified by three age-related groups, namely: A (18–64 years old, n = 989), B (65–79, n = 935), C (≥80, n = 336). Diagnostic yield (DY) was defined as any small bowel (SB) abnormality, and clinical significant findings (CSF) as SB P2 lesions, in accordance to Saurin's classification. CSF were classified in five categories using a modified Capsule Endoscopy Structured Terminology (CEST): (i) stenosis, (ii) luminal blood, (iii) inflammatory (erosion, ulcers), (iv) neoplastic (polyp, mass), (v) vascular. Chi-square for independent proportions was used to compare the three groups for the following outstanding characteristics: indication, gender, outpatient status, completion rate, retention rate, DY, CSF, and category of findings. p value < 0.05 was considered statistically significant.

Results: Suspect small bowel bleeding was the leading indication to SBCE (75.3%), without differences between groups. Males were under represented in group C (45% vs 51.6 and 56% in group A and B, respectively), without statistical significance (p = 0.28). As shown in table 1, we did not find any difference among the three groups in the frequencies of the above-mentioned variables of interest.

Conclusion: In this large prospective series, in the elderly, SBCE performed as well as adults, without difference in terms of outpatient status, diagnostic yield, completion rate, retention rate, and findings.

Group	A	B	C	*P value*
N Patients	989	935	336	–
Outpatient (%)	649 (65.6)	599 (64)	202 (60)	0.19
Completion (%)	891 (90)	836 (89.4)	310 (92.2)	0.32
Retention (%)	10 (1)	4 (0.4)	3 (0.8)	0.31
DY (%)	604 (61)	529 (56.5)	190 (56.5)	0.1
CSF (%)	509 (51.4)	477 (51)	164 (48.8)	0.7
Stenosis (%)	13/509 (2.56)	12/477 (2.5)	1/164 (0.6)	0.3
Luminal blood (%)	51/509 (10)	50/477 (10.4)	21/164 (12.8)	0.59
Inflammatory (%)	137/509 (26.9)	120/477 (25.1)	43/164 (26.2)	0.81
Neoplastic (%)	93/509 (18.2)	80/477 (16.7)	22/164 (13.4)	0.35
Vascular (%)	215/509 (42.2)	215/477 (45.6)	77/164 (47)	0.48

[Table 1]

Disclosure: Nothing to disclose

P0867 DEVELOPMENTAL INNOVATIONS WHILE PRODUCING A NOVEL CAPSULE

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Introduction: Small bowel capsule endoscopy (CE) has made tremendous technologic progress, due to its superior patient acceptability and safety profile. However, CE of the colon is held back by the need for a prep as good as or better than an average colonoscopy. C-Scan is a novel capsule which obviates the need for any cathartic or laxatives (Check Cap Ltd, Mount Carmel, Isfiya, Israel) (1). The X-ray imaging capsule overcomes the requirement for bowel preparation, a major deterrent for CRC screening. No prep, diet restrictions or medications are applied. The device records for 100 hours.

Developing this new colon capsule required various innovations, herein described, which are spinoffs with major side-benefits. Such benefits are in addition to helping achieve the primary goals of producing an efficient, safe capsule requiring no prep, which successfully identifies polyps, screens the colon, prevents cancer and thus saves lives.

Aims and Methods: A capsule has been produced and trials performed in over 200 humans. This capsule, in addition to identifying polyps, delivers novel information on motility, with pressure measurements and thermal measurements, and advances physiologic concepts and knowledge regarding native colonic functions in health and disease states. The CE- (Certificate European) approved capsule, used in over 200 humans to screen for polyps, has presented challenges and led to a series of exciting technological innovations, herein described.

Results: The three-point online monitor, embedded in a tracking unit attached to the back of the patient, has delivered patterns of capsule movement in a prep-less normal colon, leading to real-life tracks of how colonic contents move.

The performance of the 3D colon was examined in a uniquely designed mechanical phantom model of the colon and a high correlation between behavior in humans and the phantom was demonstrated. Accuracy of the capsule tracking by triangulation from the 3 sensors on the back of the patient is +/−5mm, including when patients (except morbidly obese) are in motion. This allows clinicians to localize findings correctly, facilitating the planning of subsequent interventions.

Two examples illustrate the accuracy of the system during clinical procedures: The new algorithms developed for the C-Scan detect the minute motion of the small bowel peristalsis and colon movements caused by ventilation.

The pressure monitors on the C-Scan Capsule deliver real-life measurements of the relative pressures throughout the segments of the colon, opening a path to reflecting on interventions which target specific sites within the colon.

The thermal monitor on the C-Scan capsule is being applied in efforts to determine whether differences in temperature and therefore in circulation, can be found in polyps vs. in normal colon. Total transit time [TTT] was measured from capsule ingestion to excretion while patients are free to follow their normal daily routine. The TTT is the sum of 3 distinct time segments: until the cecum, within the cecum and distal to cecum until excretion.

The results from 50 cases are presented in table 1.

Conclusion: Technical innovations often end in a different place than they initially envisioned. The development of the C-Scan capsule has stimulated the above five technologic innovations which may all continue to deliver new physiologic information allowing us to deliver better health.

	Total transit time	Time to cecum	Time in cecum	Passage in colon
Average in hours	57.5	15.3	21.0	14.9
STD (hours)	41.8	9.7	22.1	11.1

[Transit time measurement for C-Scan capsule]

Disclosure: Prof Lachter works as a paid consultant for Checkcap

Reference

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P0868 SMALL BOWEL NEOPLASIA DETECTION IN LYNCH SYNDROME USING VIDEO CAPSULE ENDOSCOPY

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Introduction: Lifetime risk of developing small-bowel cancer in patients with Lynch syndrome (LS) is estimated to be around 4%, which is more than 100-times the risk of the general population. This risk is almost similar to the lifetime risk of colorectal cancer in the general population, for which screening is generally recommended. Screening for small-bowel cancer in Lynch syndrome has, until now, not been included in guidelines for surveillance of families with Lynch syndrome. In 2016 Mallorca group gave the advise small bowel screening may be appropriate in mutation carriers MSH2 and MLH1 especially after 40 years.

Aims and Methods: The aim of the study was to determine the incidence of small-bowel neoplasia in asymptomatic LS patients by means of video capsule endoscopy (VCE).

Two prospectively maintained databases of VCE were retrospectively reviewed to identify all consecutive asymptomatic LS patients. These patients were compared with a group of patients without LS who underwent VCE for obscure gastrointestinal bleeding (OBS), with negative upper GI endoscopy and colonoscopy.

Results: 25 LS patients and 280 OBS patients were enrolled in the study by the two Italian centers.

In 91.5% of the procedures, caecal visualization was achieved.
Small-bowel neoplasia was detected in two LS patients and three OBS patients (p = 0.06). The two groups have a significant statistically different mean age (SD): 41.3 ys± 14.0 ys in LS group and 62.9 ys± 17.2 ys in OBS group (Table 1). Besides small bowel adenocarcinoma, LS patients and OBS patients have statistically significant difference in incidence of vascular lesion, angiectasia and minute polyps (Table 1).
Conclusion: The prevalence of small-bowel neoplasia in asymptomatic patients with LS was 8% vs 1.1%. Although the incidence of small bowel adenocarcinoma did not reach statistical significance difference, a trend through statistically significant difference was observed and this suggests further multicentric studies are needed.

Variable	Lynch Group N = 25	Obscure Bleeding Group N = 280	p
Male, n (%)	12 (48.0%)	163 (58.2%)	0.4
Female, n (%)	13 (52%)	117 (41.8%)	
Age, mean (SD), years	41.3 (14.0)	62.9 (17.2)	<0.0001
Adenoca Small Bowel, n (%)	2 (8.0%)	3 (1.1%)	0.06
Normal examination, n (%)	4 (16.0%)	53 (18.9%)	1.0
No caecal visualisation, n (%)	1 (4.0%)	25 (8.9%)	0.7
Vascolar lesion, n (%)	4 (16.0%)	118 (42.1%)	0.01
Emangioma/varice, n (%)	0	21 (7.5%)	0.2
Angiectasia, n (%)	3 (12.0%)	114 (40.7%)	0.005
Lymphangiectasia, n (%)	4 (16.0%)	42 (15.0%)	0.8
Submucosal lesion, n (%)	1 (4.0%)	29 (10.4%)	0.5
Minute polyps, n (%)	10 (40%)	35 (12.5%)	0.001
Red spot, n (%)	4 (16.0%)	53 (18.9%)	1.0
Erosion/ulcer, n (%)	5 (20%)	78 (27.9%)	0.5
Substenosis, n (%)	1 (4.0%)	10 (3.6%)	1.0

[Small bowel neoplasia detection in Lynch syndrome using video capsule endoscopy: Results]
Disclosure: Nothing to disclose

P0869 THE DIAGNOSTIC YIELD OF SMALL BOWEL CAPSULE ENDOSCOPY IN POSTSURGICAL CROHN'S DISEASE

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Introduction: Post-operative endoscopic recurrence (POER) of Crohn's disease (CD) is frequent and unpredictable. In clinical practice, colonoscopy is recommended 6–12 months after surgery, in order to detect early POER and guide management. The aim of our study was to determine the diagnostic yield of small bowel capsule endoscopy (SBCE) in this setting.
Aims and Methods: We reviewed the records of 5471 patients subjected to SBCE in our department from March 2003 to March 2017 (males/females: 2693/2778, mean age ± SD: 50.8 ± 28.4 years). Among these patients, we identified 677 with known CD, of whom 41 had undergone SBCE 6–12 months following ileo-colonic resection. Any lesions detected in the proximal small bowel were also recorded. All these patients had also undergone ileo-colonoscopy at the same time to assess for POER using the Rutgeerts score. The findings of the two tests were compared to examine whether SBCE can detect more proximal lesions in patients who did not exhibit POER (that is a Rutgeerts score ≤1) during ileo-colonoscopy.
Results: POER was detected in 16/41 (39%) patients by ileo-colonoscopy. SBCE detected lesions in the neoterminal ileum in 15 of these 16 patients (overall rate 36.6%) as in one patient the capsule did not reach the neo-terminal ileum during the battery's life span. Concurrent lesions in the neo-terminal ileum and more proximally were detected by SBCE in 9/15 patients; however, two patients with an ileo-colonoscopic Rutgeerts score of 0 had more proximal lesions during SBCE.
Conclusion: SBCE is not cost-effective and cannot be recommended as an adjuvant to ileo-colonoscopy to identify more proximal lesions post-operatively in CD patients. However, it may substitute for ileo-colonoscopy considering local cost, disease characteristics and patient preferences
Disclosure: Nothing to disclose

P0870 DEVELOPMENT OF QUALITY MEASURES FOR CAPSULE ENDOSCOPY REQUIRES A NOVEL APPROACH BASED ON A PERFORMANCE REVIEW OF A LARGE SINGLE CENTRE SERVICE

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Introduction: Capsule Endoscopy (CE) is a popular non-invasive technology to provide diagnostic imaging of the small bowel. As with all endoscopic techniques, quality of CE procedures will affect patient outcomes. Unlike upper and lower gastrointestinal endoscopy there is little in the literature on CE quality measures and a low evidence base to support guideline development. Analysis of current practice with reference to procedure quality and patient outcomes may highlight potential future key performance indices (KPI) and help guide future quality assurance initiatives.
Aims and Methods: To perform an analysis of our CE service with reference to procedure quality and patient outcomes.
A retrospective review of CE procedures performed in our institution from 2010 through 2015 was undertaken. CE procedures were identified from a database. Rapid Reader and other hospital electronic patient information software was used to extract essential information. Recorded data covered Pre-Procedural, Procedural and Post-Procedural domains and included patient demographics, indication, preparation quality, caecal visualisation, findings, complications, and CE reader. Data was grouped according to outcome or potential KPI and compared using a chi2 test, a $p < 0.05$ was considered significant.
Results: In all 1,227 CE's have been included and analysed; 50% (n = 615) female, median age 56 years (range 13–93). The overall diagnostic yield (DY) was 39% (n = 477). Only 85 (7%) CEs were performed for non ESGE approved indications including abnormal radiology (n = 41). The DY was similar for ESGE and non-ESGE recognised indications 34% (n = 390) and 35% (n = 30) respectively, p = 0.92.
DY did not vary significantly by indication; obscure GI bleeding (37%), anaemia (37%), suspected Crohn's disease (38%), others (34%). Similarly, age did not affect CE efficacy. In particular, DY for anaemia in patients < 50 and > 50 years was 37% (n = 124) and 40% (n = 29) respectively, p = 0.72. However CEs performed to assess known disease had a higher DY than screening CEs; known CD (65.1%) vs suspected CD (38%), p = 0.0001, OR2.9.
Overall 8% (n = 98) of CEs were incomplete. Surprisingly DY was significantly higher for incomplete, 56% (n = 55) versus complete studies 37% (n = 422), p = 0.004, likely reflecting the pathology encountered. Similarly, DY was higher in the 38% (n = 459) of CEs with a poor-quality bowel preparation; 55% (n = 254) V's 40% (n = 302), p = 0.0001. Only 2/1227 (0.1%) experienced true capsule retention.
Trainee Gastroenterologists reported 58% (n = 710) of CEs. Trainee DY was higher, 41% (n = 292) V's Trainers 35% (n = 184), p = 0.04. All (100%) of Trainees attend a certified CE course and were supervised until fully proficient.
Conclusion: Our study suggests development of quality measures for CE will require a novel approach and further research. As expected KPIs based on standard endoscopy experience have yielded contradictory results. Incomplete studies and poor preparation quality were both associated with higher diagnostic yields, which is not that surprising as bleeding is a major indication and significant findings can inhibit or slow capsule passage. In addition, the diagnostic yield for CEs is higher for disease assessment compared to screening tests. Our data also suggests that other indications including abnormal radiology can be an appropriate indication for CE. Finally, our data supports a structured approach to CE training.
Disclosure: Nothing to disclose

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P0871 LONG-TERM OUTCOME OF ENDOSCOPIC TREATMENT OF BILIARY STRICTURE FOLLOWING LIVING DONOR LIVER TRANSPLANTATION

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Introduction: Biliary strictures remain one of the most challenging aspects after living donor liver transplantation (LDLT). Endoscopic procedures are the initial choice of treatment for biliary strictures following LDLT.
Aims and Methods: The aim of this study is to assess long-term outcome of endoscopic treatment of biliary stricture occurring after LDLT and to identify risk factors of recurrent biliary stricture following endoscopic treatment in LDLT. One thousand four hundred forty one patients underwent LDLT from May 1995 to May 2014. Biliary strictures developed in 24% of patients.
Results: Among 145 patients who were successfully managed with endoscopic drainage, biliary stent could be removed in 94 patients. After for 12 months

follow up after removal of endoscopic retrograde biliary drainage (ERBD), 69 patients (66.2%) had no recurrent biliary stricture and 20 patients (21.3%) showed recurrent biliary stricture. We compared the risk factors between no recurrent biliary stricture and recurrent biliary stricture group. Younger donor age was associated with lower recurrence rate, and non-B, non-C liver cirrhosis was associated with higher recurrence rate of biliary stricture.
Conclusion: Long-term outcome of the endoscopic treatment of biliary stricture occurring after LDLT was relatively fine, but the clinician should be careful of ERBD removal and following up in the case with factors associated with recurrent biliary stricture.
Disclosure: Nothing to disclose

P0872 EUS-ANTEGRADE BILIARY STENTING VERSUS PTBD FOR DISTAL MALIGNANT BILIARY OBSTRUCTION IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Distal malignant biliary obstruction (DMBO) in patients with surgically altered anatomy (SAA) is traditionally managed with PTBD, since anatomical features complicate endoscopic approach to the biliary orifice. Recently, enteroscopy and EUS assisted approaches have emerged as alternative treatments; however, limited data comparing between the procedures has been available so far.
Aims and Methods: The aims of this study were to compare EUS-antegrade treatment (AG) with PTBD for DMBO in patients with SAA.
Patients who underwent EUS-AG or PTBD as management of DMBO and had history of upper intestinal surgery at 2 tertial centers between 4/2007 and 1/2018 were evaluated retrospectively. In EUS-AG, the bile duct was punctured under EUS-guidance, followed by guidewire placement through the obstruction, dilation of the fistula, and metallic stent placement cross DMBO. Naso-biliary drainage was placed though the fistula only if there might be any chance of stent dysfunction or active cholangitis. PTBD typically had 3 steps approach: Firstly, the bile duct was punctured under ultrasound guidance followed by external drainage tube placement. In the 2nd session, a metallic stent was deployed cross DMBO with remaining the external drainage. In the 3rd session, the external drainage was removed after confirmation of good bile flow through the stent. The study outcomes were the technical and clinical success rates and the adverse event rate. Technical success and clinical success were defined as successful internalization and decrease of serum total-bilirubin level by half, respectively. Survival duration was analyzed with Kaplan-Meier method between the groups. Possible factors which can affect the survival duration were also analyzed with multivariable analysis. Continuous valuables were described with median (interquartile range).
Results: A total of 53 patients were enrolled. Among them, 24 patients underwent EUS-AG and 29 had PTBD. Basic characteristics (EUS-AG/PTBD) were the median ages of 69.5 (61–76)/69.0 (62–74.5) ($p = 0.68$) and included 12 men/17 men ($p = 0.59$). SAAs were Billroth II (2/6), Whipple procedure (0/1), Roux-en-Y (18/19), and gastric by-pass (4/3). ($p = 0.44$) Biliary puncture was successful in 95.8%/100%. ($p = 0.45$) The median numbers of session were 1 (1-1)/3 (3–4). ($p < 0.001$) Both technical and clinical success rates were 95.8%/82.8%. ($p = 0.20$) Overall adverse event rates were 16.7%/26.4%. ($p = 0.21$) Recurrent biliary obstruction was seen in 16.7%/10.3%. ($p = 0.63$) Median survival times were 108 days (61–249)/92 days (42–277). ($p = 0.43$) Multivariable analysis showed chemotherapy after the procedure (Hazard ratio of 0.35, 95% confidential interval of 0.18–0.67) as independent risk factor for survival, but the procedure itself was not risk factor for that.
Conclusion: There were no significant differences in safety and efficacy between EUS-AG and PTBD for DMBO in patients with SAA. EUS-AG might be a treatment of choice for management of DMBO in SAA patients same as PTBD.
Disclosure: Nothing to disclose

P0873 THE USEFULNESS OF NEWLY MODIFIED NON-FLARED FULLY COVERED METAL STENT OF 12 MM-DIAMETER COMPARING WITH CONVENTIONAL STENT FOR PERIAMPULLARY MALIGNANT BILIARY STRICTURES

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Introduction: Fully covered metal stent (FCMS) can be a preferred stent for distal malignant biliary stricture (MBS). However, stent migration can be a major adverse event of FCMS, especially for far distal MBS.
Aims and Methods: The aim of this study was to evaluate the usefulness of newly modified non-flared FCMS having 12mm in diameter to minimized stent migration compared with the conventional FCMS. Total 102 patients with periampullary MBS enrolled prospectively between January 2014 and September 2017; 50 were allocated to the newly modified non-flared FCMS group and 52 to the conventional FCMS group. The primary outcome was the stent migration, and the secondary outcomes were other adverse events and stent occlusion rate during follow-up period.
Results: Baseline characteristics were not significantly different between the two groups. Endoscopic stent placement was technically successful in all patients. Stent migration was observed in 8.0% (4/50) in newly modified non-flared FCMS group in comparison to 23.1% (12/52) in conventional FCMS group ($p = 0.036$). The incidence of stent-related pancreatitis was 10.0% (5/50) with newly modified non-flared FCMS and 11.5% (6/52) with conventional FCMS ($p = 0.802$). Stent occlusion was occurred 22.0% (11/50) in newly modified non-flared FCMS and 28.8% (15/52) in conventional FCMS during follow-up period ($p = 0.428$).
Conclusion: Newly modified non-flared FCMS with large diameter of 12mm significantly decreased stent migration compared with conventional FCMS in patients with periampullary MBS.
Disclosure: Nothing to disclose

P0874 DEVELOPMENT OF A NOVEL INTERNAL FISTULA TUBE FOR ENDOSCOPIC TRANSLUMINAL BILIARY DRAINAGE

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Introduction: We developed a biliary internal fistula tube (BIFT) which has been constructed with a conventional biliary stent tube and a bioabsorbable polymer seat (BAPS) for a transluminal biliary drainage. In this study we attempted to investigate the difference between the BIFT and conventional tube (CT) in biliary-enteric fistula formation.
Aims and Methods: The BIFT is a conventional biliary tube wrapped with the BAPS, which is 0.5mm thickness. The BAPS is an ideal scaffold for tissue regeneration with porous property to allow easy penetration of cells. BIFT group ($n = 6$): The pigs were laparotomized to expose the extrahepatic bile duct (EHBD). The 5cm BIFT was placed between gallbladder (GB) and duodenum (DU). CT group ($n = 6$): The 5cm CT was placed between GB and DU in a similar manner of the BIFT group. In both group these pigs were sacrificed and re-laparotomized at 4 weeks after the placement.
Results: BIFT group: At 4 weeks after the placement, the distance between GB and DU was shortened. A biliary-enteric fistula, which had 1.5cm bore diameter and 2cm length, was constructed between GB and DU. CT group: At 4 weeks after the placement, the CT became surrounded by connective tissue, and the distance between GB and DU came closer to each other. However, the connective tissue between GB and DU was fragile and easy to be divided. The lumen of the CT has biliary sludge and almost became obstructed.
Conclusion: The placement of the BIFT between GB and DU induced rapid and good fistulization, and has the potential for application as a novel device for transluminal biliary drainage avoiding the need for exchange of tubes.
Disclosure: Nothing to disclose

P0875 EUS-GUIDED CHOLEDOCHODUODENOSTOMY USING A LUMEN APPOSING METAL STENT FOR MALIGNANT DISTAL BILIARY OBSTRUCTION: A RESTROSPECTIVE ANALYSIS OF A SINGLE CENTER EXPERIENCE

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Introduction: Endoscopic ultrasonography guided choledochoduodenostomy (EUS-CD) using a lumen apposing metal stent (LAMS) has been recently reported as an alternative approach in the management of patients with malignant obstructive jaundice and failed endoscopic retrograde cholangiopancreatography (ERCP).
Aims and Methods: The aim of this study was to analyze the safety, technical and clinical efficacy of EUS-CD in this setting of patients. Retrospective analysis of a prospectively maintained data base of consecutive patients with unresectable malignant distal bile duct obstruction who, between 10/2015 and 12/2017, underwent EUS-CD using the study device (Electrocautery enhanced (EC)-AXIOS, Boston Scientific Corp., Marlborough,Massachusetts, USA) after unsuccessful ERCP in a single tertiary-care academic medical center. Technical success was defined as accurate positioning of the stent. Clinical success was defined as resolution of biliary obstructive symptoms with a decrease in the total bilirubin level to 50% reduction of the initial level.
Results: Forty-six patients (47.8% female; median age 73.1 ± 12.6) underwent direct EUS-CD using the biliary EC-AXIOS(diameter 6x8mm in 21(45.7%); 8x8mm in 19(41.3%); 10x10 mm in 6 (13%)). ERCP failure was due to inability to get deep biliary cannulation in 30 patients (65.2%) and to duodenal obstruction in the remaining 16(34.8%) patients.
The procedure was technically successful in 43/46 (93.5%) patients, with a mean procedural time of 14.7 min (range 5–38).

Clinical success was achieved in 45/46 (97.7%) patients with a reduction in the total bilirubin level of 65.3% within 14 days of the initial levels.
Ten patients were treated with a single session sequential approach by deployment of EC-AXIOS and duodenal stent for biliary and duodenal obstruction. In 3 patients a duodenal stent insertion was performed before the procedure and in 3 patients after a median of 127 days (range 59–240 d). The median post-procedure hospitalization was 6.12 ± 5.98 days. The mean follow-up was 114.37 days (C.I. 73.2–155.4). During follow-up 19 patients died after a mean of 105.3 days ± 29.1 SE because of disease related complications.
Major complications occurred in 5(11.6%) patients after a mean of 83 days (range 17–148): 1 fatal bleeding 17 days after stent placement and 4 stent obstruction/migration requiring re-intervention (3 stent occlusion due to food impact; 1 spontaneous migration).
Conclusion: This study shows that EUS-CD using the EC-AXIOS is associated with high technical and clinical success rates. The rate of complications including one fatal event is not negligible and should be carefully considered before using the stent in this clinical setting. Future prospective studies are required to fully assess the long-term efficacy and safety of the stent.
Disclosure: Nothing to disclose

P0876 ARE PLASTIC STENTS "EXPANDABLE" IN THE TREATMENT OF BILIARY STRICTURES AFTER ORTHOTOPIC LIVER TRANSPLANTATION?

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Introduction: In the last five decades, OTL became an option for saving the life of patients with end stage liver disease, liver malignancies or acute liver failure. The purpose of liver transplantation is to prolong and to increase quality of life.
The management of these patients is better than in the past due to optimisation of surgical techniques, immunosuppression therapy, management of infections and complications. Biliary strictures are the most frequent late complication of OLT, and are now managed almost entirely by ERCP and stenting.
Aims and Methods: To assess the stricture resolution in orthotopic liver transplantation (OLT) patients by ERCP stent placement in a tertiary care hospital. This is a retrospective study which enrolled patients from January 2013 to March 2018 with OLT anastomotic strictures and the ERCP procedures. The set-up included two groups, according to the type of stent used, either plastic (PS) or covered self expandable metal stents (SEMS) with their outcomes. We assessed the indication for transplantation, the number of ERCPs per pacient, the number of stents used, early post-ERCP complications.
Results: The study included 34 patients diagnosed with anastomotic billiary strictures post OLT. The indications for transplantation were various: cirrhosis secondary to VHB+VHD (7 patients), cirrhosis secondary to VHB (6 patients), cirrhosis secondary to VHC (5 patients), alcoholic cirrhosis (6 patients), hepatocarcinoma secondary to VHB+VHD (2 patients), hepatocarcinoma secondary to VHB (one patient), cryptogenic cirrhosis (3 patients), primary biliary cirrhosis (one patient), hepatocarcinoma secondary to VHC (one patient), Caroli disease (one patient), Budd-Chiari Syndrome (one patient). A total of 100 ERCP procedures were performed, with an overall mean of 3.22 per patient. 22 patients had plastic stents inserted, 9 had SEMS, one patient had dilation of stenosis, without stent insertion, but with a good outcome. There were 2 patients to whom stenting failed. Patients required in average 4 PS and 2 SEMS ($p < 0.05$). The SEMS group (9 patients) had a lower procedure time and also fewer interventions were performed than the PS group (1.89 vs. 3.53, $p < 0.05$). Both stents were changed after 4 months, but patients with SEMS obtained resolution of strictures after 4 months on average, while those with plastic stents required 11 months on average. The most common complication was acute pancreatitis which occured in 11% of all ERCP procedures, and it was significantly more encoutered in patients with SEMS ($p < 0.05$). One patient died with massive hemobilia after plastic stent placement.
Conclusion: Patients with PS required a larger number of ERCP procedures and a mean of 4 stents per patient, which translates in higher costs for each patient; in comparison, the SEMS group needed less procedures and on average only 2 metal stents until resolution of the strictures. From our experience, SEMS seem to be the best choice of treatment and the most cost-efficient way to solve biliary strictures after OLT. Though, it is not always fesable to insert SEMS, due to technical issues, related with the location of the stenosis. That is the main reason for which plastic stents will continue to play an important role in the management of biliary strictures after orthotopic liver transplantation.
Disclosure: Nothing to disclose

P0877 LONG-TERM OUTCOME OF EUS-GUIDED GALLBLADDER DRAINAGE VS. PERCUTANEOUS GALLBLADDER DRAINAGE IN PATIENTS WHO ARE UNFIT FOR CHOLECYSTECTOMY: WHICH IS BETTER?

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Introduction: EUS guided gall-bladder drainage (EUS-GBD) has become increasingly used to treat patients with acute cholecystitis who are not eligible for surgery. However, there are limited data comparing long-term outcomes of EUS-GBD and conventional percutaneous cholecystostomy (P-GBD). We therefore performed a retrospective study to compare the efficacy and safety of EUS-GBD and P-GBD in patients with acute cholecystitis.
Aims and Methods: We studied 182 patients who required gallbladder drainage for acute cholecystitis from February 2010 to November 2014. We used propensity-score weighting to adjust for differences in all covariates (age, sex, comorbid diseases, previous drugs) between EUS-GBD and P-GBD groups, and compared early, late adverse events and need for re-intervention in each group.
Results: A total of 182 patients (75 in EUS-GBD group and 107 in PTGBD group) were enrolled in this study. The technical/clinical success rate was 98.7%/100% (74/75, 74/74) in EUS-GBD and 99.1%/98.1% (106/107, 104/106) in P-GBD group respectively. After adjustment of inverse-probability-of-treatment-weighted method, early adverse event rate was no statistical difference between two groups. However, for late adverse events including migration of stent or dislodgement of drainage tube, stent or tube occlusion, tract inflammation around percutaneous tube, bile leakage and recurrence of cholecystitis it is shown P-GBD significantly higher odds ratio compared to EUS-GBD [odd ratio 3.38 (95% CI 1.08 to 10.54)]. P-GBD also showed a higher risk of additional intervention compared to EUS-GBD [odd ratio 3.60 (95% CI 1.26 to 10.32)]. Moreover, logistic regression analysis showed that P-GBD was significantly associated with re-intervention [odds ratio 3.68, 95% CI 1.43 to 9.47, $p = 0.007$].
Conclusion: EUS-GBD and P-GBD were both effective means of achieving gallbladder drainage. However, EUS-GBD might be beneficial than P-GBD in long term management for the patients with acute cholecystitis who are not suitable for cholecystectomy.
Disclosure: Nothing to disclose

P0878 ENDOSCOPIC ULTRASOUND-GUIDED GALLBLADDER DRAINAGE VERSUS ENDOSCOPIC TRANSPAPILLARY GALLBLADDER DRAINAGE FOR ACUTE CHOLECYSTITIS IN HIGH-RISK SURGICAL PATIENTS: WHICH IS BETTER?

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Introduction: Endoscopic gallbladder drainage (GBD) has been performed as an alternative to percutaneous drainage for acute cholecystitis. To date, there has been no comparative study between endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) and endoscopic transpapillary gallbladder drainage (ETGBD).
Aims and Methods: The aim of this study was to compare the outcomes of EUS-GBD and ETGBD. Retrospective review of an endoscopic GBD database prospectively collected at the Asan Medical Center (between July 2010 and December 2014) was performed to identify consecutive patients with acute cholecystitis who underwent attempted endoscopic GBD. Procedural and long-term outcomes were evaluated using propensity score matching and inverse probability of treatment weighting (IPTW).
Results: A total of 172 patients (76 in the EUS-GBD group and 96 in the ETGBD group) were included in this study. Seven patients who failed to undergo ETGBD crossed over to the EUS-GBD group. Technical success (99.8% vs. 83.3%, $p < 0.01$) and clinical success rates (99.8% vs. 82.3%, $p < 0.01$) was significantly higher in the EUS-GBD group than in the ETGBD group. After adjustment with IPTW method, the procedure-related adverse event rate was significantly higher in the ETGBD group (5.8% vs. 19.6%, $p < 0.01$). The cholecystitis or cholangitis recurrence rate (13.3% vs. 3.5%) was also higher in the ETGBD group than in the EUS-GBD group, as identified using Cox analysis (hazard ratio, 4.61; 95% confidence interval, 0.87–18.2; $p = 0.03$).
Conclusion: In patients with acute cholecystitis and unfit for surgery, EUS-GBD may be a more suitable treatment method than ETGBD.
Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00
Surgery II – Hall X1

P0879 THE THREE-YEAR EXPERIENCE OF ENDOSCOPIC TREATMENT OF THE ZENKER'S DIVERTICULUM

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Introduction: Current surgical guidelines of Zenker's diverticulum treatment recommend incising the intersection of the cricopharyngeal muscle (cricopharyngeal myotomy) and performing a diverticulectomy. The working hypothesis of our scientific research assumes that the results of tunnel endoscopic crycopharyngo-esophagomyotomy will exceed the results of standard endoscopic treatment with respect to the effectiveness of eliminating clinical development of diseases and reducing the number of their relapses.
Aims and Methods: We report the results of a comparative study of the endoscopic treatment of Zenker's diverticulum.
In the period from July 2014 to March 2018 67 patients were included in our research. At the initial stage (until March 2017), all operations were performed according to the traditional method. Later, after the introduction of the new tunneling technique, it was given priority in application due to a number of advantages. The standard protocol for preoperative examination included the transnasal endoscopy and X-ray examination. In the presence of signs of diverticulitis, conservative treatment was performed before the reduction of inflammatory changes in the mucosa. The average age of the patients was 66 (from 34 to 86) years.
Results: According to the traditional method, 36 patients (group I) were operated. 34 patients (group II) were operated using the tunnel technique. No technical difficulties associated with the myotomy or the mucosal defect closure were noted. The average time of the surgical intervention was 56+7 in the first group и 60+4 minutes in the second.
No signs of emphysema or other pathological changes were detected postoperatively.
In both groups on the first day after the operation, all patients had a control X-ray study with water-soluble contrast. An interesting feature in the group of tunnel technique was the almost complete absence of the residual cavity of the diverticulum. All the patients were discharged on the second day after the operation.
Two patients in the group of traditional endoscopic treatment were re-operated because of complaints recurrence; each of them underwent two re-interventions. In two more cases the traditional endoscopic treatment was completed in two stages due to the large size of diverticulum. No recurrence of symptoms was observed after tunnel technique.
Conclusion: Tunnel surgery is a pathogenetically justified method of treating Zenker's diverticulum as a neuromuscular disease. We suppose that today the tunnel technique stands to be the preferable treatment option of the Zenker's diverticulum.
Disclosure: Nothing to disclose

P0880 PREVALENCE OF PRECANCEROUS CONDITIONS AND LESIONS OF THE STOMACH IN CANDIDATES FOR BARIATRIC SURGERY

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Introduction: Intestinal type gastric adenocarcinoma is preceded by a long lasting multistep precancerous process. Patients with chronic atrophic gastritis and/or intestinal metaplasia are at higher risk for gastric adenocarcinoma. Endoscopic surveillance is recommended to patients with extensive atrophy and/or intestinal metaplasia [1]. Obesity is a worldwide health problem. Surgical treatment has been shown to be the most effective treatment for severe obesity and also for its complications. Roux-en-Y gastric bypass (RYGB) is one of the most commonly performed bariatric procedures. Although gastric cancer in the excluded stomach after gastric bypass is rare [2], concerns about the risk of leaving a premalignant lesion in the excluded stomach after RYGB persist. Consensus on the necessity of esophagogastroduodenoscopy (EGD) before bariatric surgery is lacking, as well as an absence of recommendations on precancerous conditions and lesions surveillance after RYGB.
Aims and Methods: To estimate the prevalence of precancerous conditions and lesions of the stomach from patients undergoing bariatric surgery, demographics, clinical data, endoscopic and histopathological findings of preoperative EGD with biopsies performed between January 2012 and December 2017 were retrospectively reviewed.
Results: A total of 319 patients were included with a median age of 44 years (interquartile range 36–52 years); 75.2% (n = 240) were female. *Helicobacter pylori* infection was positive in 58.9% of the patients (n = 178). A positive family history of gastric cancer was present in 3.4% (n = 11). The most commonly performed bariatric procedure was RYGB (37.9%, n = 121), followed by sleeve gastrectomy (SG, 1.6%, n = 5). The remainder patients were awaiting RYGB (27.9%, n = 89), were under preoperative evaluation (24.1%, n = 77) or had contraindication/refused surgery (8.5%, n = 27). Regarding histopathological findings, 4.7% (n = 15) of the patients showed normal gastric mucosa; 63.9% (n = 204) showed chronic gastritis only; 17.5% (n = 56) atrophic gastritis; 13.7% (n = 44) intestinal metaplasia. Importantly, 11.6% (n = 37) of patients showed extensive atrophy and/or intestinal metaplasia. Thirteen of these patients were submitted to RYGB. No dysplastic lesion was found.
Conclusion: The prevalence of precancerous conditions of the stomach in candidates for bariatric surgery is considerable. The management of these patients remains unclear, both regarding the optimal surgical procedure choice (RYGB vs SG) and surveillance of the remnant gastric mucosa in those patients submitted to RYGB bariatric surgery.
Disclosure: Nothing to disclose

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P0881 GASTRIC PRESSURE AND ESOPHAGEAL REFLUX EXPOSURE SUGGEST THAT OMEGA-LOOP BYPASS IS DIFFERENT FROM BILLROTH II

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Introduction: Obesity is a global epidemic and consequently bariatric surgery is increasingly performed. More recently, omega-loop gastric bypass (OGB), consisting primarily of a long linear lesser-curvature gastric tube with a terminolateral gastro-enterostomy 180–200 cm distal to the ligament of Treitz, was introduced. Thousands of these procedures have now been performed globally, being considered a safe and effective option for morbid obese patients. Despite positive effect in terms of weight loss and improvement of obesity-related co-morbidities, there are concerns about symptomatic biliary reflux gastritis and esophagitis requiring revision. Concerns have also been expressed due to chronic biliary reflux, because of a similarity with old Billroth II (BII) procedure that exposed patients to the risk of gastric cancer. However, scarce data are available on the physiopathological effect of these two procedures on gastro-esophageal function.
Aims and Methods: Since gastric and esophageal reflux can depend from proximal gastric pressure, we aimed at assessing the esophagogastric junction (EGJ) function, esophageal peristalsis and reflux exposure using high-resolution manometry (HRM) and impedance-pH monitoring (MII-pH) after OGB and BII.
Methods: Obese (body mass index, BMI, >35) patients underwent symptomatic questionnaires (GerdQ), endoscopy, HRM and MII-pH before and one year after OGB. We enrolled only obese without dysmotilty or any evidence of GERD. Intragastric pressures (IGP) and gastroesophageal pressure gradient (GEPG) were calculated. Esophageal motor function and EGJ were classified according to Chicago Classification V. 3. EGJ contractile integral (EGJ-CI) was also calculated. Total acid exposure time (AET %), total number of refluxes and symptom association probability (SAP) were assessed. A group of patients who underwent BII, referred for follow-up, was studied with the same protocol to serve as the control population.
Results: We enrolled 22 OGB patients and 12 BII subjects. After surgery, none of the patients reported de novo heartburn or regurgitation. At endoscopic follow-up 1 year after surgery, esophagitis was absent in all patients and no biliary gastritis or presence of bile was recorded. Manometric features and patterns did not vary significantly after surgery, whereas IGP and GEPG statistically diminished (from a median of 15 to 9.5, $p<0.01$, and from 10.3 to 6.4, $p<0.01$, respectively) after OGB. BII subjects had significant lower values in IGP (a median of 4.2, $p<0.001$), and similar GEPG 4.3, p = n.s. LES pressure as well as EGJ-CI were significantly lower in BII subjects than OGB ones (13 vs 22 mmHg, $p < 0.05$, and 11 vs 21.5 mmHg*cm, $p < 0.05$, respectively). A dramatic decrease in the number of reflux events (from a median of 41 to 7; $p<.01$) was observed after OGB, whereas BII patients had a statistically significant higher values in esophageal acid exposure and number of reflux episodes (57 vs 7; $p<0.001$), in particular in weakly alkaline reflux (38 vs 0; $p < 0.001$).
Conclusion: In contrast to BII, OGB did not expose to gastroesophageal reflux and in particular to weakly alkaline reflux. Also the difference in IGP and in GEPG as assessed by HRiM suggests that gastric bile reflux can occur more easily in BII than in OGB and that these two techniques share more differences than analogies.
Disclosure: Nothing to disclose

P0882 LAPAROSCOPY AND ENDOSCOPY COOPERATIVE SURGERY FOR GASTRIC TUMOR

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Introduction: Laparoscopic wedge resection is widely performed for managing gastric submucosal tumors (SMTs) that measure ≤5 cm in diameter. Laparoscopy and Endoscopy Cooperative Surgery (LECS) is performed to ensure a sufficient margin while avoiding deformation or stenosis.
Aims and Methods: We conducted a retrospective review of the data of 83 patients who underwent LECS for SMTs or early gastric cancers at our institution between April 2012 and February 2018. While Non-exposed Endoscopic Wall-inversion Surgery (NEWS) and classical LECS predominantly were performed for intra luminal tumors, for extra luminal tumors, we adopted the combination of laparoscopic approaches to neoplasia with non-exposure technique (CLEAN-NET).
Results: The patients were 58.3 ± 14.2 years old. The male:female ratio was 44:39. The BMI was 22.5 ± 3.8 kg/m2. The tumor was located in the upper-/middle-/lower-third of the stomach in 55/21/7 cases. The operation time was 200.5 ± 66.4 min, and the intraoperative blood loss was 4.8 ± 12.2 cc. The major axis diameter of the tumors was 28.9 ± 11.8 mm. The histological tumor types included GIST (n = 41), leiomyoma (n = 17), schwannoma (n = 6), early gastric cancer (n = 8), etc. The surgical procedure consisted of classical LECS/CLEAN-NET/NEWS in 18/17/48 cases; all early gastric cancers were treated by NEWS. Postoperative resumption of water intake was 1.9 ± 0.9 days after the surgery, while that of oral meal intake was 3.3 ± 1.0 days. The postoperative hospital stay was 8.7 ± 3.8 days. The serum levels of C-reactive protein on POD1 and POD3 were 3.1 ± 1.9 and 4.3 ± 3.4 mg/dl, respectively.
The postoperative complications were anastomotic stenosis (n = 1), delayed gastric emptying (n = 5), exacerbation of GERD (>Grade II by the Clavien-Dindo classification) (n = 4).
In the patient group that developed complications, the postoperative resumption of water intake was later, and the postoperative hospital stay was longer as compared to the group without complications (p = 0.028, 0.006). There was the tendency for the tumor located in the lesser curvature or post wall to become postoperative complications (p = 0.051). No relationship was observed between the likelihood of development of complications and the tumor malignancy.
Conclusion: Use of minimally invasive surgical procedures such as LECS could allow deformation, stenosis and extent of resection to be minimized in resection of gastric tumors. LECS including NEWS and CLEAN-NET are feasible and effective for gastric tumors.
Disclosure: Nothing to disclose

P0883 SHORT-TERM OUTCOMES OF LAPAROSCOPIC DISTAL GASTRECTOMY FOR GASTRIC CANCER AMONG ELDERLY PATIENTS DETERMINED USING COMORBIDITY PREDICTIVE FACTORS

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Introduction: Laparoscopic distal gastrectomy (LADG) is a recent development in minimally invasive surgery for early gastric cancer in Japan, where the rate at which the population is aging is the highest worldwide. However, whether this procedure is safe and effective for elderly patients with preoperative comorbidities remains unknown. This report describes the short-term findings of a retrospective study of LADG.
Aims and Methods: Between January 2005 and December 2016, 166 patients with gastric cancer underwent LADG at our hospital, where the indication for LADG is cStage IA (T1N0M0) or cStage IB (T2N0M0). Patients with lymph node metastasis were excluded. We introduced a delta-shaped anastomotic procedure for gastrojejunostomy during 2012, which allowed a totally laparoscopic procedure. We compared 50 and 116 patients aged ≥75 (elderly) and <75 (younger) years, respectively, who underwent LADG. Preoperative physical status was assessed using the American Society of Anesthesiologists Physical Status (ASA-PS) Score, the Charlson Comorbidity Index (CCI), and the Prognostic Nutritional Index (PNI). The CCI is thought to predict the one-year mortality of patients with various comorbidities such as heart disease, AIDS, chronic lung disease, or cancer. The PNI was designed to indicate the risk of a poor outcome after surgery based on an assessment of nutritional status.
Results: Demographics of the patients, namely sex, tumor lesion, histology, and hemoglobin value, did not significantly differ. However, the mean ASA-PS score and CCI were significantly higher in the elderly group than in the younger group (1.29 vs. 1.14 and 0.60 vs. 0.28, respectively). In addition, the PNI was significantly lower in the elderly group than in the younger group (50.2 vs. 52.7). Surgical duration, blood loss, lymph node clearance, and length of postoperative hospital stay did not significantly differ between the groups. Cardiorespiratory and surgical complications developed in 2 (4.0%) and 3 (2.6%) of the elderly patients and in 5 (10%) and 12 (10%) of the younger patients, respectively, but intraoperative and postoperative complication rates did not significantly differ between them. Thus, significant complications did not arise in either group.
Conclusion: Laparoscopic distal gastrectomy for early gastric cancer is a safe, effective, and minimally invasive surgical procedure for elderly patients.
Disclosure: Nothing to disclose

P0884 CLINICOPATHOLOGIC CHARACTERISTICS RELATED TO LYMPH NODE METASTASIS IN EARLY GASTRIC CANCER AFTER GASTRECTOMY

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Introduction: Early gastric cancer (EGC) was defined as tumour confined to the mucosa (T1a) or submucosa (T1b), irrespective of the presence of lymph node metastasis. Endoscopic treatment has became the first choice for EGC. However, endoscopic treatment of EGC was limited to the lesions that have low risk of lymph node metastasis (LNM) because of the inability to carry out lymph node dissection. We aimed to clarify the clinicopathologic characteristics related to lymph node metastasis in early gastric cancer and provide an appropriate strategy for patients with EGC.
Aims and Methods: Clinicalpathologic characteristics of patients who underwent curative gastrectomy with lymph-node dissection and finally confirmed as EGC by pathology at the West China Hospital of Sichuan University between November 2008 and October 2017 were retrospectively analysed. The clinicopathologic characteristics of lymph node metastasis group and non-metastasis group with EGC were compared. Logistic regression was used to analyze the risk factors of lymph node metastasis by univariate and multivariate analysis.
Results: Among the 5156 gastric cancer patients who underwent gastrectomy, 1044 patients (20.2%) showed early gastric cancer. Except for 111 patients without complete pathological information, 933 patients were finally enrolled in the present study. Among these 933 patients showing EGC, 246 patients (26.4%) had lymph node metastasis. The univariate analysis revealed that LNM was significantly associated with age (p = 0.024), sex (p < 0.001), tumour size (p < 0.001), tumour depth (p < 0.001), tumour location (p < 0.001), tumour differentiation (p < 0.001), perineural involvement (p = 0.043) and lymphovascular involvement (p < 0.001). Multivariate analysis confirmed that female (odds ratio [OR] 1.603; 95% confident interval [CI], 1.155–2.255), tumour size >2 cm but ≤ 3 cm (OR 1.572; 95% CI 1.082–2.285), tumour size > 3 cm (OR 1.61; 95% CI, 1.05–2.48), location in the lower third of the stomach (OR 4.090; 95% CI 1.387–12.060), submucosa tumour (OR 3.571; 95% CI 2.473–5.157), histological undifferentiation (OR 2.066; 95% CI 1.364–3.047), and lymphovascular involvement (OR 4.073; 95% CI 2.455–6.756) were independent risk factors for lymph node metastasis (p < 0.05). The rate of LNM was 1.79% in patients with EGC who fulfilled absolute indications of endoscopic resection but actually underwent gastrectomy, while the rate of LNM in patients with EGC who met the expanded indications was 10.86%. Analysis of LNM of patients with T1a tumours showed that patients with T1a tumours, differentiation and tumour located in the upper or middle third of the stomach, irrespective of the presence of lymphovascular involvement, sex and tumour size did not show LNM.
Conclusion: Female, tumour size >2 cm, submucosal tumour, undifferentiated tumour, tumour located in the lower third of stomach and lymphovascular invasion were independent risk factors for LNM. In addition, patients with T1a tumours, differentiation and tumour located in the upper or middle third of the stomach, irrespective of the presence of lymphovascular involvement, sex and tumour size were appropriate for endoscopic resection.
Disclosure: Nothing to disclose

P0885 OPERATIVE MANAGEMENT OF PATIENTS WITH METASTATIC GASTROINTESTINAL STROMAL TUMORS: A POPULATION-BASED RETROSPECTIVE STUDY

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Introduction: Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors with a varying malignancy potential ranging from virtually indolent tumors to rapidly progressing cancers. There is no consensus about the role of surgical resection in the treatment of patients with metastatic GISTs.
Aims and Methods: We aim to evaluate the impact of operative management on survival outcomes in patients with metastatic-GIST based on US-population. Patients with GISTs were identified from the Surveillance Epidemiology and End Results (SEER) registry between 2001 to 2014. Kaplan-Meier analysis and Cox regression were performed to identify the influence of surgery on overall survival (OS) and GISTs-specific survival (GSS).
Results: A total 5773 patients diagnosed with GISTs, including 1392 metastatic-GISTs patients and 4381 non-metastatic GISTs patients. Compared with the non-metastatic GIST patients, patients with stomach GISTs had a smaller proportion among metastatic GISTs patients (621[44.6%] vs. 2611[59.6%], p < 0.001) and much less metastatic patients were managed operatively (728[52.3%] vs. 4068[92.8%], p < 0.001). Among patients with metastatic GISTs, Kaplan-Meier analysis indicated that surgical management was associated with improved survival. The five-year OS rates for metastatic patients with and without operative management were 55.3% and 27.9%, with median survival time of 85.6 and 46.5 months, respectively (p < 0.001). The five-year GSS rates were 59.5% and 32.1%, with median survival time of 94.2 and 53.0 months, respectively

($p < 0.001$). Cox regression multivariate analysis of metastatic patients showed that non-surgical management was associated with a more than 2-fold increased risk death form GISTs (RR: 2.25; 95% CI, 1.88–2.69; $p < 0.001$).
Conclusion: Surgical resection is associated with improved OS and GSS in metastatic GISTs patients.
Disclosure: Nothing to disclose

P0886 BILE DUCT INJURY AFTER CHOLECYSTECTOMY: NEW CLASSIFICATION AND NOVEL APPROACH FOR THE MANAGEMENT IN EMERGENCY SITUATIONS. DATA OF 178 CASES

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Introduction: We have analysed our data or managing bile duct injury and have put forth a new classification more relevant in our clinical practice.
Aims and Methods: From October 2010 to May 2017, total 178 patients of mean age 51 (range 30–74) years were referred to our unit with bile duct injury following or during laparoscopic cholecystectomy. Laparoscopic cholecystectomy was described as 'uneventful' in 45% and 'difficult' in 55% patients; 19 injuries were recognized at operation. Rest patients were transferred on 7th post operative day on an average. Exploration and complete diversion of bile was done in initial 12 patients along with feeding jejunostomy (for bile refeeding) of type II & III. Later on all patients were internally drained irrespective of type II / type III, and feeding jejunostomy was not done. Average time for hepatico jejunostomy – day 62 following initial surgery. Out of 74 patients of type II and III only 39 patient required Hepatico jejunostomy (52.7%), one needing surgery was lost to follow up, rest 34 (45.9%) were managed successfully with endobiliary repeat/multiple stenting. All patient with type I injury were subjected to ERC-papillotomy and stenting of common bile duct was done successfully. Out of 102, 91 patients had drains kept during surgery and was draining bile, 11 patients had Biloma which was drained with pigtail catheter percutaneously. Two patients died, one was referred on day 11, after redo laparoscopy which was done on post of day 6, patient was in sepsis, ARDS & MODS. Was operated for biliary peritonitis but could not be saved. Another patient was referred on post operative day 12 with biliary fistula from drain and peritonitis with liver failure. On exploration found to have type 3B Bile duct injury with portal vein clipping and complete thrombosis with ischemic liver. This patient died of liver failure with sepsis post operatively.
Results: We propose new classification for bile duct injury according to its prevalence in our region and our management recommendations.
TYPE I: Cystic duct stump blow out.
TYPE II: Partial clip on CBD with or without cystic duct stump blow out or lateral injury.
TYPE III: a. Segment loss of CBD < 2cm.
b. CBD / CHD > 2 cm extending upto hilum.
c. Hilar injury with separate sectoral ducts. T
d. Any of above with ligation of right hepatic artery.
TYPE IV: Isolated sectoral duct injury.
Distribution of our cases according to types.
Number of patients: Type I – 102, Type II – 34, Type IIIA – 19, Type IIIB – 15, Type IIIC – 4, Type IIID – 2, Type IV – 2
Conclusion: Bile duct injury following laparoscopic cholecystectomy is a complex management problem and results in significant postoperative morbidity.
Bile duct injury recognized intraoperatively always does better irrespective of severity of injury.
More complex injuries are better drained first and then later date reconstruction is advisable.
We propose use of endobiliary plastic stents (routinely used following ERC) for internal drainage and repair of bile duct over stent without use of conventional T tube and if required later date hepatico jejunostomy can be done.
ERC is used in type I and II injury and use of multiple stents after a salvage surgery and placing intra operative stents in 45.9% cases.
In presence of biliary sepsis and peritonitis, surgical lavage and endobiliary stenting is advisable before subjecting patients to ERC.
Disclosure: Nothing to disclose

P0887 BRAUN ENTEROENTEROSTOMY AFTER PARTIAL PANCREATICODUODENECTOMY AND CHILD RECONSTRUCTION DECREASES MORBIDITY, CLINICALLY RELEVANT PANCREATIC FISTULA, CLINICALLY RELEVANT DELAYED GASTRIC EMPTYING AND BILE LEAKS – A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Due to its high rates of postoperative mortality and morbidity, resections of the pancreas remain a high-risk operation. Since its first description by Kausch et al. and Whipple et al., several surgical reconstruction techniques have been introduced to minimize the risk for postoperative mortality and morbidity after pancreaticoduodenectomy/PD. These reconstruction techniques include the standard Child reconstruction defined as pancreatojejunostomy/PJ followed by hepaticojejunostomy/HJ and the gastrojejunostomy/GJ (s-Child), the s-Child reconstruction with an additional Braun enteroenterostomy (BE-Child) and the Isolated-Roux-En-Y-pancreaticojejunostomy (ISRY), in which the pancreas anastomosis is reconstructed in a separate loop after the GJ. Yet, no comparative systematic review with meta-analysis has been performed to assess the impact of these most commonly used reconstruction techniques on the postoperative course of patients undergoing PD.
Aims and Methods: This systematic review with meta-analysis aims to compare the effect of different reconstruction techniques on the postoperative course of patients after PD.
For this purpose, the Preferred-Reporting-Items-for-Systematic-review-and-Meta-Analysis/PRISMA-guidelines were used to conduct a systematic review with meta-analysis. Databases of Pubmed/Medline, Scopus, Cochrane Library and Web-of-Science were screened for relevant articles meeting predefined inclusion and exclusion criteria. Afterwards, data were extracted and pooled in meta-analysis calculating risk ratios/RR for postoperative complication rates between s-Child vs. BE-Child and s-Child vs. ISRY.
Results: Thereby, a total of 18 studies comparing the postoperative outcome of BE-Child or ISRY against s-Child could be identified. Neither BE-Child ($p = 0.47$) nor ISRY ($p = 0.95$) displayed any impact on postoperative mortality. Accordingly, the meta-analyses of ISRY could not reveal any relevant effect on postoperative morbidity ($p = 0.73$), postoperative pancreatic fistula/POPF Grade A/B/C ($p = 0.61$), clinically relevant POPF ($p = 0.79$), delayed gastric emptying/DGE Grade A/B/C ($p = 0.36$), clinically relevant DGE ($p = 0.16$) or bile leaks ($p = 0.56$) compared to s-Child. However, although the meta-analyses of BE-Child vs. s-Child could also not detect any differences in POPF ($p = 0.27$) and DGE ($p = 0.06$) in general, BE-Child was strongly associated with a decreased risk for overall morbidity ($p = 0.0002$), clinically relevant POPF ($p < 0.00001$), clinically relevant DGE ($p = 0.004$) and bile leaks ($p < 0.01$). In line with these results, BE-Child showed a decreased hospital stay ($p = 0.05$) but also an increased operation time ($p = 0.0002$) with no impact on haemorrhage ($p = 0.52$), surgical site infections ($p = 0.97$) and pulmonary complications ($p = 0.85$) compared to s-Child.
Conclusion: BE-Child favorably affects the outcome of patients after PD by decreasing the risk for morbidity, clinically relevant POPF, clinically relevant DGE and bile leaks. In contrast, no effect was visible for ISRY compared to s-Child. However, because of the low evidence of the included studies caused by the low number of participants of the randomized controlled trials and the retrospective character fo the studies, a randomized controlled trial is planned to confirm these results of the recent meta-analysis.
Disclosure: Nothing to disclose

P0888 PREVENTION OF POSTOPERATIVE BILE-LEAKAGE BY A NEWLY DESIGNED TISSUE SEALANT PATCH

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Introduction: Up to 10–15% of patients develop a bile-leakage after liver surgery, which increases the length of hospital stay as well as overall mortality and morbidity. However, with no effective preventive measure at hand, the surgical community is forced to accept bile-leakage as an unavoidable post-surgery complication.
Aims and Methods: To overcome the clinical challenge of post-operative bile leakage we developed a new tissue sealant patch to prevent this complication. The tissue sealant patch was designed in a multi angle approach including *in-vitro* comparison on tensile, burst pressure measurements and testing in a liver perfusion model with clinically relevant competitors. For *in-vivo* evaluation a porcine bile-leakage model was established and the tissue sealant patch was investigated in a prospective randomized animal trial with a suturing group and Veriset® group as controls.
Results: More than 30 different prototypes were screened *in-vitro*. The final selected sealant prototype showed superiority compared to clinical used competitors Tachosil®, Hemopatch® and Veriset® in tensile and burst pressure testing ($p < 0.05$ each). Moreover, the newly developed patch reduced the leakage rate in the liver perfusion model ($p < 0.05$). The pre-clinical performance of the sealant patch was confirmed in a porcine bile-leakage model. 21 animals were included in the study and randomized for treatment with the sealant, Veriset® or suturing ($n = 7$ each). After 7 days incidence of bile leakage was significantly lower in the sealant group compared to the Veriset® group ($p < 0.05$) and comparable to the suturing control group. These promising results were supported by strong bile containment and the formation of a smooth fibrous capsule by the sealant within one week. This was paralleled by the formation of neo bile ducts. Furthermore, no systemic or local side effects (e.g. bilioma) were seen.
Conclusion: The new designed sealant was as effective as suturing in preventing bile-leakage in our animal model. This was due to strong bile containment and formation of a fibrous capsule by the sealant within one week. The efficacy of the sealant was also histologically proven, as formation of neo bile ducts – which indicates a biliary obstruction – was detected. More importantly, no clinical relevant side effect of the sealant became evident. To our knowledge, this is the first report of a randomized trial showing the efficacy of a tissue sealant device for preventing postoperative bile leakage.
Disclosure: Nothing to disclose

P0889 SHORT-TERM SURGICAL MORBIDITY AND MORTALITY OF DISTAL PANCREATECTOMY PERFORMED FOR BENIGN VS MALIGNANT DISEASES: A NSQIP ANALYSIS

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Introduction: Distal pancreatectomy (DP) accounts for 25% of all pancreatic resections. Complications following DP occur in around 40% of the cases.

Aims and Methods: Few studies compared the clinical outcomes of distal pancreatectomy in benign versus malignant diseases.

We studied all patients undergoing DP from the National Surgery Quality Improvement Program (NSQIP) pancreatectomy participant use data specific file from 2014–2016. NSQIP includes prospective validated outcomes and anonymized data for patients' demographics, functional statuses, preoperative risk factors, laboratory data, and 30-day postoperative outcomes for patients undergoing major surgery in more than 500 hospitals. The primary outcome in this study was short term surgical morbidity and mortality. The patients were divided into 2 groups, those who underwent DP for benign diseases (DP-B) and those who underwent DP for malignant diseases (DP-M). We used the chi square test or Fisher's exact (when one or more cells had an expected frequency lower than 5) to compare categorical variables between the 2 groups. We used the independent t-test for continuous variables. We performed multivariate logistic regression to evaluate the association between benign or malignant distal pancreatectomies and 30-day postoperative outcomes. We included confounders into the models based on both clinical and statistical significance.

Results: Over the specified period, 1685 (47%) patients underwent DP-B and 1894 (53%) patients underwent DP-M. DP-M patients were significantly older, had significant longer operation time and hospital stay. The most common indications of DP-B and DP-M were mucinous cystic neoplasm (26.4%) and pancreatic adenocarcinoma (75%), respectively. Open DP was the most performed type of surgery for both benign (39%) and malignant (60%) lesions while laparoscopic DP was performed at a higher rate for benign indications (29%) compared to malignant ones (15%). Thirty-day mortality occurred in 0.4% of DP-B compared to 1.3% DP-M. Pancreatic fistula occurred in 20% of DP-B compared to 18% of DP-M. Moreover, composite morbidity (including thromboembolism, sepsis, wound infection, cardiac, respiratory, and urinary complications) were significantly higher in DP-M. On multivariate analysis, after adjusting for clinically relevant confounding factors, no significant difference was found in mortality or in developing a pancreatic fistula between the 2 groups. Bleeding ($p = 0.002$) and composite morbidity ($p = 0.01$) were significantly higher in the DP-M group. Among composite morbidities, thromboembolism was shown to be significantly associated with DP-M (OR = 2.1, $p = 0.0004$).

Conclusion: Our study showed that DP-M is significantly associated with higher composite morbidity, sepsis, and thromboembolism. However, no significant difference in mortality was found between DP-B and DP-M groups.

Disclosure: Nothing to disclose

P0890 VALIDATION OF DAY 1 DRAIN FLUID AMYLASE LEVEL FOR PREDICTION OF CLINICALLY RELEVANT FISTULA FOLLOWING DISTAL PANCREATECTOMY USING THE NSQIP DATABASE

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Introduction: In a previous multicenter study, post-operative day 1 drain fluid amylase level (DFA-1) level of 2000 was found to be most predictive of the development of clinically relevant post-operative pancreatic fistula (CRPOPF).

Aims and Methods: We aimed to validate the previously established cut-off level for DFA-1 after distal pancreatectomy using the NSQIP database.

Methods: Patients undergoing distal pancreatectomy from the National Surgery Quality Improvement Program (NSQIP) pancreatectomy specific PUF file from 2014–2016 were studied. We applied the DFA-1 of 2000 cut off to compare clinical outcomes in both groups. In order to validate the previously defined DFA-1 level, we performed a receiving operating characteristic (ROC) curve to independently determine the optimal cut-off value of DFA1.

Results: 1012 patients underwent DP. CRPOPF occurred in 206 (20.4%). Patients with DFA1 levels $\geq$ 2000 U/L were more likely to develop CR-POPF (32.5% vs 11.3%, $p < 0.0001$), to have a higher mean number of days before drain removal (8.86 versus 5.59, $p < 0.0001$), to have a drain 30-days post-operatively (12.7% versus 3.6%, $p < 0.0001$) and to undergo percutaneous drainage (13.8% vs. 9.7%, $p = 0.04$). Application of maximal Youden index calculated the DFA-1 level value at 2000 U/L with a sensitivity of 68.45% and a specificity of 63.65% for CR-POPF, with PPV and NPV of 32.49% and 88.75%, respectively and a Youden index of 0.32.

Conclusion: Using a different population of patients and a different data set as well as an independent analysis, we successfully validated a DFA1 of 2000 as striking the best balance of sensitivity and specificity for the detection of CR-POPF. The identified cut-off might be employed in the design of a trial of early drain removal in patients undergoing distal pancreatectomy.

Amylase cutoff	Sensitivity	Specificity	Youden's Index	Positive Predictive Value	Negative Predictive Value
500	84.95	34.86	0.20	25.00	90.06
1000	76.21	47.27	0.23	26.98	88.60
1500	71.84	55.96	0.28	29.42	88.61
2000	68.45	63.65	0.32	32.49	88.75
2500	61.17	70.10	0.31	34.33	87.60
3000	57.77	73.70	0.32	35.95	87.22
3500	55.83	75.43	0.31	36.74	86.98
4000	52.91	78.78	0.32	38.93	86.75
4500	49.03	81.51	0.30	40.40	86.22
5000	46.60	83.00	0.30	41.20	85.88

[Analyzing different cut-off values, using sensitivity, specificity, negative predictive value (NPV), Positive predictive value (PPV) and Youden Index]

Disclosure: Nothing to disclose

P0891 VALIDATION OF THE REVISED 2018 EUROPEAN GUIDELINE ON THE MANAGEMENT OF SURGICALLY REMOVED PANCREATIC CYSTIC NEOPLASMS WITH REGARD TO PATHOLOGICAL OUTCOME

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Introduction: The primary goal of management of patients with pancreatic cystic neoplasm (PCN) is to prevent malignancy, while avoiding unnecessary surgery.

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	Benign (n = 1,685)	Malignant (n = 1,894)	Unadjusted		Adjusted	
			OR (95% CI)	p-value	OR (95% CI)	p-value
Mortality	7 (0.4)	24 (1.3)	3.08 (1.32–7.16)	0.006	2.29 (0.93–5.62)	0.07
Bleeding	180 (10.7)	268 (14.1)	1.38 (1.13–1.69)	0.002	1.37 (1.12–1.68)	0.002
Return to Operation Room	49 (2.9)	79 (4.2)	1.45 (1.01–2.09)	0.04	1.42 (0.98–2.07)	0.07
Composite morbidity	282 (16.7)	397 (21.0)	1.32 (1.11–1.56)	0.001	1.26 (1.05–1.50)	0.01
Thromboembolism	33 (2.0)	77 (4.1)	2.12 (1.40–3.21)	0.0003	2.12 (1.40–3.21)	0.0004
Sepsis	97 (5.8)	130 (6.9)	1.21 (0.92–1.58)	0.17	1.32 (1.00–1.74)	0.05

[Table comparing outcomes between benign and malignant distal pancreatectomies, before and after adjusting for clinically confounding variables]

Surgical resection is generally accepted in patients with advanced neoplasia (AN) (high-grade dysplasia (HGD) or malignancy). Currently, the main challenge is to determine the risk of progression to AN in patients with PCNs. It is unclear whether the revised 2018 European guideline is more accurate for predicting AN than the 2013 European guideline. Therefore, the aim of this study was to evaluate the clinical usefulness of the predictors of malignancy listed in the 2018 European guideline and to validate the diagnostic accuracy of the 2018 European guideline with reference to the 2013 European guideline and to the revised 2017 IAP guideline.
Aims and Methods: Patients who underwent pancreatic resection were extracted from our prospective pancreatic cyst database (2006-present). The final histopathological diagnosis was compared with the initial indication for surgery stated by the 2013 European, 2017 IAP and 2018 European guidelines. We considered surgery in retrospect justified for AN, solid pseudopapillary neoplasms, cystic neuroendocrine tumors, and symptom improvement. Furthermore, we evaluated the patients with IPMN separately: receiver operating characteristics (ROC) curves were calculated and compared to measure diagnostic value.
Results: Overall, 172 underwent surgical resection. In hindsight, based on the histopathological outcomes and symptom improvement, surgery was indicated in 72/172 patients (41.9%). Ninety-two patients with IPMN (11 MD-IPMN, 55 MT-IPMN, 26 SB-IPMN) were included in the analysis to identify the value of the 2018 European guideline in identifying AN preoperatively. Of these, 44 were diagnosed with AN pathologically. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the 2018 European criteria were 94.7%, 29.6%, 48.7%, 88.9%, 56.5%, respectively. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the 2013 European guideline and 2017 IAP guideline were 100.0%, 9.3%, 43.7%, 100.0%, 46.7% and 94.7%, 22.2%, 46.2%, 85.7%, 52.2%, respectively. ROC comparison analysis showed that the 2018 European guideline criteria were superior to the 2013 European guideline criteria ($p = 0.02$) and to the 2017 IAP guideline ($p = 0.04$) in identifying AN in IPMN.
Conclusion: The revised 2018 European guideline criteria were superior to the 2013 European guideline criteria and 2017 IAP guideline criteria in identifying AN in IPMN in this retrospective analysis.
Disclosure: N.C.M. van Huijgevoort: None S. ten Bokkel-Huinink: None S.J. Lekkerkerker: None I. Somers: None M. Del Chiaro: None O.R. Busch: None P. Fockens: received consulting fees from Boston Scientific, Cook Medical, Fujifilm, Medtronic and Olympus. M.G. Besselink: None J.E. van Hooft: received research grants from Cook Medical and Abbott, and consulting fees from Boston Scientific and Medtronic

TUESDAY, OCTOBER 23, 2018 09:00–17:00

IBD II – Hall X1

P0892 *ENTEROBACTERIACEAE* ARE ESSENTIAL FOR BENEFICIAL EFFECTS OF *SACCHAROMYCES BOULARDII* CNCM I-745 AND DELETERIOUS EFFECTS OF *CANDIDA ALBICANS* IN COLITIS

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Introduction: The balance between host and microbes in the gut drives the intestinal homeostasis and prevents inflammatory situations such as inflammatory bowel disease (IBD). However, interactions between different microbial kingdoms, bacteria and fungi for example, and their effects on the intestinal homeostasis remain poorly understood. Here, we studied specific bacteria – fungi interactions and their implications in intestinal inflammation.
Aims and Methods: Female C57BL/6 mice were treated for 7 days with 1g/L vancomycin in drinking or 1g/L colistin (oral gavage) in order to deplete Gram positive and *Enterobacteriaceae* respectively. In addition, the effect of oral gavage with either the probiotic yeast *Saccharomyces boulardii* CNCM I-745 (Biocodex-Gentilly) or the pathogenic yeast *Candida albicans* were evaluated. After 7 days of antibiotic treatment and fungi supplementation, colitis was induced with 2% Dextran Sodium Sulphate (DSS) in drinking water for 7 days followed by a recovery period of 5 days with water. Mice were sacrificed at day 0, day 7 and day 12 post-DSS. The development of colitis and its recovery were assessed by monitoring daily weight loss and disease activity index from day 0 to day 12. Lipocalin levels, histological analysis as well as bacterial (16S sequencing) and fungi (ITS2 sequencing) microbiota compositions and diversity were monitored after antibiotic exposure and during colitis.
Results: In wild-type conventional mice, administration of *Saccharomyces boulardii* reduced DSS-induced colitis severity while administration of *Candida albicans* had the opposite effect. Antibiotics treatments strongly modified the observed phenotype. Vancomycin-treated mice were fully protected from colitis. Colistin treated-mice had a conserved colitis phenotype but were not affected anymore by administration of beneficial (*S. boulardii*) or pathogenic (*C. albicans*) fungi. 16S and ITS2 sequencing analysis showed that both fungal and bacterial microbiota were altered in colistin-treated mice. Bacteria-fungi abundance correlations were dramatically decreased in colistin-treated mice compared to vancomycin-treated and control mice suggesting that colistin-sensitive bacteria are involved in interactions with fungi. As expected, microbiota composition analysis showed that *Enterobacteriaceae* were depleted in colistin treated-mice. To test whether *Enterobacteriaceae* are required for positive or negative effects of fungi in colitis setting, colistin-resistant *Escherichia coli* (a major *Enterobacteriaceae* member) were administered in colistin-treated mice and then submitted to colitis. Restoring an *Enterobacteriaceae* population by administrating colistin-resistant *E. coli* reestablished both the beneficial effects of *S. boulardii* and the pathogenic effects of *C. albicans* on colitis severity. The mechanisms are not fully identified but involve an improved gut colonization of fungi in presence of *Enterobacteriaceae*.
Conclusion: The probiotic yeast *Saccharomyces boulardii* CNCM I-745 reduces colitis severity whereas the pathogenic yeast *Candida albicans* worsens it. These effects are influenced by *Enterobacteriaceae*, at least partly through an improved gut colonization of fungi. These results provide new insights into the role of interkingdom functional interactions in intestinal physiopathology and in IBD pathogenesis.
Disclosure: Nothing to disclose

P0893GUT INFLAMMATION DEMONSTRATES A CIRCADIAN RHYTHM AND THE CLOCK IS DISRUPTED IN A MURINE MODEL OF COLITIS

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Introduction: The circadian clock oscillates over a 24-hour (or circadian) cycle and is entrained to external stimuli such as light and food availability. At the molecular level, these circadian oscillations are generated by transcriptional-translational feedback loops. Immune cells show circadian rhythms in their function and consequently the symptoms of many inflammatory diseases are diurnal. Phenotypically, patients with IBD do not have diurnal symptoms, but there is emerging evidence of circadian dysrhythmia at a cellular level in the gut and gastrointestinal conditions are more prevalent in shift workers.[1,2] The interplay between gut inflammation and circadian biology requires further investigation.
Aims and Methods: The aim of this study was to examine circadian variation in inflammation within the colonic lamina propria, using a mouse model of colitis. To achieve our aims, C57BL/6 mice were given 2% (w/v) DSS in drinking water *ad libitum* for 4 days, followed by 4 days of water. Control mice drank water throughout. Mice were sacrificed at 4 different times across the circadian day: Zeitgeber Time (ZT)0 (lights on); ZT6 (mid-light); ZT12 (lights off) or ZT18 (mid-dark). Samples of colon were taken for histological staining and analysis of clock and inflammatory gene expression. Faeces were isolated for calprotectin assessment by ELISA. Colonic lamina propria immune cells were isolated from inflamed and naïve mice by enzymatic digestion and immune cell populations were quantified using flow cytometry.
Results: Mice administered DSS developed colitis, demonstrated by an average weight loss of −15% body weight (compared with +5% weight gain in controls), significantly greater spleen weight and reduced colon length. Furthermore, histological analysis confirmed inflammation within the colon. Flow cytometry revealed increased populations of neutrophils, monocytes, macrophages and dendritic cells within the lamina propria following DSS treatment.
Gene expression of pro-inflammatory cytokines (*il-1b*, *il-6*, *ccl2, cxcl1* and *cxcl5)* was significantly elevated in mice with DSS compared with controls at all time points. However, a subset of cytokines (*ccl2* and *cxcl1*) showed dramatically enhanced expression during the night (ZT18) compared to the day (ZT6), with up to a 40-fold increase in *ccl2*.
This localised inflammation was accompanied by dampening of the diurnal variation of clock gene expression, most notably *rev-erbα*, in the colon. Of interest, attenuated expression of *rev-erbα* was also noted in the liver of DSS treated mice.
Conclusion: We have demonstrated circadian variation in pro-inflammatory responses in a murine model of colitis, which coincides with dampening of rhythms in clock gene expression. This early work suggests colitis is a circadian disease and opens the possibility of identifying the circadian clock mechanism as a potential therapeutic target.
Disclosure: Nothing to disclose

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P0894 ADMINISTRATION OF IMM-124E AMELIORATES COLITIS

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Introduction: Inflammatory bowel disease (IBD) is accompanied by lesions in the epithelial barrier, which allow translocation of bacterial products from the gut lumen to the host's circulation. Systemic exposure to certain bacterial products, including lipopolysaccharide (LPS) elicits strong immune responses, and thereby contributes to the pathogenesis and perpetuation of IBD. LPS exposure in

particular, promotes production of pro-inflammatory cytokines, and affects immune cell activation. Colostrum contains high levels of immunglobulins (Ig), which neutralize bacteria-derived antigens in the intestine, and thereby prevent systemic translocation of bacterial products. IMM-124E is a colostrum-based product, containing high levels of anti-LPS IgG, and therefore prevents systemic exposure to LPS. Since LPS is involved in IBD pathogenesis, we here investigated whether IMM-124E can ameliorate symptoms of intestinal inflammation.
Aims and Methods: Acute colitis was induced in WT C57B6 mice by administration of 2% DSS in the drinking water for 7 days. T cell transfer colitis was induced via transfer of 0.25x10^6 naïve T cells into $RAG2^{-/-}$ C57B6 mice. IMM-124E was administered daily by oral gavages throughout the experiment (acute DSS colitis) or upon onset of colitis symptoms, namely weight loss and macroscopically inflamed colon as visible by colonoscopy (T cell transfer colitis).
Results: In acute DSS-induced colitis, treatment with IMM-124E significantly ameliorated colitis, as observed by reduced weight loss ($p < 0.01$), lower endoscopic colitis score (MEICS score; $p < 0.05$), decreased myeloperoxidase levels ($p < 0.01$), and reduced shortening of the colon ($p < 0.05$). Histology of the terminal and proximal colon confirmed reduced colitis ($p < 0.05$). In the T cell transfer colitis model, therapeutic IMM-124E administration had similar effects and resulted in significant alleviation of colitis symptoms, including reduced disease activity scores and reduced levels of macroscopically detectable colitis in mouse endoscopy ($p < 0.05$ for both). Maximum anti-inflammatory effects were detected by an IMM-124E concentration of 100 mg/kg body weight. At 25 and 500 mg/kg IMM-124E, the anti-inflammatory effects were also detectable, but clearly less pronounced. Further, histology revealed reduced levels of infiltrating immune cells, and less pronounced mucosal damage ($p < 0.05$). In line with these findings, levels of IFN-g+ T cells and IL-17+ T cells were clearly reduced in mesenteric lymph nodes ($p < 0.01$) and the lamina propria ($p < 0.05$), while levels of FoxP3+ regulatory T cells were enhanced ($p < 0.01$) in mice treated with IMM-124E, when compared to control mice that received BSA.
Conclusion: Our results demonstrate that treatment with IMM-124E significantly reduces intestinal inflammation via reducing the accumulation and differentiation of pathogenic T cells, while concomitantly enhancing the induction of regulatory cells. This may suggest that inhibiting LPS-mediated effects on the mucosal immune system ameliorates colitis. Summarized, our findings indicate that IMM-124E administration might represent a novel therapeutic strategy to induce or maintain remission in IBD patients.
Disclosure: Nothing to disclose

P0895 EPITHELIAL FERROPTOSIS IS A FEATURE OF CROHN'S DISEASE WHICH IS INDUCED BY WESTERN-DIET-DERIVED ARACHIDONIC ACID

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Introduction: Ferroptosis is an iron-dependent cell death mechanism which is defined by increased lipid peroxidation (LPO) and the inability of inhibitors for other cell death mechanisms to interfere with the ongoing process of cellular demise. Glutathione peroxidase 4 (GPx4) regulates this non-apoptotic cell death mechanism [1, 2]. A genome-wide association study identified GPx4 as a risk gene for the development of Crohn's disease (CD) [3]. However, CD has not been linked to ferroptosis or LPO in the intestine.
Aims and Methods: In this study we analysed ferroptosis and LPO in intestinal epithelial cells from patients with inflammatory bowel disease and analyzed the impact of GPX4-deficiency on intestinal-epithelial-cell (IEC)-derived inflammation.
Biopsies were obtained from lesional and non lesional mucosa of CD patients and healthy controls undergoing routine colonoscopy. One biopsy was paraffin embedded and used for IHC analysis. From a second biopsy an epithelial cells enriched single cell suspension was isolated and used for protein and RNA expression measurements. For in vitro experiments MODE-K cells, a murine small intestinal cell line, were used. Silencing for GPx4 was done for 24 hours prior to stimulating cells. ACSL4 knockout was obtained by CrisprCas9 editing of MODE-K cells. LPO was measured by staining for 4-HNE (human samples), BodipyC11 assessed lipid peroxidation by flow cytometry.
Results: In IEC enriched fractions from biopsies derived from the lesional mucosa of CD patients GPx4 activity and expression is diminished, compared to healthy controls. In line with this, CD patients exhibited increased LPO indicated by increased 4-HNE immunoreactivity. To further investigate the effect of diminished GPx4 in IECs we silenced MODE-K cells for GPx4 (siGPx4). SiGPx4 cells underwent ferroptosis, shown by increased LPO and increased cell death which could be prevented by vitamin e and ferrostatin, but not by inhibitors of necrotic or apoptotic cell death. SiGPx4 cells showed a markedly increased pro-inflammatory response to stimulation with arachidonic acid (AA), a polyunsaturated fatty acid largely contained within a westernised diet. Similar to ferroptosis, AA-induced inflammation was controlled by ACSL4 and lipoxygenases.
Conclusion: Reduced GPx4 activity in intestinal epithelial cells, as observed in Crohn's disease, leads to ferroptosis and promotes inflammation induced by arachidonic acid. This inflammatory response is controlled by ACSL4 and lipoxygenase-mediated LPO within intestinal epithelial cells. We suggest that ferroptosis is a feature of Crohn's disease which could be triggered by dietary-derived compounds such as long-chain fatty acids.
Disclosure: Nothing to disclose

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P0896 LESION-SPECIFIC GENE EXPRESSION IN THE EPITHELIAL CELLS OF CROHN'S DISEASE BY COMPARING SMALL INTESTINAL ORGANOIDS FROM ACTIVE AND INACTIVE LESION IN THE SAME PATIENT

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Introduction: Patients with inflammatory bowel disease (IBD) mainly present with ulcerative colitis (UC) or Crohn's disease (CD). Recently, it has been recommended that mucosal healing is therapeutic goal of IBD because dysfunction of epithelial cells might cause frequent relapse. However, the pathogenesis of epithelial cells in IBD remains unknown. Especially, although skip lesions in small intestine are often shown in the patients with CD, the mechanism to develop ulcer and stenosis at a certain part in entire small intestine remains unknown. We have previously identified the lesion-specific epithelial cell function in UC to compare the gene expression between organoids generated from active and inactive lesion of colon in the same patient with UC (DDW 2018).
Aims and Methods: We therefore aimed to identify lesion-specific genes to compare the gene expression between the organoids generated from active and inactive lesion of small intestine in same patient with CD.
Human small intestinal organoids were generated from both active and inactive lesion of the small intestinal tissue surgically resected from an identical patient with CD. Both organoids were cultured for a month to remove the effect of inflammation in tissue before the resection. Comprehensive gene expression profiles in the organoids were assessed by microarray analysis. The expression of genes upregulated or downregulated (>2 fold change) between active and inactive lesion-derived organoids were selected. The expression of selected genes was confirmed by RT-PCR using three pairs of small intestinal organoids in addition to another two patients with CD. This study was approved by the ethics committee.
Results: We have established both small intestinal organoids generated from active and inactive lesion of same CD patient. The configuration and growth patterns of the organoids from active lesion were the same as the organoids from no-active lesion. There was no significant difference of phenotypes such as stem cell and differentiation markers in the organoids. In spite of no significant difference of phenotypes, microarray analysis identified 7 upregulated genes in the organoids from active lesion more than 2 times compared to the organoids from inactive lesion. 3 downregulated genes in the organoids from active lesion less than half were also identified. 3 of 7 upregulated genes and all downregulated genes were preserved in the organoids from another patient but not all three patients.
Conclusion: Comparison of gene expression between organoids from active and inactive lesion of same patient might reveal the fundamental pathogenesis in intestinal epithelial cells of CD. The identification of lesion specific genes might also be useful for the elucidation of molecular mechanism and therapeutic target for mucosal healing in CD.
Disclosure: Nothing to disclose

P0898 THE EFFECT OF NEW HERBAL PRESCRIPTION DERIVED FROM *BOJANGGUNBI-TANG* ON INFLAMMATORY BOWEL DISEASE

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Introduction: *Bojanggunbi-tang* (BGT) is one of the most frequently used herbal prescription in Korea for colon diseases and the pharmacological activities of BGT on digestive system are also well-documented. However, BGT consists of 16 herbs, which makes it difficult to standardize and quality-control due to high cost in industrial manufacture.
Aims and Methods: The purpose of the current study is to develop a new simple and effective prescription derived from original prescription. We developed the essence of BGT (BGT-E) by mixing three herbs of BGT. Two herbs are *Lonicera japonica* Thunb. and *Alisma orientalis*, known as the most effective herbs in BGT. The other herb is *Atractylodes macrocephala* selected by literature review and screening test of total 16 kinds of components in BGT. Colitis mouse model was induced by 5% Dextran Sulfate Sodium (DSS) and body weight, histological damage, clinical score, gross anatomy and colon length were investigated to compare the effects between BGT and BGT-E. The mechanisms of action were analyzed by production of cytokines in colon tissue.
Results: We found that 300 mg/kg of BGT-E showed similar effect with same dose of BGT on colon shortening, clinical score, gross anatomical score and histological damage in the model. In addition, BGT-E showed dose-dependent decrease of pro-inflammatory cytokines including IL-1β, TNF-α, and IL-17.
Conclusion: Therefore, BGT-E could be a substitute prescription of BGT in clinical practice and a new candidate for alternative medicine for inflammatory bowel disease.
Disclosure: Nothing to disclose

P0899 UPON AIEC INFECTION, CROHN'S DISEASE-ASSOCIATED CIRCULATING MICRORNAS ARE TRANSFERRED BETWEEN HUMAN MACROPHAGES *VIA* THE EXOSOMAL SHUTTLE

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Introduction: The intestinal mucosa of CD patients is abnormally colonized with adherent-invasive *E. coli* (AIEC) strains, which are able to adhere to and to invade intestinal epithelial cells, to survive and replicate within macrophages and to induce a strong pro-inflammatory response. Exosomes, small extracellular vesicles of 30–100 nm, play a role in cell-to-cell communication by transferring their content from a donor cell to a recipient cell. We recently reported that upon AIEC infection, human macrophages secrete exosomes that induce a pro-inflammatory response and enhance the intracellular replication of AIEC bacteria in recipient cells.
Aims and Methods: This study aimed at investigating whether exosomes can transfer the microRNA (miRNA, miR) content between human macrophages during AIEC infection, and whether these miRNAs may contribute to the increased inflammation and AIEC replication observed in exosome-receiving cells. Exosomes released by human THP-1 macrophages uninfected (Exo-uninfected) or infected with the AIEC LF82 strain (Exo-AIEC) or the commensal *E. coli* HS strain (Exo-HS) were purified using the ExoQuick reagent and used to incubate with naïve THP-1 macrophages. The levels of the previously reported CD-associated circulating miRNAs in the purified exosomes and in exosome-receiving THP-1 macrophages were analyzed by qRT-PCR. *In silico* analysis was performed to predict the biological processes in which these miRNAs are potentially involved.
Results: Most of the CD-associated circulating miRNAs were detected in the purified exosomes. The levels of some miRNAs were increased in Exo-AIEC compared to Exo-uninfected or Exo-HS. The levels of these dysregulated exosomal miRNAs were also increased in THP-1 macrophages incubated with Exo-AIEC compared to those incubated with Exo-uninfected or Exo-HS. This suggests an efficient miRNA transfer *via* exosomes. *In silico* analysis revealed that the dysregulated exosomal miRNAs might be implicated in inflammatory responses and autophagy, which is required to restraint AIEC intracellular replication, among other biological processes.
Conclusion: Although functional studies are required to investigate the role of the exosomal miRNAs, our study suggests that during AIEC infection, miRNAs can be transferred between human macrophages *via* the exosomal shuttle to mediate their role as regulators of innate immune responses.
Disclosure: Nothing to disclose

P0900 CYR61 EXPRESSION IN INFLAMMATORY BOWEL DISEASE

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Introduction: The pro-angiogenic cysteine-rich protein 61 (Cyr61) is a novel proinflammatory factor. Whether Cyr61 is involved in the development of inflammatory bowel disease (IBD) remains unknown. The purpose of this study is to investigate the expression of Cyr61 in patients with IBD.
Aims and Methods: We achieved the colonic mucosae from 23 patients with IBD who had undergone colonoscopy. We measured the expression of Cyr61 and inflammatory markers in the biopsy specimens using the real-time PCR. And, we determined the expression of Cyr61 in LPS (Lipopolysaccharide) -treated colonic epithelial cells (Caco-2 and HCT 116).
Results: Expression of Cyr61 in the inflamed mucosae was 2.5 times higher than that of the non-inflammed mucosae ($p = 0.002$). Expression of TNF(tumor necrosis factor)-a, IL(interleukin)-6 and TLR(toll-like receptor)-4 increased significantly in inflamed mucosae than that of the non-inflamed mucosae (all $p < 0.05$). Time-dependent increase in Cyr-61 expression was observed in Caco-2 and HCT 116 after the treatment with LPS.
Conclusion: Our results reveal a novel mechanism suggesting the role of Cyr61 and therapies targeting Cyr61 in patients with IBD.
Disclosure: Nothing to disclose

P0901 SUCCINATE INDUCES EMT THROUGH SUCNR1

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Introduction: Epithelial-to-mesenquimal transition (EMT) is a process which allows a switch of the phenotype from epithelial cells towards a fibrotic behavior. This process has been widely associated with the development of fistulas, a complication in IBD patients associated with an activation of the inflammation. Under inflammatory conditions, the metabolite succinate is accumulated and its receptor, called SUCNR1, mediates profibrotic responses in hepatic stellate cells; however, there is no study analyzing its role specifically in epithelial cells and in EMT.
Aims and Methods: We aim to analyze the role of succinate and its receptor in EMT.
HT-29 intestinal epithelial cells were treated with different concentrations of succinate (0, 0.1, 0.5, 1, 5mM) or TGF-β (5ng/ml) during 48 hours. In some experiments, HT-29 cells were transfected with a specific SUCNR1 siRNA or with a negative control siRNA using Lipofectamine. The expression of EMT markers (Snail1, Snail2, Vimentin and E-Cadherin) was analyzed by qPCR and Western Blot. Intestinal fibrosis was induced *in vivo* using the heterotopic transplant model. Briefly, one intestinal graft from WT or KO mice was transplanted into the neck of a receptor mice for 7 days. The expression of EMT markers was analyzed by qPCR. Intestinal resections from CD patients were obtained and the expression of SUCNR1, Snail1, Snail2 and E-Cadherin was analyzed by qPCR. Results are expressed by mean ± SEM ($n \geq 5$). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test. Correlations were analyzed with the Spearman coefficient.
Results: In HT-29 cells, succinate induces in a dose-dependent manner: a) a significant increase in both mRNA and protein levels of SUCNR1; b) a significant increase in the mRNA expression of Vimentin, Snail1 and Snail2 and c) a significant reduction in the mRNA and protein expression of E-Cadherin. In HT-29 cells transfected with SUCNR1-specific siRNAs, the mRNA expression of Vimentin, Snail1 and Snail2 induced by succinate was significantly lower than that detected in HT-29 transfected with negative control siRNA (1.12 ± 0.12 vs 1.87 ± 0.09, 0.90 ± 0.09 vs 1.85 ± 0.18, 1.07 ± 0.26 vs 2.57 ± 0.19, respectively). In murine intestinal fibrotic tissue from WT mice we detected, seven days after transplantation a significant increase in the mRNA expression of Vimentin (3.50 ± 0.48), Snail1 (4.87 ± 0.79) and Snail2 (2.45 ± 0.25) and a significant reduction in the expression of E-Cadherin (0.60 ± 0.06) compared with that detected at day 0 (1.01 ± 0.07, 1.06 ± 0.13, 1.04 ± 0.10, 1.00 ± 0.04 respectively). In intestinal tissue from SUCNR1-/- mice, 7 days after transplantation we detected no significant changes in the expression of Vimentin, Snail1, Snail2 and E-cadherin vs KO-grafts at day 0 and levels of these markers were significantly lower than those detected in WT mice at day 7. Finally, SUCNR1 expression positively and significantly correlates with the expression of Snail1 ($r_{Spearman} = 0.6925$, $p < 0.0001$, $n = 36$) and Snail2 ($r_{Spearman} = 0.6305$, $p < 0.0001$, $n = 36$) in intestinal resections from CD patients.
Conclusion: Succinate activates EMT in intestinal epithelial cells through its receptor SUCNR1, which identifies a new molecular mechanism involved in EMT and points to a new possible target for fistula-treatment.
Disclosure: Nothing to disclose

P0902 ECTOPIC EXPRESSION OF REG3A IN THE MICE DISTAL COLON IS MEDIATED BY INTERACTIONS BETWEEN NOTCH AND IL-22 SIGNALING PATHWAYS, AND PROMOTES TISSUE REPAIR BY THE AUGMENTATION OF EGFR SIGNALING

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Introduction: Members of the Reg gene family share common upstream regulation pathway mediated by the IL-22-STAT3 axis, and encode multifunctional secretory proteins. Each Reg gene shows a distinct region-specific expression pattern in the colon. For example, REG3A is exclusively expressed in the intestinal epithelial cells (IECs) of the mouse proximal colon. In contrast, disease-active ulcerative colitis or Crohn's disease patients show ectopic expression of REG3A in rectal IECs. Those ectopically expressed REG3A may contribute to initiating tissue repair partly through its ROS scavenger activity. In our previous study, we have demonstrated the importance of Notch signaling in colonic tissue repair, and also its dominant role in IL-22-induced Reg gene family expression. However, the precise role of Notch signaling in "ectopic" expression of REG3A, or the comprehensive functional role of REG3A in the inflamed colonic environment is poorly understood.
Aims and Methods: The role of Notch signaling in REG3A expression was examined by immunohistochemical analysis of REG3A and HES1 in Villin-cre^{ER}; RBP-J$^{fl/fl}$ (RBP-J$^{\Delta IEC}$) mice and wild-type (WT) mice, under homeostatic and DSS-induced colitic conditions. Organoid culture system was used to analyze colonic region-specific regulation of REG3A expression, in regard to extrinsic IL-22 stimulation or intrinsic Notch signaling activity. To evaluate the direct effect of REG3A on IECs, organoid re-construction assay was performed under the presence of recombinant mouse REG3A. Those REG3A-treated organoids were also subjected to microarray analysis and immunoblotting to identify the IEC-intrinsic molecular pathway (s) regulated by REG3A.
Results: Under homeostatic condition, REG3A was specifically expressed in the proximal colon of WT mice. However in RBP-J$^{\Delta IEC}$ mice, IEC-specific deletion of RBPJ resulted in complete loss of both Hes1 and REG3A expression in the proximal colon. In DSS-colitis mice, REG3A was ectopically expressed by rectal IECs during the mucosal regeneration phase. In vitro analysis using distal colon-derived organoids confirmed IL-22-induced REG3A expression via STAT3 phosphorylation, which was completely cancelled by DBZ-mediated blockade of Notch signaling. Immunoprecipitation assay further revealed the direct interaction between STAT3 and HES1 in distal colon-derived organoid IECs. Furthermore, addition of recombinant mouse REG3A clearly promoted the organoid re-construction efficiency of single isolated distal colon-derived IECs. Microarray analysis of REG3A-treated distal colon-derived organoids revealed enhancement of EGF signaling pathway by REG3A, which was confirmed by immunoblotting analysis demonstrating REG3A-induced phosphorylation of EGFR and AKT. Consistently, addition of REG3A efficiently rescued the organoid re-construction ability of distal colon-derived IECs under a EGF-depleted environment.
Conclusion: Ectopic expression of REG3A in the inflamed distal colon is mediated by the interaction between IL22-STAT3 and Notch-Hes1 pathways. Ectopically secreted REG3A functions as a positive regulator of IEC-intrinsic EGF signaling, and thereby contribute to the repair of the inflamed colonic epithelium.
Disclosure: Nothing to disclose

P0903 3,25-$(OH)_2D_3$ STIMULATES NHE8 EXPRESSION *VIA* ERK1/2 SIGNALING PATHWAY IN DSS COLITIS MICE

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Introduction: Vitamin D (VitD) and vitamin D receptor (VDR) have been regarded as protective factors for colonic mucosa in ulcerative colitis (UC) patients. Recent epidemiological studies have suggested that UC patients commonly suffered from VitD deficiency. However, the potential molecular mechanisms by which VitD/VDR protects colonic mucosa in UC remain poorly understand. Sodium/hydrogen exchanger 8 (NHE8) is reported to play a protective role in colitis, and we have previously found that stimulating NHE8 expression could ameliorate mucosal injury in dextran sulphate sodium salt (DSS) colitis mice. However, whether NHE8 involves in VitD/VDR-mediated mucosa protection is still unclear.
Aims and Methods: The main objective of this study is to test whether VitD/VDR protects colonic mucosa through mediating NHE8 expression. VitD-deficient mice were established by feeding VitD-deficient chow for 8 weeks. VitD supplementary mice were gavaged with 1,25-$(OH)_2D_3$ (0.2ug/25g/d) daily for 7 days in the eighth week. DSS colitis mice were induced by drinking 3% DSS containing water *ad libitum* for 7 days; treatment mice received 1,25$(OH)_2D_3$ (0.2ug/25g/d) daily intragastrically three days prior to DSS administration. The histological score and disease activity index (DAI) score were assessed, respectively. For mechanism study, caco-2 cells were incubated with TNF-α (100ng/ml) for 18 hours to induce inflammation and followed by incubating with ERK1/2 specific inhibitor PD98059 (25μM) for 1 hour.
Results: NHE8 protein expression was significantly decreased in VitD-deficient mice compared with the control (1.74 ± 0.06 vs. 2.02 ± 0.06, $n = 6$, $p < 0.05$). However, 1,25-$(OH)_2D_3$ supplementation effectively recovered NHE8 expression compared with VitD-deficient mice (2.12 ± 0.09 vs. 1.74 ± 0.06, $n = 6$, $p < 0.05$). In DSS colitis mice, the colonic histological score and DAI score were dramatically increased compared with the control ($n = 16$, $p < 0.05$), respectively. Whereas, 1,25$(OH)_2D_3$ treatment obviously declined the histological score and DAI score compared with DSS colitis mice ($n = 22$, $p < 0.05$). Moreover, DSS administration remarkably compromised NHE8 expression compared with the control (1.24 ± 0.11 vs. 1.73 ± 0.11, $n = 16$, $p < 0.05$), but that 1,25$(OH)_2D_3$ treatment partly restored NHE8 expression from 1.24 ± 0.11 to 1.65 ± 0.19 ($n = 22$, $p < 0.05$). Of note, Pearson correlation analysis showed that colonic NHE8 protein expression was positively associated with VDR ($R = 0.628$, $p < 0.0001$, $n = 28$). Furthermore, 1,25$(OH)_2D_3$ treatment significantly suppressed DSS induced ERK1/2 phosphorylation levels (0.42 ± 0.03 vs. 0.54 ± 0.02, $n = 22$, $p < 0.05$). In caco-2 cells, TNF-α intervention significantly downregulated NHE8 (0.43 ± 0.03 vs. 0.94 ± 0.12, $n = 3$, $p < 0.05$) and VDR (0.46 ± 0.03 vs. 0.63 ± 0.06, $n = 3$, $p < 0.05$) proteins expression compared with the control cells. Consistently, 1,25$(OH)_2D_3$ treatment dramatically upregulated NHE8 (0.78 ± 0.09 vs. 0.43 ± 0.03, $n = 3$, $p < 0.05$) and VDR (0.76 ± 0.05 vs. 0.46 ± 0.03, $n = 3$, $p < 0.05$) proteins expression compared with TNF-α treated cells. In addition, in TNF-α pretreated cells, PD98058 dramatically upregulated NHE8 expression from 0.21 ± 0.02 to 0.44 ± 0.04 ($n = 3$, $p < 0.05$).
Conclusion: The present study suggested that NHE8 decrease is responsible for colonic mucosa injury caused by VitD deficiency. 1,25$(OH)_2D_3$ supplementation could ameliorate DSS colitis via VDR-ERK1/2-NHE8 pathway.
Disclosure: Nothing to disclose

P0904 ASSESSMENT OF AUTONOMIC FUNCTION IN INFLAMMATORY BOWEL DISEASE BY HEART RATE SPECTRAL ANALYSIS

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Introduction: Heart rate variability (HRV) are used to evaluate of autonomic dysfunction in various clinical disorders. In this study, we examined HRV in patients with inflammatory bowel disease (IBD) to evaluate autonomic nerve function.
Aims and Methods: A total of 136 IBD patients (98 Crohn's disease and 38 ulcerative colitis) from the First Affiliated Hospital of Nanjing Medical University were evaluated. Demographic data and clinical characteristics were collected. HRV in IBD patients were compared with those in the healthy controls. HRV parameters the power of high-frequency (HF) and the ratio of HF and low frequency (LF), reflects vagal/sympathetic balance were assessed.
Results: The power of HF component was significantly decreased in CD ($n = 98$), UC ($n = 38$) and IBD ($n = 136$) patients respectively, compared with health controls ($n = 16$) ($p < 0.001$). Patients with CD or UC in state of different disease activity had significantly lower levels of HF compared with health control. However, there was no significant differences of HF levels in mild CD, moderate and severe CD patients. UC patients also had the same alterations at stage of different disease activity.
Conclusion: Altered HRV were found in both CD and UC patients, implicated impaired autonomic function in patients with IBD.
Disclosure: Nothing to disclose

P0905 CLASS-1-HISTONE DESACETYLASES AS A NEW THERAPEUTIC TARGET FOR THE CONTROL OF ADHERENT-INVASIVE E. COLI-INDUCED INTESTINAL INFLAMMATION

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Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease with a complex etiology including genetic, environmental, infectious and also epigenetics factors. Adherent-invasive *E. coli* (AIEC) are clearly involved in triggering and maintaining ileal CD. AIEC bacteria adhere to the enterocytes through high affinity interaction between their variant type one pili and abnormally expressed CEACAM6 receptor on host cells. Once internalized, AIEC bacteria replicate within host cell (macrophages and intestinal epithelial cells). Intestinal mucosa colonization by AIEC alters intestinal barrier function, inducing chronic inflammation in CD patients. Controlling the invasion, intra-cellular replication and inflammatory response induces by AIEC could be a new promising strategy for CD patients. To date, no specific therapeutic targets were identified for AIEC positive CD patients.
Aims and Methods: The aim of this work are to (1) identify histone post-translational modifications altered during the course of AIEC colonization using intestinal epithelial cells (IECs) in culture infected by AIEC reference strain LF82 and non-pathogenic *E. coli* through immunofluorescence and western-blot approaches; (2) to assess the role of HDAC during infection using specific inhibitors (MS 275 and SAHA) on AIEC-intracellular replication in IECs cells and

during the course of colonization in humanized CEACAM6-expressing mice (CEABAC10 mice). These mice received SAHA intra-peritoneally for two weeks and were challenged with AIEC by oral gavage. Colonization was monitored for 3 days after infection (AIEC numbering in feces). AIEC associated to intestinal tissues were numbered at the time of sacrifice and inflammatory response was analyzed by ELISA.
Results: AIEC infection leads to an important increase in acetylated and crotonylated form of histone H3 in three different IECs lines. H3K9ac (acetylation) and H3K18cr (crotonylation) marks were significantly increased six hours after infection, in comparison to non-infected and non-pathogenic *E. coli*-infected cells. These observations suggest that AIEC infection could interplay with histone ''eraser''/''writer'' pathways leading to changes in genome organization in host cell. We focused the analysis on the erasers HDAC using pharmacological inhibition of HDAC. HDAC inhibitors pre-treatment of IECs led to a significant reduction of invasion and multiplication capacity of AIEC within IECs. Finally, in vivo approach using CEABAC10 mice treated with HDAC inhibitors revealed a decrease in AIEC colonization ability and decreased inflammatory response in the group treated with HDAC inhibitor compared to the untreated mice.
Conclusion: This work shows that AIEC infection alters the epigenetic landscape of host cell which could modify gene expression favoring the infection process. We reveal that pharmacological inhibition of HDAC limits AIEC colonization in vitro and in vivo in CEABAC10 mice and prevents intestinal inflammation, suggesting that HDAC could be an interesting target for controlling AIEC-induced intestinal inflammation in Crohn's disease patients.
Disclosure: Nothing to disclose

P0906 A PATHWAY TO UNDERSTAND COLITIS-ASSOCIATED CARCINOMA: GENE EXPRESSION ANALYSIS IN HUMAN COLON

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Introduction: Long-term Inflammatory Bowel Disease (IBD) patients have a higher risk of developing colorectal cancer (CRC), namely, colitis-associated carcinoma (CAC). However, its tumorigenesis occurs differently from the model described for CRC tumorigenesis due to the active participation of inflammatory signaling pathways [1]. It is known that in CAC, cytokines such as TNF, PEG2, IL-6 and IL-1 can activate signaling pathways such as ERK, NFκB, PI3K-Akt and STAT3, promoting transformation and tumor progression [2,3]. However, most of the knowledge about CAC pathogenesis comes from mouse models, indicating the need for studies in human samples. Thus in this study we performed a comparative gene-expression analysis in surgical samples of IBD patients, and we intend to contribute to a better understanding of the carcinogenesis of CAC
Aims and Methods: Colon samples were collected from 60 patients divided in 6 groups: Control, Ulcerative Colitis (UC), Crohn's Disease-colitis (CD), UC- or CD-related CAC and CRC. Gene expression analysis was performed on RNA extracted from paraffin-embedded samples using the Nanostring amplification-free technique. A set of 624 genes related to immunology or epithelial barrier function and cell polarization was analyzed. Statistics and preliminary analyses were performed using the nSolver software and Pathway analysis was performed using the free platform ConsensusPathDB (http://ConsensusPathDB.org).
Results: The analysis of differentially expressed genes between CD-CAC and CD as well as UC-CAC and UC rendered 203 and 271 differentially expressed genes, respectively. Among the major up-regulated genes in both comparisons were genes related to inflammation and cell cycle progression, such as SPP1, DUSP4 and CCND1. Among the most down-regulated genes were cytokines, genes related to T-cell activation and to NFκB activation such as CXCL13, CD45RA, TNFRSF13B and TNFRSF17. The enrichment analysis of up-regulated genes resulted in 49 enriched pathway-based sets for UC-CAC and UC as well as 213 enriched pathway-based sets for CD-CAC and CD. Among the statistically significant pathways present in both analyses were pathways related to cancer, JAK STAT signaling pathway and cytokine-cytokine receptor interaction.
Conclusion: The customized gene expression panel offered a comprehensive analysis of the differences in expression between CAC and the underlying inflammatory diseases UC and CD. Identified upregulated or downregulated genes indicate signal transduction pathways that are crucial for CAC tumorigenesis, corroborating to the existing knowledge about CAC progression.
Disclosure: Nothing to disclose

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P0907 CB2 INHIBITOR PROMOTES FACTORS ASSOCIATED WITH MUCOSAL HEALING IN COLON EPITHELIAL CELLS OF IBD PATIENTS: AN *EX-VIVO* AND *IN VITRO* STUDY

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Introduction: Accumulating data from animal models and clinical data from our group and others suggest beneficial effects of cannabis in the treatment of patients with inflammatory bowel diseases (IBD). Cannabinoid receptors are expressed on epithelial and immune cells throughout the gastrointestinal (GI) tract and CB2 immunoreactivityis specifically found in epithelium area of inflamed colonic tissue, thus suggesting a role for the endocannabinoid system inmodulating IBD disease activity. However, the mechanisms by which cannabis affects the inflammatory processes and/or the clinical presentation of IBD is not yet clear. Experimental mouse models of IBD have limited use in predicting the clinical relevance of therapeutic targets in relation to human IBD. Therefore, in the current study we used human-originated tissuemodelsto evaluate mechanisms for the beneficial effects of cannabis inpatients with IBD.
Aims and Methods: To investigate the effects of CB2 activation on colon epithelial cells, which are exposed to IBD microenvironment.
In the current study weused 2 biological systems: 1. mucosal samples were collected during endoscopy from inflamed and non-inflamed areas ofIBD patients. Samples were cultured for 7 hours with medium or CB2 agonist (JW-133, 10mM) or ethanol (the solvent). Samples (time 0, after 7hr) were analyzed for epithelial cells Ki67 (proliferation) and fragmented caspase 3 (apoptosis) expression by immunohistochemistry and quantified by ImageJ software. The secretomes of the explants were collected and analyzed for MMP9 activity (zymogram), which is known to impair colonic epithelial permeability.2) The effect of soluble IBD microenvironment and CB2 agonist directly on the epithelial cells was evaluated by culturing CaCO-2 (colon carcinoma cells) for 48hr with secretomes collected from the biopsies (treated with JW-133 or ethanol) and analyzing their effects on the cells' viability (alamar-blue), number (automatic cell counter), death (trypan blue) and migration (scratch assay). All experiments were done at least 3 times.
Results: We found: I. Higher epithelial cell proliferation in biopsies obtained from healthy areas of the colon compared to biopsies from inflamed areas (Ki67 expression: 64 vs 32%, $p < 0.05$). No difference was found in apoptosis (expression of caspase 3) between the two areas (both at time 0 and 7hr). II. Higher level of MMP9 activity was found in secretomes collected from inflamed biopsies in comparison to non-inflamed areas (79%↑, $p < 0.05$). III. Treatment with CB2 agonist (JW-133) returned epithelial Ki67 and MMP9 activity levels of the inflamed area to the level of the non-inflamed areas. IV. Secretomes collected from the inflamed biopsies, significantly ($p < 0.05$) reduced CaCO-2 cell viability (30%↓), number (40%↓) and migration (45%↓), while secretomes collected from CB2 agonist treated biopsies reversed these cell characteristics to the control levels (all $p < 0.05$). Direct addition of CB2 agonist (in the same concentration) to the CaCO-2 cells had no effect on theirviability and number, yet it facilitated cell migration (40%, $p < 0.05$).
Conclusion: Our study demonstrated in a human *ex-vivo* and *in-vitro* human models that cannabinoids alter epithelial cells phenotype in a way that may facilitate mucosal healing.
Disclosure: Nothing to disclose

P0908 LONGER DISEASE COURSE IS ASSOCIATED WITH REDUCED SYSTEMIC ANTI-INFLAMMATORY RESPONSE IN ULCERATIVE COLITIS PATIENTS

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Introduction: Interleukin 10 (IL-10), representing the anti-inflammatory mechanisms of the human body, is a well-known marker used to characterise the course of ulcerative colitis (UC). Although many mechanisms of UC are well understood, some of them still remain unclear, including the exact factors that could attribute to better prognosis and more favourable outcome of the disease.
Aims and Methods: The aim of the study was to determine the association between the systemic anti-inflammatory state of the body and UC disease length and analyse the possible factors attributing to that. A cross-sectional

study was conducted analysing all patients with clinically, endoscopically and histologically confirmed UC diagnosis previously hospitalized in two largest tertiary medical care centres in Riga, Latvia during a 6-year period (2012–2017). Patients participated in out-patient interviews, blood samples were obtained and analysed for IL-10 using ELISA, UC disease activity was evaluated according to the full Mayo score.
Results: Out 65 UC patients – 34 (52.3%) male and 31 (47.7%) female patients with the mean age of 41.95 (SD = 15.1) years, who enrolled in the study – only one (1.5%) had increased IL-10 levels (more than 20 pg/ml). The levels of IL-10 in the study group ranged from 0 pg/ml to 55 pg/ml with a mean of 3.4 (SD = 7.9) pg/ml. Statistically significant negative correlation (RS = −0.35; p = 0.004) was found between IL-10 levels and the number of years since the patient experienced their first UC symptoms, showing that the longer the patient had UC, the lower their IL-10 levels were. The mean age when the first UC symptoms appeared in the study group was 32.1 (SD = 14.6) years, ranging from 2 to 48 years. The possible confounding factors that could influence the IL-10 levels in these patients, including UC disease activity, UC treatment, UC complications, the number of UC exacerbations, patient's BMI, smoking history, concomitant diseases, previous hospitalizations and CRP levels did not show any statistically significant effect. The only exception was systemic corticosteroid use, were IL-10 levels were significantly higher – 8.93 (SD = 13.84) in patients who had received Methylprednisolon therapy in the past 12 months, comparing to the patients who did not receive Methylprednisolon in the last 12 months – 1.65 (SD = 3.8) (p = 0.004). This finding is well known and described in the literature before. 81.5% (n = 53) of the study group had received conservative UC treatment in the last 12 months and 23% (n = 15) of the patients had received systemic corticosteroids in the last 12 months.
Conclusion: Patients with shorter UC disease history may still have well working anti-inflammatory defence mechanisms (elevated IL-10 levels), which however decline over the course of the disease. This could be valuable knowledge, when recommending to diagnose and treat UC patients as soon as possible, so that the course of the disease is not getting worse and more advanced treatment options have to be used.
Disclosure: Nothing to disclose

P0909 HYPERMETHYLATION PATTERNS IN DYSPLASIA IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Inflammatory Bowel Disease (IBD) with colonic involvement has been associated to an increased colorectal cancer (CRC) risk – several guidelines recommend screening/surveillance strategies based on the early detection of dysplasia in colorectal mucosa. However, agreement in the definitions of IBD associated dysplasia or sporadic dysplasia in IBD patients is far from ideal. IBD associated carcinogenesis has distinctive features – some data favors the importance of abnormal DNA methylation.
Aims and Methods: This study aims to define methylation patterns of several genes presumably implicated in colorectal carcinogenesis, in patients with a CRC or colonic dysplasia diagnosis following an IBD diagnosis.
In the pilot phase, 25 samples from colonic mucosa with and without dysplasia from 3 patients with IBD associated dysplasia (multifocal/on random biopsies/lesions with ill-defined limits) and 3 patients with IBD and sporadic dysplasia were studied. The Cpg islands methylation patterns of 70 genes' promoter regions were analyzed by the MS-MLPA (methylation-specific multiplex ligation-dependent probe amplification) technique, using commercial kits (ME001, ME002, ME004, ME011, ME042) and Coffalyser.NET (MRC-Holland®) software.
Results: *NEUROG1, IGF2, CDKN2B, CDH13, ESR1, WT1, GATA5, GATA4, SFRP1* and *TERT* genes' promoters were frequently methylated. Regarding *ESR1* and *SFRP1* genes, dysplasia/CRC samples showed more frequent methylation (6/10 *vs.* 3/15); all high-grade dysplasia and CRC samples showed *SFRP1* gene methylation. The same tendency was seen for the *IGF2* gene (7/10 *vs.* 2/15); the 2 samples without dysplasia that showed methylation were active disease samples. No methylation pattern differences were seen between CRC/dysplasia samples and the remainder in any other genes.
Conclusion: Methylation analysis, particularly in the *ESR1*, *SFRP1* and *IGF2* genes, may contribute to the prediction of CRC risk in IBD – to be further tested in a larger number of patients/lesions.
Disclosure: Nothing to disclose

P0910 DEVELOPMENT OF A CHRONIC DEXTRAN SULFATE SODIUM-INDUCED COLITIS MODEL IN THE NONHUMAN PRIMATE

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Introduction: The dextran sulfate sodium (DSS)-induced model of colitis is frequently used as a preclinical model of inflammatory bowel disease (IBD). The chronic phase of DSS-induced colitis shares pathophysiological aspects of human ulcerative colitis (UC). Therefore, DSS-induced colitis is suitable for evaluating the therapeutic potential of treatments for UC. However, some treatments for IBD, such as prednisolone (PSL), show poor efficacy or even worsen colitis in the rodent model. Differences in inflammatory/immune mechanisms between humans and rodents are potential sources of this issue. Nonhuman primates are phylogenetically closer to humans than rodents and useful in investigating mucosal immunity.
Aims and Methods: In the current study, a nonhuman primate model of chronic colitis was created and the effect of PSL was assessed in this model. Eight male cynomolgus macaques were used. Macaques were allowed free access to 0.25% DSS in distilled water. Daily total intake of DDS-water was 100 mL/kg. One treatment cycle consisted of DSS-water for 2 weeks followed by 2 weeks without DSS-water. Macaques underwent a total of three treatment cycles. A modified Mayo score (0–12) was used to quantify the extent of colitis. The sum of the following parameters was calculated: stool consistency (0–3), gross bleeding in stool (0–3), colonoscopy examination (0–3), and general symptoms (0–3). Endoscopic findings were also classified according to the Rachmilewitz Endoscopic Index (EI, 0–12). Fecal calprotectin was measured using an ELISA kit. Macaques received either vehicle (control, N = 4) or PSL (treatment, N = 4). Prednisolone (1 mg/body, BID) was administered for 14 days during the third DSS-water treatment cycle.
Results: In the control group, during all three cycles of DSS treatment, increased feces scores (stool consistency and fecal bleeding) were observed. Colonoscopy revealed reduced vascularization and mucosal erythema, edema, and erosion in the mucosa of the rectosigmoid colon in three macaques. Ulceration of colonic mucosa was observed in one macaque. Similar modified Mayo scores (mean ± SEM), indicating moderate severity, were observed during all three cycles (Cycle 1, 4.0 ± 0.0; Cycle 2, 3.5 ± 0.6; Cycle 3, 4.2 ± 0.6). The EI indicated consistent and moderate colitis severity during all three DSS treatment cycles (Cycle 1, 4.3 ± 0.5; Cycle 2, 4.5 ± 0.6; Cycle 3, 5.5 ± 1.3). In between DSS treatments, Mayo scores recovered to the remission level. In the PSL-treated macaques, mean Mayo scores during the first and second DSS-treatment cycle were similar to that of the control group. However, a significantly lower score was obtained in the third DSS-treatment cycle (1.8 ± 0.5). The mean EI for PSL-treated macaques was also lower (1.8 ± 0.6) than of the control-treated macaques. Mean fecal calprotectin was higher in the control group compared to that of naïve macaques. By contrast, fecal calprotectin values of the PSL-treated animals indicated remission (< 70 μg/g).
Conclusion: A chronic DSS-induced colitis model was developed in macaques that showed similar symptomatic and endoscopic features to those seen in clinical UC, including repeated relapse and remission. In this model, PSL clearly inhibited disease relapse. Therefore, the macaque model, compared to the rodent model, could show better predictiveness of clinical outcome of compounds that are currently under evaluation for the treatment of UC.
Disclosure: All the authors are employees of Hamamatsu Pharma Research, Inc.

P0911 INCREASED ALVEOLAR NITRIC OXIDE CONCENTRATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SIGN OF SUBCLINICAL SMALL AIRWAY INFLAMMATION?

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Introduction: Among extraintestinal complications of inflammatory bowel diseases, pulmonary manifestations are rarely recognized in clinical practice. Exhaled nitric oxide (eNO) is an established biological marker of airway inflammation, one that can be potentially used to identify these manifestations.
Aims and Methods: Fractional eNO (FeNO) was measured in multiple flows, allowing us to assess alveolar concentration (C_ANO) and bronchial flux (JawNO) of nitric oxide in 27 patients with inflammatory bowel disease (17 with Crohn's Disease and 10 with Ulcerative Colitis) and in 39 healthy controls. Patients or healthy controls exhibiting factors that have been correlated in past studies with eNO measurements were excluded from the study. In patients with Crohn's Disease, Crohn's Disease Activity Index (CDAI) was used to define clinical disease activity, while Partial Mayo Score was used in patients with Ulcerative Colitis.
Results: Patients with inflammatory bowel disease had significantly higher C_ANO, compared to the control group (p < 0.0001). FeNO was significantly increased in patients with inflammatory bowel disease (p = 0.023), while there was no statistical significance found regarding levels of JawNO in patients with inflammatory bowel disease (p = 0.106), both compared to controls. Patients with Crohn's disease in clinical remission (CDAI < 150, n = 12) or patients

with UC that had inactive or mild disease (Partial Mayo Ranking of 0 or 1, n = 8), had significantly higher C_ANO levels compared to the control group (p = 0.024 and p = 0.005 respectively). None of the eNO components was correlated with markers of disease activity (CDAI, Partial Mayo score, CRP, ESR).
Conclusion: There seems to be a significant elevation of the alveolar concentration of nitric oxide in patients with inflammatory bowel disease, regardless of disease activity. Alveolar concentration of nitric oxide has been shown to be a marker of small airway inflammation. This may suggest that subclinical small airway inflammation is present in patients with inflammatory bowel disease, even those with mild or inactive disease.
Disclosure: Nothing to disclose

P0912 LOW VITAMIN D RECEPTOR PROTEIN LEVELS IN MURINE AND HUMAN INTESTINAL FIBROSIS

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Introduction: Vitamin D signals through the vitamin D receptor (VDR) which is a member of the nuclear receptor family of transcription factors that play an immunoregulatory role in the gut. Vitamin D deficiency is associated to Crohn's disease (CD).
Aims and Methods: The aim was to analyse the levels of VDR in murine and human intestinal fibrosis. We used intestinal tissue from CD patients as well as epithelial cells and fibroblasts isolated from intestinal tissue. Control tissue and control cells were obtained from the non-damaged intestine of patients with colorectal cancer. Fibroblasts were treated with 1,25 Vitamin D_3 (100nM) for 24 hours. A murine model of intestinal fibrosis was established by the transplant of one intestinal graft from C57BL/6 mice into the neck of receptor mice for 7 days. VDR, pSTAT3, STAT3 protein levels were determined by Western Blot and VDR and CYP24A1 gene expression by qPCR. Statistical significance was measured by t-test.
Results: VDR protein levels were significantly lower in intestinal tissue, epithelial cells and fibroblasts obtained from CD patients than that the obtained from controls (18.7 ± 9.1 vs 100 ± 35.1, 48.5 ± 23.9 vs 100 ± 3.7, 57.2 ± 13.2 vs 100 ± 16.7, respectively). Vitamin D_3 significantly increased the mRNA and protein expression of VDR and CYP24A1 (a VDR gene target) in human isolated fibroblasts. In the murine model of intestinal fibrosis, compared with control, we detected reduced VDR protein levels (18.5 ± 9.8 vs 100.3 ± 25.9) and increased levels of the ratio pSTAT3/STAT3 (149 ± 10 vs 100 ± 1).
Conclusion: Our study indicates reduced VDR protein levels in murine intestinal fibrosis and intestinal tissue from CD patients. Diminished VDR protein levels were also detected in isolated epithelial cells and fibroblasts from human intestine in which exogenous administration of Vitamin D_3 increases the VDR signaling pathway.
Disclosure: Nothing to disclose

P0913 CLINICAL ASPECTS AND PROGNOSES OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND AUTOIMMUNE LIVER DISEASE

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Introduction: Inflammatory bowel diseases (IBD) are associated with autoimmune liver diseases (AILD) and numerous studies have been published, however, almost all of them have focused on Primary Sclerosing Colangitis (PSC).
Aims and Methods: This is a retrospective, observational, case-control study aimed to evaluate the clinical features of PSC and non-PSC autoimmune diseases in patients with IBD and compare the course of both groups. Distribution of data was assessed for normality test (Shapiro-Wilk), chi-square test was used to assess the association between variables and variables with $p < 0.2$ were included in regression binary logistic model. p values < 0.05 were considered statistically significant.
Results: Fifty-four patients were included. The median age was 34 years (17–74) and 31 were males (53.4%). Ulcerative colitis was present in 48 patients (88.8%) and Crohn's disease in six (11.2%). The follow-up time median was 8 years (1–28 years). PSC was present in 35 patients (64.8%). Non-PSC in 19 (35.2%), and it was: autoimmune hepatitis in seven patients; five patients had autoimmune hepatitis with PSC; variant type of autoimmune hepatitis with cholestasis was present in two; autoimmune cholangiopathy and primary biliary cholangitis were present in two patients each and one patient had autoimmune hepatitis with PSC small duct. The median IBD diagnosis time was 5 years (1–30). The median of liver disease diagnosis time was 7 years (1–26). Thirty-three patients underwent liver biopsy and of these, 19 (57.5%) were staged as F0 or F1 of Metavir Classification and 14 (42.5%) were F2-F4. Portal hypertension was observed in 19 patients at diagnosis. Twenty-two patients were submitted to liver transplant. Colon adenocarcinoma was detected in one patient and there were six deaths of all patients. There was no difference between two groups in regard diagnosis time, drug therapy, liver disease staging, liver transplantation and need for proctocolectomy and death. When multiple logistic regression was performed to evaluate factors associated with liver transplant it was observed that only the liver disease diagnosis time persisted with $p < 0.05$ (p = 0.001). The value of Odds Ratio was 1.792 (95% CI 1.689–1.911). Regarding the need for surgery to approach IBD, the time of diagnosis of IBD remained in the final model (p = 0.041; Odds Ratio 1.861 – 95% CI 1.745–1.994). Other variable that was analyzed was the recurrence of IBD after liver transplantation: the diagnosis of autoimmune hepatitis remained in the final model (p = 0.012; Odds Ratio 7.1 (95% CI 1.215–42.43).
Conclusion: Clinical features and evolution of both groups were the same, but this population had liver transplant chance increased by 20.1% for each year of diagnosis of liver disease. Besides, how longer was the time of IBD diagnosis, the chance of needing surgical treatment is greater and patients with previous diagnosis of autoimmune hepatitis have increased in 7 times the chance of *de novo* IBD
Disclosure: Nothing to disclose

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P0914 MEDIATORS OF APOPTOSIS IN CIRCULATING LYMPHOCYTES OF IBD PATIENTS ARE DECREASED AND BCL-2 IS AN ACCURATE MARKER OF IBD

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Introduction: Despite uncertain pathogenesis of IBD, deregulation of the mechanisms of adaptive immunity, including excessive T-cell responses towards gut microbiota as well as lymphocyte resistance to desensitization signals, is paramount for the initiation and perpetuation of inflammatory response. Essential role in the resolution of inflammation is played by apoptosis, which is strictly regulated by among others transcription factor p53 and the members of Bcl-2 family. An increased level of anti-apoptotic mediators as well as an aberrant response to pro-apoptotic signals have been previously observed in lymphocytes isolated from intestine in IBD whereas little is known about the susceptibility to apoptosis of peripheral lymphocytes (PBLs).
Aims and Methods: Study was performed to evaluate the concentrations of p53, cytochrome c and Bcl-2 in PBLs in healthy volunteers and IBD patients with respect to the disease type and activity. Diagnostic utility of apoptosis mediators using ROC analysis was assessed as well.
A group of 64 individuals was enrolled: 42 IBD patients (25 ulcerative colitis (UC) and 17 Crohn's disease (CD)) from the Department of Gastroenterology and Hepatology, Wroclaw Medical University and 22 apparently healthy volunteers. Cytochrome c, Bcl-2 and p53 were quantified immunoenzymatically in lysates of peripheral lymphocytes.
Results: The concentrations of Bcl-2 in PBLs from IBD patients were significantly lower as compared to healthy volunteers (17 vs.35 ng/ml, $p < 0.001$) without significant difference between CD and UC (p = 0.063) or disease activity in CD. However, patients with active UC had significantly lower Bcl-2 as compared to patients with inactive UC (18 vs. 28 ng/ml, p = 0.044). Also cytochrome c was lower in IBD than controls (294 vs. 406 ng/ml, p = 0.003) without significant difference between CD and UC (p = 0.060). Patients with active CD, but not UC, had significantly higher cytochrome c than these with inactive disease (213 *vs.* 75.5 ng/ml, p = 0.039). Yet, cytochrome c tended (p = 0.070) to increase along with increased Truelove and Witts severity index with 244, 339, and 349 ng/ml in mild, moderate and severe UC. In turn, p53 did not differ significantly between IBD patients and controls (p = 0.080) but was significantly lower in CD than UC (3.1 vs. 8.5 ng/ml, p = 0.039). There was no difference in p53 concentrations with respect to CD (p = 0.477) or UC (p = 0.351) activity. None of the apoptosis mediators correlated with CDAI or MDAI. In a whole cohort, there were positive correlations between Bcl-2 and p53 ($r = 0.56$, $p < 0.0001$) and cytochrome c and p53 ($r = 0.25$, p = 0.049). In subgroups, Bcl-2 and p53 were positively correlated in healthy controls ($r = 0.69$, $p < 0.001$) as well as CD ($r = 0.50$, p = 0.041) but not UC patients. Bcl-2 was characterized by good accuracy as an IBD marker (86% at ≤25 ng/ml) and p53 by moderate accuracy as a CD/UC differentiating marker (70% at ≤6.8 ng/ml).
Conclusion: IBD is associated with decreased concentrations of apoptosis modulators in peripheral lymphocytes and the deregulation seems to be more pronounced in CD. Bcl-2 has a good overall accuracy as an IBD marker while p53 is moderately accurate in differentiating CD from UC.
Disclosure: Nothing to disclose

P0915 DISEASE COURSE AND PROGNOSIS OF INCIDENT PATIENTS WITH MICROSCOPIC COLITIS – ONE YEAR FOLLOW-UP RESULTS. THE EUROPEAN PRO-MC COLLABORATION, A LINK AWARD PROJECT

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Introduction: The PRO-MC Collaboration is a European prospective registry for incident cases of Microscopic colitis (MC)[1]. Follow-up data from patients at 15 different European centres are accured to provide real life data on disease activity, treatment response, and long-term prognosis. One-year follow-up data on the first 71 patients are reported.

Aims and Methods: Incident cases of MC prospectively followed for 12 months were eligible for inclusion. Patient characteristics and data on pathology, medical history and performed diagnostics were registered at baseline. Disease activity, quality of life and treatment strategies were registered at baseline and after 3, 6 and 12 months. Data are reported numerically and as percentages. Non-parametric statistics were used

Results: By March 2018, 71 of 318 patients included in the registry had been followed for 12 months. Mean age 64 years, 70% females. In total, 52% had collagenous colitis (CC), 39% lymphocytic colitis (LC) and 8% incomplete MC (MCi).

At baseline 42 (59%) presented with active disease according to Hjortswang criteria[2]. Twenty (28%) were in remission due to budesonide initiated before baseline visit in the study, 9 (12%) were in spontaneous remission.

Treatment in patients with active disease at baseline was initiated in 29 patients, of which 19 were treated with budesonide. Ten patients were treated with bulging agents (cholestyramine, loperamide, fibres). Thirteen patients received no medical treatment. Patients were classified according to disease behaviour during the first year in four groups, see Table.

Patients with chronic active or chronic relapsing disease did not differ from patients with mild or quiescent disease concerning smoking habits or subtype of MC ($p > 0.05$, Chi-square). Quality of life (Short Health Score) improved significantly from baseline visit to week 52 in patients with mild/quiescent disease ($p = 0.02$, Wilcoxon). No improvement in quality of life was detected in patients with chronic relapsing disease.

Conclusion: The prognosis for MC after one year appears good. The majority of patients (63%) have a quiescent or mild disease course. Bulging agents and on-demand use of budesonide are frequently applied. The PRO-MC cohort will provide further information on long term prognosis, identify predictive factors for disease activity and generate proposals for new treatment algorithms.

Disease behaviour	Total N = 71	n CC / LC / MCi
Quiescent	Only one flare at onset of disease subsided spontaneously or after one course of budesonide, N = 19	12 / 6 / 1
Mild	Treatment with bulging agents or occasional use of budesonide on demand), N = 26	12 / 11 / 3
Chronic relapsing	Disease activity or budesonide treatment at ≥ two visits, N = 24	11 / 11 / 2
Chronic active	Disease activity or in budesonide treatment at every visit, N = 2	2 / 0 / 0

[Microscopic colitis disease behaviour during the first year after diagnosis]

Disclosure: Nothing to disclose

Reference

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P0916 OPPORTUNISTIC INFECTIONS ARE MORE PREVALENT IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS: A LARGE POPULATION-BASED STUDY

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Introduction: Inflammatory bowel diseases (IBD) comprising of Crohn's disease (CD) and Ulcerative Colitis (UC) are chronic inflammatory disorders that have been associated with an increased risk of opportunistic infections (OIs)[1,2]. While OIs like Clostridium difficile have been extensively studied, there is limited data on the prevalence of other OIs in a large cohort of IBD patients.

Aims and Methods: The aim of this study was to investigate the epidemiology of seventeen OIs in IBD in a large, population-based database. Data was collected from a commercial database (Explorys Inc, Cleveland, OH, USA) that provided electronic health records (inpatients and outpatients) from 26 major integrated United States healthcare systems from March 2013- March 2018. We identified a cohort of patients with CD, UC, and OIs based on Systemized Nomenclature of Medicine – Clinical Terms. We compared the prevalence of seventeen OIs in this cohort of CD and UC patients to controls without IBD[2] and characterized the distribution of these OIs with age.

Results: Of the 35,420,110 individuals in the database, we identified 153,290 patients with CD and 128,540 patients with UC. The overall prevalence rate of CD and UC was 432.8/100,000 persons and 362.9/100,000 persons respectively. Both UC and CD patients had significantly increased odds for OIs compared to controls (OR, 2.87 in CD; $p < 0.0001$, and OR, 3.15 in UC; $p < 0.0001$). The OIs with the highest odds ratios (OR) in IBD patients were *Clostridium difficile* followed by cytomegalovirus and tuberculosis (Table 1 for ORs). The most prevalent opportunistic infections in IBD patients by numbers were candidiasis followed by *Clostridium difficile*, human papilloma virus, influenza, and herpes simplex virus (Table 1). Viral infections i.e influenza (OR, 2.56 in CD; $p < 0.0001$ and OR, 1.75 in UC, $p = 0.0001$) and Epstein-Barr virus [EBV] (OR 2.69 in CD; $p < 0.0001$, and OR, 2.82 for UC; $p < 0.0001$) were more common in children (< 18 years of age). On the other hand, fungal and bacterial infections i.e aspergillosis (OR, 2.93 in CD; $p < 0.0001$, and OR, 3.21 in UC; $p < 0.0001$), histoplasmosis (OR, 1.60 in CD; $p = 0.003$, and OR, 2.14 in UC; $p < 0.0001$) and pneumococcal disease (OR, 3.36; $p < 0.0001$, and OR, 3.09 in UC; $p < 0.0001$) were more prevalent in the elderly (> 65 years). Tuberculosis was more common in CD and *Clostridium difficile* and cytomegalovirus infections were more common in UC.

Conclusion: OIs are more prevalent in patients with CD and UC. Children with UC and CD tend to have a higher prevalence of viral OIs and older adults with UC and CD tend to have a higher prevalence of fungal and bacterial OIs.

Disclosure: Nothing to disclose

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Opportunistic infection	Prevalence in CD /100,000	Prevalence in UC /100,000	Prevalence in non IBD /100,000	Odds Ratio CD	Odds Ratio UC	Odds Ratio CD vs UC
Histoplasmosis	104.4	93.4	22.9	4.57, 95% CI 3.91 to 5.35, p < 0.0001	4.09, 95% CI 3.41 to 4.90, p < 0.0001	4.09, 95% CI 3.41 to 4.90, p < 0.0001
Cryptococcosis	26.1	15.6	4	6.50, 95% CI 4.75 to 8.91, p < 0.0001	3.88, 95% CI 2.49 to 6.03, p < 0.0001	1.68, 95% CI 0.98 to 2.87, p = 0.059
Pneumocystis jiroveci	39.1	38.9	9.4	4.16, 95% CI 3.22 to 5.37, p < 0.0001	4.13, 95% CI 3.12 to 5.46, p < 0.0001	1.01, 95% 0.69 to 1.46, p = 0.974
Aspergillosis	71.8	85.6	16.6	4.33, 95% CI 3.59 to 5.24, p < 0.0001	5.17, 95% CI 4.28 to 6.24, p < 0.0001	0.84, 95% CI 0.64 to 1.09, p = 0.191
Candidiasis	5858.2	5702.1	1995	3.06, 95% CI 2.99 to 3.12, p < 0.0001	2.97, 95% CI 2.90 to 3.04, p < 0.0001	1.03, 95% CI 1.00 to 1.06, p = 0.078
Strongyloides	3.3	7.8	1.4	2.34, 95% CI 0.97 to 5.65, p = 0.059	5.58, 95% CI 2.98 to 10.44, p < 0.0001	0.42, 95% CI 0.14 to 1.23, p = 0.113
Listeriosis	6.5	7.8	0.9	7.64, 95% CI 4.07 to 14.35, p < 0.0001	9.11, 95% CI 4.85 to 17.11, p < 0.0001	0.84, 95% CI 0.35 to 2.01, p = 0.694
Legionella	19.6	31.1	11.4	1.72, 95% CI 1.20 to 2.46, p = 0.0031	2.73, 95% CI 2.00 to 3.73, p < 0.0001	0.63, 95% CI 0.39 to 1.01, p = 0.055
Pneumococcus	293.6	303.4	89.1	3.30, 95% CI 3.01 to 3.62, p < 0.0001	3.41, 95% CI 3.09 to 3.77, p < 0.0001	0.97, 95% CI 0.884 to 1.11, p = 0.633
Nocardiosis	6.5	7.8	1.8	3.64, 95% CI 1.95 to 6.80, p = 0.0001	4.34, 95% CI 2.32 to 8.10, p < 0.0001	0.84, 95% CI 0.35 to 2.01, p = 0.694
Clostridium difficile	2596.4	3905.4	226.5	11.74, 95% CI 11.37 to 12.13, p < 0.0001	17.90, 95% CI 17.39 to 18.43, p < 0.0001	0.66, 95% CI 0.63 to 0.68, p < 0.0001
Tuberculosis	156.6	124.5	29.5	5.31, 95% CI 4.67 to 6.04, p < 0.0001	4.22, 95% CI 3.61 to 4.94, p < 0.0001	1.26, 95% CI 1.03 to 1.54, p = 0.0245
Influenza	2322.4	2341.7	1468.4	1.60, 95% CI 1.54 to 1.65, p < 0.0001	1.61, 95% CI 1.55 to 1.67, p < 0.0001	0.99, 95% CI 0.94 to 1.04, p = 0.734
HPV	3901.1	4092.1	1966.6	2.02, 95% CI 1.97 to 2.08, p < 0.0001	2.13, 95% CI 2.07 to 2.19, p < 0.0001	0.95, 95% CI 0.92 to 0.99, p = 0.0099
EBV	241.4	225.6	131.9	1.83, 95% CI 1.65 to 2.03, p < 0.0001	1.71, 95% CI 1.52 to 1.92, p < 0.0001	1.07, 95% CI 0.92 to 1.25, p = 0.389
CMV	228.3	319.0	21.9	10.45, 95% CI 9.39 to 11.64, p < 0.0001	14.62, 95% CI 13.2 3to 16.14, p < 0.001	0.72, 95% CI 0.62 to 0.83, p < 0.0001
HSV	1937.5	1913.8	1019.5	1.92, 95% CI 1.85 to 1.99, p < 0.0001	1.89, 95% CI 1.82 to 1.97, p < 0.0001	1.01, 95% CI 0.96 to 1.07, p = 0.648

[OIs in patients with CD and UC from 2013 to 2018 in a large population based database in United States]

P0917 NON-CELIAC WHEAT SENSITIVITY AND CELIAC DISEASE IS STRONGLY AND INDEPENDENTLY ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY OF 3542 RANDOMLY SELECTED SUBJECTS

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Introduction: Diet may be involved in the pathogenesis of inflammatory bowel disease (IBD) but this is controversial, as is an association between IBD with celiac disease (1). Wheat sensitivity has been reported in Crohn's disease, and associated with more severe disease (2). A diet which excludes gluten (along with other dietary components) has been shown to induce clinical remission in 79% of treated patients with Crohn's disease (3). These findings suggest gluten may aggravate IBD.

Aims and Methods: The aims of this study were to evaluate if wheat sensitivity and celiac disease are risk factors for physician-diagnosed IBD in a general community and determine which symptoms and factors are associated with wheat sensitivity in IBD. A total of 3542 people randomly selected from the Australian population returned a mail survey (Digestive Health & Wellbeing Survey, response rate = 43%) which contained questions on gastrointestinal (GI) symptoms (present in the last 3 months), medical and lifestyle factors including a self-reported physician diagnosis of celiac disease and IBD. Response bias was minimal. Wheat sensitivity was defined as people without celiac disease who reported GI symptoms on wheat ingestion. Associations between categorical variables were evaluated using the Pearson chi-square test.

Results: The prevalence of IBD by self-report in our cohort was 1.9% (95% CI 1.5–2.5). Of those with IBD, 13% reported celiac disease compared with 1.2% of those without IBD (unaffected cohort) (OR 12.9, 95% 6.0–27.7). In addition 26.7% of those with IBD reported wheat sensitivity, compared with 14.8% of the unaffected cohort (OR 2.1, 95% CI 1.2–3.7, Attributable Risk 11.9% 95% CI 0.7–23.2). There was no significant association between wheat sensitivity in IBD and age (p = 0.27), gender (p = 0.16) or psychological distress (p = 0.93). There was a significant association with modified Rome IV criteria for functional dyspepsia (OR 3.49, 95% CI 1.03–11.82), particularly epigastric pain syndrome subtype (OR 4.11, 95% CI 1.15–14.73), but not irritable bowel syndrome. Symptoms significantly associated with wheat sensitivity in the IBD cohort included epigastric pain and constipation (see Table 1).

Conclusion: In this cohort, celiac disease and wheat sensitivity are both significantly associated with a diagnosis of IBD, and wheat sensitivity is associated with constipation and epigastric pain in particular. This suggests exacerbation of symptoms in IBD may be related to wheat sensitivity. These results suggest that it is worth testing for celiac disease in IBD, and asking patients whether wheat sensitivity worsens symptoms if the present results are confirmed.

Disclosure: This abstract has been presented at DDW 2018

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P0918 LONGITUDINAL IMPACT OF IBS-TYPE SYMPTOMS ON DISEASE ACTIVITY, HEALTHCARE UTILISATION, PSYCHOLOGICAL HEALTH, AND QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE

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Introduction: Irritable bowel syndrome (IBS)-type symptom reporting in quiescent inflammatory bowel disease (IBD) is associated with anxiety, depression and reduced quality of life when compared with patients who do not report these symptoms (1,2). However, the impact of IBS-type symptom reporting on disease activity, healthcare use and psychological well-being over protracted follow-up is uncertain. This was addressed in a longitudinal study of secondary care IBD patients.

Aims and Methods: Longitudinal disease activity was defined by glucocorticosteroid prescription or disease flare identified by physician's global assessment, escalation of medical therapy, hospitalisation, or intestinal resection. The number of investigations performed and clinics attended determined healthcare utilisation. Psychological well-being, including assessment for the presence of anxiety, depression or somatisation, and quality of life, was determined using

validated questionnaires. These outcomes were compared over a minimum period of 2 years between patients reporting IBS-type symptoms and patients with quiescent disease, occult inflammation, and active disease at baseline. A χ^2 test was used to compare categorical variables and an independent samples t-test to compare continuous data. Due to multiple comparisons, a 2-tailed p value of <0.01 was considered statistically significant for these analyses. Independent predictors of the occurrence of any of the objective disease activity outcomes of interest were determined by performing multivariate Cox regression analysis to control for baseline demographic, disease related and psychological characteristics. Results were expressed as hazard ratios (HR) with 95% confidence intervals (CI).
Results: In 360 IBD patients, there were no differences in longitudinal disease activity between patients reporting IBS-type symptoms and patients with quiescent disease or occult inflammation. Glucocorticosteroid prescription or disease flare identified by physician's global assessment, and escalation of medical therapy, was more common in patients with active disease than in patients reporting IBS-type symptoms (HR = 3.16; 95% CI 1.93–5.19 and HR = 3.24; 95% CI 1.98–5.31, respectively). A significantly greater mean number of investigations were performed in patients reporting IBS-type symptoms than those with quiescent disease (p = 0.008), but not compared with patients with occult inflammation or active disease. Anxiety, depression, and somatisation scores at follow-up were significantly higher, and quality of life scores significantly lower, in patients reporting IBS-type symptoms when compared with patients with quiescent disease, but were similar to patients with active disease.
Conclusion: The reporting of IBS-type symptoms in IBD was associated with increased healthcare utilisation, psychological co-morbidity, reduced quality of life, but not adverse objective disease activity outcomes during longitudinal follow-up.
Disclosure: Nothing to disclose

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P0919 EVIDENCE OF A BI-DIRECTIONAL EFFECT OF THE BRAIN-GUT AXIS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Evidence to support the existence of a bi-directional relationship between the presence of mood disorders and gastrointestinal symptom reporting has been previously described (1,2). Whether a similar bi-directional relationship exists between psychological co-morbidity and disease activity in inflammatory bowel disease (IBD) is uncertain. We aimed to resolve this issue during longitudinal follow-up in secondary care patients.
Aims and Methods: The hospital anxiety and depression scale (HADS) and clinical disease activity indices were administered at baseline and after ≥2 years. Faecal calprotectin (FC) was collected at baseline. Objective markers of disease activity during longitudinal follow-up were assessed via case note review. These included glucocorticosteroid prescription or flare of disease activity defined by physician's global assessment, escalation of medical therapy, hospitalisation and intestinal resection. Brain-to-gut interactions were defined as development of new-onset disease activity in patients with quiescent disease and abnormal baseline HADS scores. Gut-to-brain interactions were defined as *de novo* abnormal HADS scores in patients with active disease and normal HADS scores at baseline. Multivariate Cox regression analysis was performed to control for baseline characteristics and duration of follow-up, with results expressed as hazard ratios (HRs) with 95% confidence intervals (CI).
Results: 405 (50.7%) of 799 patients with baseline data were followed up. Baseline clinical disease activity was associated with an almost six-fold increase in subsequent development of abnormal anxiety scores (HR 5.77; 95% CI 1.89–17.7). In patients with clinically quiescent disease at baseline, abnormal anxiety scores were associated with need for glucocorticosteroid prescription or flare of disease activity (HR 2.08; 95% CI 1.31–3.30) and escalation of medical therapy (HR 1.82; 95% CI 1.19–2.80), but not hospitalisation (HR = 1.59; 95% CI 0.77–3.31) or intestinal resection (HR = 0.79; 95% CI 0.22–2.84). Abnormal baseline anxiety scores remained associated with subsequent flare of disease activity or escalation of medical therapy when both normal clinical disease activity indices and FC $<250\mu g/g$ were used to define quiescent disease at baseline (HR = 2.29; 95% CI 1.03–5.07 and HR = 2.43; 95% CI 1.13–5.20, respectively). There was no association between depression and disease activity during longitudinal follow-up.
Conclusion: We provide evidence of a bi-directional relationship between psychological co-morbidity and disease activity in IBD, suggesting that brain-gut axis activity may have a significant effect on the natural history of IBD. These findings underline the need for the development of novel approaches towards IBD management, away from one that focuses solely on the management of inflammatory activity, to one that integrates this with the need for proactive management of psychological well-being. Novel therapeutic interventions are much needed.
Disclosure: Nothing to disclose

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P0920 HOSPITALIZATION AND RE-HOSPITALIZATION IN INFLAMMATORY BOWEL DISEASE: REASONS FOR A GROWING REALITY

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Introduction: Inflammatory Bowel Disease (IBD) is a chronic disease with a significant burden of healthcare utilization and hospitalizations.
Aims and Methods: The aim of this study was to evaluate the causes of hospitalization and readmission, therapeutic intensification and surgery rates, in patients with Inflammatory Bowel Disease admitted to our department.
This was a retrospective study of all patients with acute exacerbation of Inflammatory Bowel Disease admitted in our department from January 2011 to December 2016.
Results: We included 446 admissions from 278 patients, 51% male, with mean age of 38.3 ± 14.3 years, 338 with Crohn's disease (CD) (47 newly diagnosis) and 108 with ulcerative colitis (UC) (21 newly diagnosis). The median time of hospitalization was 7 [5–10] days.
The large proportion of the patients (67.6%) with UC presented pancolitis, and in CD 46.5% had ileal involvement and 46.3% had penetrant disease. Twenty four percent took oral corticosteroids in the previous 3 months, 43.9% were under azathioprine and 20% under infliximab. The vast majority (95%) had had one clinic appointment in the previous 3 months.
The main causes of admission were acute exacerbation of CD (39.9%) e UC (24.2%), being 3 patients admitted to an intermediate care unit. The most common symptoms were abdominal pain (83%), diarrhea (54%), nausea (44%) and reduction in bowel movements (26%).
During the hospital stay, 65.2% were treated with intravenous corticosteroids, 41% with antibiotics, 14.8% with infliximab and one patient was submitted to surgery.
After discharge, more than an half needed to intensify therapy and 21.5% were submitted to surgery.
The readmission rate at 30, 90, 180 and 360 days were, respectively, 9.4%, 20%, 27.1% and 34.5%. The factors associated with readmission at 180-days were therapy with intravenous corticosteroids ($p < 0.05$) and reduction in bowel movements ($p < 0.05$).
Conclusion: Patients with Inflammatory Bowel Disease present with multiple exacerbations of the disease, needing multiple admissions and therapeutic intensification.
The readmission rate in patients with IBD is high and intravenous corticosteroids use during hospitalization ($p < 0.05$) and reduction in bowel movements ($p < 0.05$) were statically associated with 180-days readmission.
Disclosure: Nothing to disclose

P0921 IS FATIGUE COMMON IN INFLAMMATORY BOWEL DISEASE AND IS IT A SEPARATE ENTITY?

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Introduction: Fatigue in inflammatory bowel disease (IBD) is a significant problem, reported to affect between 44–86% of patients with active disease [1,2] and 22–54% of patients in remission [1–5]. Fatigue has been demonstrated to have a substantial effect on quality of life [4] with IBD patients reporting fatigue as one of their main concerns [6,7].
However, the aetiology and pathogenesis of fatigue in IBD is unknown. Proposed mechanisms frequently centre around inflammation but this does not fully explain the persistence of fatigue in quiescent disease.
Little consideration has been given to the idea that fatigue may be a separate entity: could it be possible that it is actually a result of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME)?
Through our study, we wished to assess the burden of fatigue in a cohort of patients with IBD in Tayside and gain a better understanding of it by evaluating whether those reporting fatigue fulfilled criteria for CFS/ME.
Aims and Methods: We designed a questionnaire to assess the prevalence of fatigue in patients attending IBD clinics in Tayside and whether they met the diagnostic criteria for CFS/ME.
Given numerous guidelines for the diagnosis of CFS/ME exist we followed the recommendations from BMJ Best Practice and based our questionnaire on the following four criteria: Centres of Disease Control (CDC) which was the most widely used, International Consensus Criteria (ICC) which is the most widely accepted, Institute of Medicine (IOM) and the National Institute for Health and Care Excellence (NICE) guidance.
NICE guidelines, whilst suggested to be less clinically appropriate, were included as, in the UK, these may be the guidelines with which practitioners are most familiar.
All guidelines required specific patterns of fatigue in addition to associated symptoms; the biggest differences are in requirements for post exertional malaise and numbers of associated symptoms.
All patients attending the IBD clinics between 3rd−24th November 2017 were given the anonymous questionnaire to complete. Exclusion criteria were age < 16, incapacity and/or absence of an established diagnosis of IBD.

Questionnaire responses were analysed to determine whether the criteria for a diagnosis of CFS/ME in the context of each of the four guidelines had been reached.
Results: Of 130 patients approached, 113 met the inclusion criteria and 99 returned a completed questionnaire, forming the study group: 52 female; 47 male, median age 41 (range 18–84 years). 46 had Crohn's disease (CD), 38 ulcerative colitis (UC) and 12 IBD unclassified (3 did not state IBD type).
Fatigue was experienced by 65% (n = 64) and was more prevalent in CD than UC (74% vs 52%) and in females than males (77% vs 51%). 64% of those experiencing fatigue reported fatigue persisting in the absence of gastrointestinal symptoms.
Of these patients with fatigue, 26 patients (41%) with IBD fulfilled the NICE CFS/ME diagnostic criteria, 13 (20%) the ICC, 6 (9%) the IOM criteria and 13 (20%) the CDC criteria.
Conclusion: Fatigue is commonly reported in this population even when disease is reportedly in remission. Although there may be other confounding factors contributing to fatigue in our cohort, such as concurrent medication or co-morbidity, a small proportion nevertheless meet recognised diagnostic criteria for CFS/ME and this should not be overlooked when managing fatigue in IBD.
Disclosure: Nothing to disclose

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P0922 PREVALENCE AND FEATURES OF SPONDYLOARTHRITIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory Bowel Diseases (IBD) are associated with the variety of Extra-intestinal Manifestations (EIM), axial involvement is common. Sacroiliitis on different imaging modalities is detected in 20–50% of patients with IBD (both in ulcerative colitis (UC) and Crohn's Disease (CD)). Ankylosing spondylitis (AS) occurs in 1–10% of patients [1].
Aims and Methods: The aim of the study is to determine the prevalence of Spondyloarthritis (SpA), AS and incidence of Inflammatory Back Pain (IBP) according to ASAS criteria in patients with IBD and to analyze the clinical features in patients with SpA and IBD compared to patients with IBD alone.
The single-center observational cross-sectional study included 91 patients with IBD: 52 (57.1%) with UC, 39 (42.9%) with CD, males – 47 (51.6%), mean age – 40.2 years (95% CI 39.0 to 41.0), duration of IBD – 7.7 years (95% CI 5.9 to 8.1). Seven (7.7%) patients had an established diagnosis of AS. Inflammatory Back Pain (IBP) was determined according to ASAS criteria (2009), which include five clinical signs. If suspected with SpA, patients underwent X-ray and/or MRI of sacroiliac joints. Secondary SpA was diagnosed in compliance with ECCO recommendations, AS was defined according to the modified New-York Criteria (1984). Mann-Whitney test and Fisher's Exact Test were performed for group comparisons between patients with SpA and IBD and IBD alone, with $p < 0.05$ considered statistically significant. Univariate binary logistic regression models were constructed to assess the ORs.
Results: Chronic Back Pain was observed in 58 patients (63.7%), IBP was detected in 39 (42.9%) patients with IBD. Diagnosis of SpA was established in 26 (28.6%) patients. Significant sacroiliitis, sufficient for the diagnosis of AS according to modified New York criteria was found in 14 (15.4%) patients. Patients with CD had higher chance of being diagnosed with SpA compared to patients with UC (41.0% vs. 19.2%, OR 2.92 (CI 1.14–7.48)). In patients with a combination of IBD and SpA, the incidence of chronic back pain (41.3% and 0%, p = 0,00), arthralgia (45.7% and 15.4%, p = 0.29), arthritis (75% and 20%, p = 0.00) and inflammatory back pain (51.3% and 11.5%, p = 0.00) was higher compared to patients with IBD alone. Clinical and laboratory signs of IBD, such as frequency of bowel movement, abdominal pain, ESR, CRP and hemoglobin values, were similar between the groups. There was also no difference between the patients with SpA and IBD and with IBD alone in the duration of IBD, disease activity and smoking.
Conclusion: Almost half of the patients with IBD had signs of inflammatory back pain according to ASAS criteria; one-third of them was classified as SpA. Patients with CD had higher chance of having of SpA compared to UC. Performing of pelvis X-ray in patients with IBD increased the number of diagnosed cases of AS by twofold.
Disclosure: Nothing to disclose

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P0923 FACTORS ASSOCIATED WITH GUT COLONIZATION AND DECOLONIZATION WITH EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING ENTEROBACTERIA IN ULCERATIVE COLITIS PATIENTS: PRELIMINARY STUDY RESULTS

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Introduction: Extended spectrum beta-lactamase producing Enterobacteria (ESBL-E) are the most frequently found multi-drug resistant bacteria colonizing the gut of ulcerative colitis (UC) patients.[1] Changes in the microbiome may act as a trigger in UC inflammation process. Previous studies have shown that gut colonization with ESBL-E might increase UC disease severity.[2]
Aims and Methods: The aim of the study was to analyze whether gut colonization with ESBL-E in UC patients is a constant state or changing over time and what are the factors attributing to that. A prospective study was conducted analysing patients with clinically, endoscopically and histologically confirmed UC diagnosis previously hospitalized in two largest tertiary medical care centres in Riga, Latvia. During the two study visits (2015 and 2017) the same patients participated in out-patient interviews regarding factors for gut colonization and decolonization with ESBL-E, UC disease activity was evaluated according to the full Mayo score (FMS), faecal samples were obtained and analyzed for ESBL-E presence according to EUCAST guidelines.
Results: 102 patients with UC participated in the fist study visit in 2015 and gut colonization with ESBL-E was found in 12% (n = 12) of the patients. 29 patients participated in the second study visit in 2017 and gut colonization with ESBL-E was found in 7% (n = 2) of the patients. The analyzed reasons for not participating in the second study visit showed that patients with previous gut colonization with ESBL-E were feeling bad (8 vs 1 patient) or had traveled abroad (17 vs 8 patients) more often at the time of the visit, comparing to the patients which were not previously colonized with ESBL-E. In between the two study years, two patients had become newly colonized with ESBL-E, whereas two other patients became decolonized. Patients who became newly colonized with ESBL-E were only women and were 11 years older in comparison to the patients who became decolonized. Both patients who become decolonized, had not used any antibiotics during the study period, while all the patients who became newly colonized with ESBL-E had used antibiotics during the study period. Patients newly colonized with ESBL-E had more exacerbations – 11, in comparison to decolonized patients, who only had 1 exacerbation during the study period. All patients who became colonized with ESBL-E had severe UC disease activity, while patients who became decolonized had either mild or moderate UC disease activity, according to the FMS. Also the mean FMS in patients who became colonized with ESBL-E was much higher – 11 (severe disease), comparing to the patients who became decolonized – 6 (moderate disease). There were no differences found in patients who became colonized and decolonized with ESBL-E regarding hospitalization times, UC conservative treatment and surgical interventions.
Conclusion: Gut colonization with ESBL-E in UC patients is not a constant state and is changing over time. Older age, female gender, previous antibiotic use, patients with more UC exacerbations and higher UC disease activity may act as risk factors for gut colonization with ESBL-E in UC patients. Inversely – younger age, male gender, abstention from antibiotic use, less UC exacerbations and lower UC disease activity may act as factors for gut decolonization from ESBL-E in UC patients.
Disclosure: Nothing to disclose

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P0924 INCIDENCE AND DISEASE PRESENTATION OF ELDERLY-ONSET IBD IN A EUROPEAN POPULATION-BASED INCEPTION COHORT – AN ANALYSIS OF THE EPI-IBD 2010-2011 COHORTS

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Introduction: Previous reports have indicated that the clinical presentation and initial treatment of patients with elderly-onset inflammatory bowel disease (IBD), defined as patients diagnosed ≥60 years, differs from that of younger patients.

Aims and Methods: To assess the age-specific incidence, initial presentation and treatment of elderly-onset IBD, compared with IBD diagnosed in patients aged 15–39 and 40–59, in a European population-based inception cohort.

The EPI-IBD cohort is a prospective, population-based inception cohort of patients diagnosed 2010 and 2011 in 36 European and 1 Australian centres. Background population was available for 35 centres representing 14,119,004 person-years; incidence was calculated considering only the patients diagnosed in those centres. For this study, data regarding disease characteristics and medical or surgical treatment during the first three months from diagnosis were analysed. All data were entered in a secure web-based database, www.epi-com-ecco.eu. Early, intensive treatment was defined as the need of immunomodulators (IMM), biologicals or surgery. Patients were classified according to age at diagnosis into 15–39y, 40–59y and ≥60y, and the results are presented in this sequence.

Results: In total, 2000 IBD patients (53.6% males) were included in the cohort, 747 (37.4%) CD, 1106 (55.3%) UC and 147 (7.4%) IBDU. The CD incidence was 7.18, 3.95 and 2.70 cases/10^5, in each age group respectively ($p < 0.001$). The UC incidence rate was 9.58, 6.30 and 5.68, respectively (40–59y vs ≥60y, $p = 0.257$). In elderly-onset IBD, overall more patients were diagnosed with UC, and the frequency of proctitis at diagnosis was lower (Table). In CD patients, elderly-onset patients more often had colonic location, while no differences were observed in disease behaviour (Table). Within the first three months, elderly-onset CD patients were less likely to be treated with IMM or biologicals. Elderly-onset UC patients received more frequently topical steroids and were less frequently treated with 5-ASA or IMM. No difference was observed between the age groups in the need of abdominal surgery, in CD or UC (Table). In CD patients, a regression analysis found that the need of early, intensive treatment was inversely associated to elderly-onset (OR 0.29, 95% CI 0.16–0.51) and inflammatory behaviour (OR 0.24, 95% CI 0.1–0.35). In UC patients, it was associated to extensive disease (OR 12.03, 95% CI 3.71–39.05) and inversely associated to elderly-onset (OR 0.35, 95% CI 0.16–0.75).

Conclusion: In this large population-based inception cohort, the age-specific incidence of CD decreases with age, while UC incidence shows a peak in young ages and it decreases to a plateau in adult and elderly individuals. Elderly-onset IBD shows a different phenotype from that of young patients: elderly patients are more likely to be diagnosed from UC, and in case of CD it is more frequently associated to colonic localisation. At diagnosis, elderly-onset IBD patients were less aggressively treated than other age groups; this differences in the management might be due to differences in severity but this should be confirmed with the analysis of the long-term follow-up of the cohort.

Disclosure: Nothing to disclose

P0925 USEFULNESS OF SYSTEMATIC LIVER BIOPSY DURING A SURGERY FOR INFLAMMATORY BOWEL DISEASE FOR THE DIAGNOSIS OF PRIMARY SCLEROSING CHOLANGITIS

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Introduction: PSC associated to IBD drastically increases the risk of liver and colonic complications. However, no specific screening is recommended. The local IBD unit proposed to perform systematic screening by liver biopsy during surgery.

Aims and Methods: The aims of the study were to assess the frequency, characteristics and outcomes of inflammatory bowel disease (IBD) patients diagnosed with primary sclerosing cholangitis (PSC) on systematic liver biopsy during a surgery for IBD.

In a retrospective monocentric study, all patients who underwent a major abdominal surgery related to IBD were included. IBD phenotype and outcomes were assessed according to the presence of PSC.

Abstract No: P0924

	15-39 years	40-59 years	≥60 years	p
IBD (CD -UC – IBDU)	40.5%–52.6%–6.9%	35.4%–56.3%–8.3%	29.7%–62.9%–7.4%	0.006
CD behaviour (B1 – B2 – B3 – B1+p – B2+p – B3+p)	64.8%–16.8%–8.3%–7.2% –1.7%–1.1%	63.6%–19.8%–9.1%–5.3% –1.1%–1.1%	66.0%–22.0%–6.0%–4.0% –1.0%–1.0%	0.912
CD location (L1 – L2 – L3 – L4–1+4 – L2+4 – L3+4)	30.4%–22.6%–23.3%–5.1% –5.1%–5.5%–7.7%	26.3%–29.0%–22.0%–7.5% –7.5%–1.6%–5.9%	22.7%–38.1%–19.6%–5.2% –9.3%–3.1%–2.1%	0.022
UC extent (E1 – E2 – E3)	23.2%–38.0% -38.7%	24.0%–42.5%–33.6%	16.2%–45.7%–38.1%	0.087
CD TREATMENT (5ASA – Systemic STEROIDS/Topic STEROIDS – IMM – BIOLOGICALS – ABDOMINAL SURGERY)	50.2%–46.5%/16.1%–37.6% –8.3%–7.4%	50.3%–38.3%/17.6%–27.8% –5.3%–8.6%	53.3%–37.0%/16.6%–14.0% (*)–1.0% (**)–10%	(*): $p < 0.001$ ///—/// (**): $p = 0.022$
UC TREATMENT (5ASA – Systemic STEROIDS/Topic STEROIDS – IMM – BIOLOGICALS – ABDOMINAL SURGERY)	89.9%–34.0%/8.9%–7.7% –2.2%–1.2%	90.2%–26.3%/7.4%–4.4% –1.3%–0.7%	83.5% (*)–29.2%/12.7% (**)–3.3% (***)–0.9%–0.5%	(*) $p = 0.025$ ///—/// (**) $p = 0.026$ ///—/// (***) $p = 0.027$

[Phenotype at diagnosis and initial (first 3 months) treatment]

Results: Between 1998 and 2011, 390 IBD patients were operated and followed-up for 68 months [14; 118], 255 systematic peroperative liver biopsies were performed. The incidence of PSC was 12.8%. Twenty-two patients with PSC on 29 (75.9%) had normal liver biochemistry at the time of surgery, and 18 PSC patients on 41 (43.9%) presented no abnormality during the follow-up. Hepatic pejorative outcomes were infrequent, no patient underwent liver transplantation. Demographic, IBD phenotype and IBD outcomes were broadly comparable according to PSC status except for disease location. Among the IBD population, 27 (6.9%) colorectal neoplasia occurred, including 8 (29.6%) in patients with PSC. The cumulative risk of developing colorectal neoplasia from IBD diagnosis were 1.1%, 3.5%, 10.6%, 19.6% at 5, 10, 20, 30 years respectively. Neoplasia was mostly multifocal (40.7%). By multivariate analysis, PSC strongly increased the risk of developing neoplasia, with an HR = 2.51 [1.01; 5.8]. Extensive colitis also increased the risk of neoplasia (HR = 2.71 [1.004; 9.49]). The use of immunosuppressant drugs and/or biotherapy trended to be independently associated with colorectal neoplasia (HR = 0.46 [0.21; 1.02], p = 0.05).
Conclusion: Asymptomatic forms of PSC are frequently associated to IBD and alter the prognosis of patients with colitis through colorectal neoplastic complications, favouring a systematic screening of PSC in these patients, including peroperative liver biopsy.
Disclosure: G Bouguen declares COI with abbvie, MSD, Takeda, Janssen, Pfizer, Hospira, Diasorin, Ferring

P0926 MARIA INDEX AT DIAGNOSIS AS A PREDICTOR OF DISABLING CROHN'S DISEASE

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Introduction: MaRIA index is the most well-characterized MRI index to measure activity in Crohn's Disease (CD). This index was validated with ileocolonoscopy as a reference. However, there are no data on its applicability as a predictor of disease course.
Aims and Methods: A retrospective study that included patients with ileal/ileocolic CD with initial diagnosis between 2013 and 2014 who underwent MRI prior to initiating treatment. MaRIA index was calculated in the worst affected segment taking into account the formula: 1.5x wall thickness (mm) + 0.02x relative enhancement + 5x edema + 10x ulceration. Disabling DC was defined as ≥1 of the following: ≥2 cycles of corticoid therapy/year, cortico-dependence or cortico-refractoriness; immunomodulatory/anti-TNF modulation or dose escalation; ≥2 hospitalizations; new events (perianal, penetrating and / or stenosis); ≥1 surgery. The aim of this study was to evaluate MaRIA index at diagnosis as a predictor of disabling CD.
Results: Included 26 patients – mean age 37 ± 13 years; 58% female; 62% inflammatory, 30% penetrating, 8% stenosing; 46% ileal, 54% ileocolic. At follow-up (mean 31 ± 9months), 65% of the patients had disabling CD- corticosteroid therapy in 31% (n = 8), immunomodulator / anti-TNF modification or dose escalation in 46% (n = 12), hospital admission in 27% (n = 7), new events in 27% (n = 27) and surgery in 15% (n = 4).
The MaRIA score was a predictor of disabling CD (12 vs 21; p = 0.001). From the formula, wall thickness (3,8mm vs 6,7mm; p = 0.02) and ulceration (0% vs 21%; p = 0.02) were predictors of disabling CD.
Conclusion: The MaRIA score at diagnosis in this group of patients was a predictor of disabling DC during the course of the disease.
Disclosure: Nothing to disclose

P0927 DYSPLASIA SURVEILLANCE IN INFLAMMATORY BOWEL DISEASE – A COHORT STUDY

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Introduction: Patients with inflammatory bowel disease (IBD) are at increased risk for developing colorectal cancer (CRC) – this risk is modulated by several factors. Currently, surveillance colonoscopy is recommended to detect and treat neoplastic lesions.
Aims and Methods: A cohort study was conducted in order to determine clinical and endoscopic variables associated with dysplasia in IBD patients who were part of a colonoscopy surveillance program between 2011–2016.
Statistic tests: Chi-square, Fisher's Exact Test, Mann-Whitney U test, Multivariate Logistic Regression.
Results: A total of 162 patients (51.2% men, mean age at diagnosis 36.8 ± 13.5 years, mean duration of IBD at the start of the program: 11.0 ± 8.9 years) were included.
105 patients had Ulcerative Colitis (UC) (70.5% having extensive colitis) and 57 patients had Crohn's Disease (CD), 82.5% of which with > 50% surface of the colon affected. Only 6 patients had concurrent primary sclerosing cholangitis, 18 had a family history of CRC and 6 had personal history of colorectal dysplastic lesions.
The majority of patients (95.7%) were or had been under 5-ASA; half (55.6%) of the patients received thiopurines and 24.1% were or had been under anti-TNF alpha.
A total of 342 colonoscopies were performed during the 5 years period (2.1 ± 1.2 colonoscopies/patient). Random biopsies were performed at least once in 81.5% of patients with a mean 27.5 ± 6.4 biopsy samples per colonoscopy and 33.3% of the patients underwent chromoendoscopy (CE) at least once.
During the surveillance period, endoscopically resectable lesions were detected in 55 patients (34%) and visible lesions deemed unfit for endoscopic resection were found in 5 patients (3.1%). Overall, 61 dysplastic visible lesions (58 with low grade dysplasia and 3 with high grade dysplasia) and 1 adenocarcinoma were found in 34 patients.
Dysplasia in random biopsies was present in 3 patients, the yield of random biopsies for dysplasia being 1.85% per-patient (3/162), 1.75% per-colonoscopy (6/342) and 0.25% per-biopsy (9/3637). Dysplasia detected in random biopsies was associated with a personal history of visible dysplasia (p = 0.006).
The presence of dysplasia, either in targeted samples or random biopsies, was significantly associated, on univariate analysis, with type of IBD (26.7% in UC vs 10.5% in CD) (p = 0.016), with the performance of random biopsies (p = 0.009), and CE (p = 0.05) and with previous ileo-colonic surgeries (p = 0.002). On multivariate analysis, dysplasia was associated with type of IBD (p = 0,034), with the performance of random biopsies (p = 0.09) and with previous ileo-colonic surgeries (p = 0.001). Median disease duration was superior in patients with dysplasia compared with those without dysplasia (14.0 (IQR 5.75–21.0) vs 9.0 (IQR 3.25–15.0) years, p = 0.03). There was no significant association between the presence of dysplasia and family history of CCR or personal history of PSC.
The presence of endoscopically resectable lesions was associated, on multivariate analysis, with duration of disease (p = 0.03), with the presence of histologic inflammation (p = 0.017) and with the performance of random biopsies (p = 0.02).
Conclusion: Our data confirm that patients with longstanding IBD, in particular UC, should be enrolled in dysplasia surveillance programs and that perfoming CE and random biopsies helps in the detection of colonic neoplastic lesions.
Disclosure: Nothing to disclose

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P0928 DISCRETE TERMINAL ILEAL ULCERS IN ULCERATIVE COLITIS PATIENTS: CLINICAL SIGNIFICANCE AND NATURAL COURSE

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Introduction: Aphthous or small ulcerations in terminal ileum are infrequently observed in patients with ulcerative colitis (UC) without evidence of backwash ileitis. However, clinical significance and natural course of terminal ileal (TI) ulcers in UC are unclear.
Aims and Methods: This study was conducted to demonstrate the frequency and prognostic implication of UC patients with TI ulcer. We retrospectively reviewed 1,585 UC patients with successful TI intubation among 2,211 UC patients, excluding 626 patients with no available images. To evaluate the frequency, we compared with those of historic healthy cohort (n = 26,735)[1] who had no gastrointestinal symptom and history of NSAIDs use at the same center. Regarding the clinical characteristics, we compared the 87 UC patients with TI ulcer (group A) and the 1,498 UC patients without TI ulcer (group B). The natural courses of TI ulcers were also investigated during the follow-up periods.
Results: Of 1,585 UC patients**,** 87 patients (5.5%) showed TI ulcer without the evidence of inflammation in the cecum and right colon, which was higher than the frequency of healthy cohort (106/26,735, 0.4%), (p < 0.001). There was not any difference in age, sex, smoking history, family history, and the incidence of extraintestinal manifestations between the group A and group B. The group A had more proctitis and left-sided colitis than the group B (p = 0.001). However, disease activity and maximal disease extent during follow-up periods were not different between the two groups. The histories of medication use including corticosteroids, azathiopurine, and anti-tumor necrotizing factor and the colectomy showed also no significant differences. Of the 55 patients who underwent follow-up colonoscopy, 36 patients (65.5%) showed a resolution of TI ulcer.

Conclusion: Discrete TI ulcers are more common in UC patients, compared with healthy control. Two third of them, lesions were resolved. Clinical impact on disease extension and severity seems not to be significant.
Disclosure: Nothing to disclose

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P0929 MAGNETIC RESONANCE ENTEROGRAPHY DEPLOYMENT IN AN INTERNATIONAL MULTICENTRE CLINICAL TRIAL OF VEDOLIZUMAB IN CROHN'S DISEASE: AN ANALYSIS OF TECHNICAL FEASIBILITY FROM THE VERSIFY TRIAL

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Introduction: Radiologic imaging is used as a method to monitor Crohn's disease (CD) activity in clinical practice. Magnetic resonance enterography (MREn) depicts the transmural extent of disease, and can be performed on equipment commonly available at most hospitals and many outpatient clinics globally. There is a growing interest in implementing MREn in clinical trials and in research. The magnetic resonance index of activity (MaRIA) score requires quantitative assessment of MREn imaging sequences before and after intravenous gadolinium. To date, assessment of MREn in the research setting has been largely restricted to single centre studies, and use of MREn in a prospective multicentre trial has not previously been reported.
Aims and Methods: The aim of this report was to evaluate the deployment of a standardised MREn protocol execution in a clinical trial setting in CD. VERSIFY (NCT02425111) was an international, multicentre, phase 3b, open-label study of mucosal healing with vedolizumab (VDZ) in a difficult-to-treat population (n = 101) with moderate-severe CD (≥3 months; CD Activity Index 220–450; Simple Endoscopic Score for CD ≥7; ≥1 mucosal ulceration on central endoscopy; prior failure with corticosteroid, immunomodulatory and/or ≥1 tumour necrosis factor antagonist). In the MREn substudy (n = 37), scanner and protocols were qualified and expert-to-site technologist training was delivered, either face-to-face or via conference call. Sites were qualified after submitting a test scan from a healthy volunteer. All MREns from Weeks 0 (baseline) and 26 (follow up) were consensus reviewed by two radiologists. Missing sequences were counted. Exam-adequacy was measured as critical sequences that allowed calculation of MaRIA score present (including T2 with/without fat saturation and T1 coronal pre-/post- gadolinium), sequence order correct and full anatomy covered. Image quality (5-point scale: 1–2 = failure; 3–5 = success) and artefact frequency were assessed. Per patient and per sequence analyses were performed for each visit. Data were summarised descriptively by time point (compared using McNemar's test).
Results: All MREns (37 patients with 302 sequences at baseline, 30 patients with 255 sequences at follow up) were reviewed. At baseline and follow up, 92% and 83% of patients had all critical sequences present, 97% and 93% had execution order that matched prescribed order, and 100% and 97% had full anatomy. The majority of sequences (98%; 98%) were rated as 3–5 on the quality scale. At baseline and follow up, artefacts were observed in 152 and 132 sequences (36 and 30 patients, respectively), most frequently: breath-motion (13%; 15% of sequences); low signal:noise ratio (15%; 15%); segmental signal loss (15%; 19%); and faeces/gas (6%; 9%).
Overall, 89% of patients at baseline and 83% at follow up had MREns suitable for assessing activity. In patients evaluated at both time points (n = 30), no significant change in the proportion of patients with inadequate examinations was observed (p = 0.51 missing sequences, p = 0.13 missing critical sequences, p = 1.00 acquisition order, p = 1.00 full anatomy, p = 0.73 complete readability; no patient had a quality score of 1 or 2 for any critical sequence at either time point).
Conclusion: MREn is considered an accurate, minimally invasive tool for monitoring CD activity in clinical practice and in research. In our study, MREn was technically feasible, indicating it also has the potential to be successfully deployed in an international multicentre clinical research setting.
Disclosure: Jordi Rimola: Robarts Clinical Trials – advisor; TiGenix – advisor; AbbVie – speaker fees, research grant; Takeda – honoraria fees; Genentech – research grant. Daniel Vas: Takeda – research consultancy. Silvio Danese: Speaker, consultant, and/or advisory board member for: Abbvie, Allergan, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Ferring, Hospira, Janssen, Merck, MSD, Mundipharma, Pfizer Inc, Sandoz, Takeda, Tigenix, UCB Pharma, Vifor. Cong Han, Ozlem Yardibi, Stephen Jones and Jenifer Siegelman: Employees of Takeda

P0930 THE TORONTO IBD GLOBAL ENDOSCOPIC REPORTING (TIGER) SCORE: A SINGLE, EASY TO USE ENDOSCOPIC SCORE FOR ALL IBD PATIENTS

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Introduction: It can be difficult to differentiate the various forms of inflammatory bowel disease (IBD) endoscopically. There is a need for a single endoscopic score for all IBD patients to simplify and unify mucosal assessment for Crohn's disease (CD), ulcerative colitis (UC) and inflammatory bowel disease – unclassified (IBDU). Although the Mayo score for UC is relatively simple to use, it does not account for the entire colonic burden of disease as it is not scored by segment and there is no agreement on how IBDU should be assessed and with which score.
Aims and Methods: The aim of this study was to develop an endoscopic scoring tool for all IBD patients and to compare it with existing endoscopic scoring tools for UC and CD.
The TIGER score was developed as a modified endoscopic mucosal scoring tool using renewed parameters and specifications (mucosal appearance, ulcer/erosion size, percent ulcerated/erosion mucosal surface, segmental involvement and presence of luminal narrowing) that can be applied during ileocolonoscopy to any IBD patient. A unique property of the TIGER score is that it adds extra points for segments showing moderate to severe mucosal involvement thereby allowing a global assessment of the total endoscopic severity. Three blinded IBD experts reviewed and scored anonymized ileocolonoscopy videos for 200 intestinal segments in 40 IBD patients (20 CD and 20 UC). In addition to the TIGER score, the Mayo score and the SES-CD were simultaneously determined for UC and CD subjects respectively. Reviewers' inter-rater reliability for the TIGER score was explored using the interclass correlation coefficient (ICC) with 95% confidence intervals (CI) for all 200 ileocolonic segments (5 segments per patient X 40 patients). The TIGER score was categorized into two distinct levels: a score of 0–4 represented a mild/inactive disease segment and ≥5 represented a moderate to severely active segment. Agreement in the categorized score was estimated using Cohen's kappa coefficient as well as the overall agreement percentage. Clinical application of the scores were determined a priori as follows: TIGER score >4, Mayo >1 and SES-CD > 5 per segment were all considered to be consistent with moderate to severe mucosal disease. The agreement between the TIGER score and the conventional scores was estimated using Cohen's kappa coefficient as well as by reporting the overall agreement with 95% confidence intervals (CI).
Results: The ICC per segment between reviewers was excellent (ICC = 0.94; 95% CI: 0.92–0.96). In the categorized TIGER score the lowest overall agreement was 96.9% [95% CI: 93.5%−98.6%] and the lowest kappa was 0.91 [95% CI: 0.84–0.98], reflecting excellent agreement. The overall agreement per segment between the SES-CD and TIGER was 91% [95% CI: 84%−95%] with a kappa coefficient of 0.74 [95% CI: 0.59–0.90]. The overall agreement between the Mayo and the TIGER scores was 84% with a kappa coefficient of 0.61 [95% CI: 0.42–0.80], indicating moderate to good agreement. Per patient analysis for the 3 total scores included all 40 patients and yielded overall agreement of 88% [95% CI: 74%−94%] and kappa coefficient 0.66 [95% CI: 0.39–0.93]. McNemar's test (p = 0.1797) reflected no significant difference in clinical application between the TIGER score and the conventional scoring methods.
Conclusion: The TIGER endoscopic score is comparable to existing endoscopic scoring tools for ileocolonoscopy in terms of assessing disease severity and was shown to be reproducible and easy to use for both CD and UC patients.
Disclosure: E. Zittan-None AH. Steinhart-received research Grants – Abbvie, Amgen, Pfizer, Millennium. Honorarium for Educational Event Presentations – Abbvie, Janssen, Takeda, Shire Advisory Board – Abbvie, Actavis, Janssen, Takeda, Pharmascience, Shire. R. Milgrom-none N. Schwartz-none M. Zelcer-none IM. Gralnek-none S. Zelber-Sagi-none MS. Silverberg-received research support and consulting fees from Janssen, Abbvie, Takeda, and Prometheus.

P0931 HISTOLOGICAL FEATURES OF ULCERATIVE COLITIS IN NON-OPERATED PATIENTS WITH *CLOSTRIDIUM DIFFICILE* INFECTION

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Introduction: The incidence of *Clostridium difficile* infection (CDI) is increasing both in general population and in patients with ulcerative colitis (UC). Available studies provide contradictory results: several studies demonstrated higher mortality and surgery rate following a CDI diagnosis [1] while another showed negative association between CDI and colectomy [2].
Aims and Methods: The aim of the study was to evaluate the impact of CDI in non-surgical patients with ulcerative colitis (UC), to estimate association between CDI and disease severity in patients with UC, to examine histologic features suggestive of CDI in patients with UC.
A cross-sectional study included 70 consecutive inpatients or outpatients with UC (37 males, 33 females, aged 19 to 65 years, mean age 37.97 ± 1.53 years) with disease duration of 1 to 10 years. Patients received no antibiotic medications for at least 6 months prior to the study. None of the patients was operated or died during hospital admission or was operated previously. No patents were diagnosed to have pseudomembranous colitis. Patients were enrolled after history and clinical examination, stool samples and were evaluated for the presence of C. difficile toxins A and B (CDT) by ELISA. UC severity was assessed according to Mayo Score/disease activity index (DAI): mild in 24 cases (34.3%), moderate — in 26 (37.1), severe — in 20 (28.6%). All patients underwent hi-resolution colonoscopy in white and NBI modes with mucosa biopsies (1 per each segment of the colon and terminal ileum). Colonic biopsies were scored 0 through 3 for lymphocytic, neutrophilic infiltration and atrophy. Slides were also reviewed for evidence of pseudomembranes, ischemic-like changes and *lamina propria* hemorrhage. Bacterial overgrowth syndrome (BOS) was diagnosed by hydrogen breath test with lactulose.
Results: Thirty one UC patients (44.3%) had no CD toxins, 33 (47.1%) —toxin B only, 6 (8.6%) — both A and B toxins. Demographic data and laboratory values upon admission did not differ between subgroups of patients with and without CDT. BOS was revealed in 17 of 30 cases (56.7%). Colon histology revealed no signs consistent with pseudomembranous colitis. As determined by Kruskal-Wallis one-way ANOVA and chi-square test there was no statistically significant difference in gender, age, education level, duration of UC history, stool frequency, type of immunesuppressive therapy, other clinical, endoscopic or histological features of UC or in the presence of BOS in patients with and without CDT. No difference was found in UC severity according to DAI: mild/moderate/severe distribution was 9/12/10 for CDT-negative and 15/14/10 for CDT-positive patients respectively ($\chi^2 = 0.749$, $p = 0.688$).
Conclusion: CDT may play important role for the outcomes of severe UC patients undergoing surgery, who receive potent broad-spectrum antibiotics. However, no significant differences in severity of UC in our group of patients in relation to the presence of CDT were found.
Disclosure: Nothing to disclose

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P0932 COMPARISON OF BOWEL ULTRASONOGRAPHYAND MAGNETICRESONANCE ENTEROGRAPHY FOR DETECTING ENDOSCOPY-BASED DISEASE ACTIVITY IN ILEOCOLONIC CROHN'S DISEASE

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Introduction: Cross-sectional imaging techniques, including bowel ultrasonography (BUSG) and magnetic resonance enterography (MRE) are increasingly used for evaluation of Crohn's Disease (CD). Various clinical, laboratory and imaging indices have been derived to evaluate disease activity in CD.
Aims and Methods: The aim of the present study was to compare the diagnostic accuracy of BUSG and MRE for detecting disease activity in CD using simple endoscopic score for CD (SES-CD) as reference standard. A total of 71 consecutive adult patients with known CD underwent ileocolonoscopy, BUSG and MRE within one month prospectively, and comparisons were made as per-patient. The SES-CD > 6 was accepted as active disease. Sensitivity of BUSG and MRE for detection of disease activity was compared with the McNemar test, with results of SES-CD > 6.
Results: The sensitivity and specificity of BUSG lesions in detecting patients with SES-CD > 6 were as follows; bowel wall thickening 62.3/50, loss of wall stratification 66.7/34, color Doppler USG signal (Limberg 3–4) 78.6/36.8, rigidity 81/40, mesenteric fibro-fatty proliferation 76.9/40, and fistula 66.7/33.8, respectively. Noteworthy MRE lesions in detecting patients with SES-CD > 6 were as follows; bowel wall thickening 70.2/50, loss of wall stratification 69.6/40, bowel wall edema 74.4/43.8, ulcers 65.3/31.8, total hyperenhancement 67.9/37.9, layered enhangement 64.3/32.6, homogenous enhangement 70/36.6, comb sign 69.2/35.6, mesenteric fibro-fatty proliferation 79.4/45.9, and lymphadenopathy 69.6/35.4, respectively.
Regarding the fallowing uniform parameters, there was a significant correlation between BUSG and MRE in detecting endoscopically active CD (SES-CD > 6): bowel wall thickening ($p = 0.727$), prestenotic dilatation ($p = 0.210$), mesenteric fibro-fatty proliferation ($p = 0.167$), mesenteric lymphadenopathy ($p = 0.815$), and fistula ($p = 1.000$). Compared to BUSG, the diagnostic accuracy of MRE was significantly higher in detecting loss of wall stratification and strictures ($p = 0.000$). On the other hand, diagnostic accuracy of BUSG color Doppler signal (Limberg 3–4) was significantly higher than MRE comb sign in detecting hyper vascularity ($p = 0.030$).
Conclusion: BUSG and MRE are equally accurate to detect disease activity in CD. MRE was more sensitive than BUSG for detection of loss of wall stratification and strictures. BUSG was significantly more sensitive than MRE in detecting hyper vascularity. In this study, bowel wall thickening, loss of wall stratification, rigidity, increased color Doppler signal, fistula and mesenteric fibro-fatty proliferation come into prominence on the BUSG examination in active CD. BUSG may denote an alternative technique to MRE in evaluating disease activity and follow-up of CD.
Disclosure: Nothing to disclose

P0933 PLATELET INDICES IN THE COURSE OF INFLIXIMAB INDUCTION REGIMEN IN ULCERATIVE COLITIS PATIENTS – EXPERIENCE OF A SINGLE CENTRE – A PILOT STUDY

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Introduction: Platelet (PLT) abnormalities are known to participate in the pathological appearance of inflammatory bowel disease (IBD). Chronic inflammatory process in patients with IBD is connected with elevated PLT count and changes in PLT activation.
Aims and Methods: The aim of the study was to assess the correlation between PLT indices: MPV (mean platelet volume), PCT (plateletcrit), PDW (platelet distribution width), C-reactive protein (CRP) and endoscopic picture in the course of infliximab (IFX) induction regimen in ulcerative colitis (UC) patients. 46 patients with UC, 32 men and 16 women, were enrolled to the study. They were administered IFX (standard induction therapy). Laboratory tests (CRP and PLT indices) and colonoscopy were performed in all patients during induction regimen – at 0, 2, and 6 weeks and in follow-up six weeks after finished induction therapy.
Results: The study revealed statistically significant ($p < 0.01$) decrease in mean CRP level (from 32.35 to 7.05 mg/L) and mean PLT count (from 398 to 315 x 10^9/L) together with improvement of endoscopic picture (MAYO score; $p < 0{,}01$) in all patients. Mean MAYO score prior to BT and after finished induction therapy were 9.78 and 2.76 points, respectively; mean MAYO endoscopic subscore decreased from 2.8 to 1.84 points ($p < 0.01$). Mean PCT values were too high prior to BT (0.46%) and normalized after induction therapy (0.22%) ($p < 0.01$). On the other hand, mean MPV measurements were under normal range during qualification to BT (6.8 fl) and obtained adequate values after BT (8.08 fl) ($p = 0.01$). Subsequently, CRP and PCT levels correlated positively with each other before the introduction of BT ($p = 0.02$). Negative correlations between PDW level and PLT count and positive correlations between PCT level and PLT count were noticed before IFX induction regimen and in follow-up after finished therapy, too ($p < 0.01$).
Conclusion: Chronic inflammatory process in patients with IBD is connected with elevated PLT count and changes in PLT activation and morphological parameters. Our data suggest that PLT indices might be useful biomarkers for determining active UC and for assessing the efficacy of BT. However, further studies are required to establish a correlation between platelet functions and BT in IBD patients.
Disclosure: The work was presented as a poster at one international meeting – Falk Symposium 209 October 6–7, Berlin, Germany IX GASTRO-CONFERENCE (Part II) IBD 2017 – Therapeutic and Biological Barriers

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P0934 DISEASE SEVERITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE ASSOCIATED WITH CARDIOVASCULAR DISEASES

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Introduction: Patients with inflammatory bowel disease (IBD), i.e. Crohn's disease (CD) and ulcerative colitis (UC), may be at increased risk for cardiovascular disease (CVD) even in the absence of documented risk factors. Data linking the severity of IBD to coexisting CVD are rather scarce.
Aims and Methods: This is a retrospective analysis from IBD patients with concurrent CVD derived from 3 participating IBD Centers. Patient demographic and clinical characteristics, routine laboratory tests including serum biomarkers, disease activity scored by the Harvey-Bradshaw Index (HBI) for CD and the Simple Colitis Activity Index (SCCAI) for UC, quality of life scores based on the short inflammatory bowel disease questionnaire (SIBDQ), and health care resources utilization were compared to those of IBD patients without CVD. Statistical analysis was performed with the SPSS 24.
Results: Overall, 321 IBD patients (167 CD, 154 UC, 192 males, median [IQR] age 55[42–65] years) with a mean (±SD) follow-up of 12.6 ± 9.3 years were included. Of these, 82(35.5%) patients, mainly with UC (59.8% vs 43.8%, $p = 0.015$) had a history of CVD. CVD followed IBD diagnosis in 51.2% of cases. Among patients with CVD, 53 (64.6%) reported coronary artery disease (4/53 had at least another one CVD comorbidity), 22 (26.8%) were diagnosed with stroke, 10 (12.2%) with heart failure, and 2 (2.4%) with peripheral artery disease. Patients with CVD were smoking more frequently (75.6% vs 66.5%, $p < 0.001$), had hypertension (65.9% vs 18%, $p < 0.001$) and diabetes mellitus (34.1% vs 6.3%, $p < 0.001$) as well as older age at diagnosis (53.6 ± 15.2 vs 38.2 ± 14 years, $p < 0.001$) and elevated body mass index (28.8 ± 0.6 vs 26.7 ± 0.4, $p = 0.04$). Patients without CVD were receiving more often anti-TNFa (53.6% vs 26.8%, $p < 0.001$), steroids (81.2% vs 59.8%, $p < 0.001$), immunomodulators (61.1% vs 36.6%, $p < 0.001$) but no 5-ASA ($p = 0.285$). HBI, SCCAI, or SIBDQ scores did not differ between the two groups. Rates of hospitalization and/or surgery after diagnosis were not different between the two groups. Endoscopic activity was milder when CVD was present ($p = 0.018$ and $p = 0.002$ respectively for UC and CD).
Conclusion: The results of this study did not confirm the hypothesis that IBD patients with CVD have a more severe disease. Inflammatory burden possibly plays a less important role in the development of CVD in IBD patients. Data from larger prospective studies are essential to confirm our findings.
Disclosure: Nothing to disclose

P0935 THE ROLE OF SERUM IL-17 AND IL-23 IN ASSESSING INFLAMMATORY BOWEL DISEASE SEVERITY

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Introduction: Interleukin-17 (IL-17) and Interleukin-23 (IL-23) play a critical role in inflammatory bowel disease (IBD) immune response and are currently being targeted by therapeutic agents in clinical trials. High serum levels of IL-17 and IL-23 in IBD patients with active disease has been reported before, but the relationship between these cytokines and disease severity has not been thoroughly assessed.
Aims and Methods: We aimed to investigate if the levels of IL-17 and IL23 in the serum of patients with Crohn's disease (CD) and ulcerative colitis (UC) reflect disease severity and if they correlate with standard inflammatory biomarkers, such as C-reactive protein (CRP) and fecal calprotectin (FC).
We prospectively included in the study 62 IBD patients and 15 healthy controls. Using disease activity scores, disease pattern, serum and fecal inflammatory biomarkers we further classified the patients into severe and mild or moderate disease. Serum levels of IL-17 and IL-23 were determined using sandwich enzyme-linked immunosorbent assays (ELISA). Mann Whitney U test was used to assess distribution among groups, and Spearman's rank correlation for describing relationship among variables. Numerical data was presented with median and interquartile range.
Results: In Crohn's disease, IL-17 had with 930.48pg/mL lower serum levels in mild/moderate disease group vs severe disease group, $p = 0.119$. As for IL-23, mild/moderate group had with 699.86pg/mL lower serum levels than severe disease group, $p = < 0.001$. In UC, mild/moderate group had with 1328.13pg/mL lower levels of IL-17 ($p = 0.003$) and with 723.62pg/mL lower levels of IL-23 ($p = < 0.001$) comparatively to the severe group. Spearman's rank correlation test between IL-17, IL-23 and Fcal showed a correlation coeficient of 0.52 for IL-17 ($p = 0.003$) and 0.67 for IL-23 ($p = < 0.001$). The median distribution of IL-23 serum levels among patients with intestinal complications showed with 622.1pg/mL higher values in fistula group ($p = 0.035$) vs other types of complications.
Conclusion: IL-17 and IL-23 serum level can differentiate between IBD patients with severe and non-severe disease and can assess disease severity in the clinical practice. Further monitorization of these cytokins in larger IBD groups might be a promissing tool in assessing disease progression.
Disclosure: Nothing to disclose

P0936 SYMPTOMS OF ANXIETY AND DEPRESSION IN INFLAMMATORY BOWEL DISEASE

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Introduction: Treatment of Crohn's Disease (CD) and Ulcerative Colitis (UC) is usually directed at organic aspects of the disease, often disregarding psychosocial factors. A comprehensive strategy including identification of anxiety and depression are possible therapeutic targets to increase quality of life in inflammatory bowel disease (IBD).
Aims and Methods: The present study aims to test the association between anxious and depressive symptoms with IBD activity and course.
Of 221 patients followed in outpatient setting in October and November of 2017, 64 patients with confirmed IBD who accepted to participate in the study were selected. Patients with known mental illness followed by Psychiatry were excluded. Anxiety symptoms were quantified by Spielberg's Anxious State Inventory (STAI) and symptoms of depression by the Beck II Depression Scale (BDI-II).
Results: Sixty-four patients were included, of which 75% with CD and 25% with UC. The mean age was 40 ± 13.99 years and 53.1% were female. Clinical remission rate was 87.5% in CU and 75% in CD, with an endoscopic remission rate of 25% in CU and 50% in CD. The correlation between anxiety and depression symptoms was significant ($p < 0.001$, $r = 0.73$). There was no statistically significant difference in anxiety and depression scores between patients with CD and CU. The correlation of number of disease flairs with STAI and BDI-II scores was significant (STAI $p = 0.023$; BDI-II $p = 0.017$). In IBD patients, there was also a statistically significant association between STAI score (anxiety) and clinical remission, endoscopic remission and need for therapy step-up ($p < 0.05$). In CD patients there was a significant association between anxiety and the presence of perianal disease ($p = 0.035$). In UC patients, there was a significant association between anxiety and recent flair ($p = 0.021$), use of emergency room ($p = 0.029$), hospitalization ($p = 0.029$) and therapy step-up ($p = 0.013$). In this group of patients a significant association between depressive symptoms and immunosuppressant or anti-TNF therapy was seen ($p = 0.009$).
Conclusion: In the analyzed patients there was an association of anxious and/or depressive symptoms with frequency of disease flairs and disease activity. Screening for anxious and depressive symptoms may have a significant impact on the quality of life of patients with IBD.
Disclosure: Nothing to disclose

P0937 QUALITY OF CARE AND OUTCOMES IN A TERTIARY HOSPITAL INFLAMMATORY BOWEL DISEASE (IBD) CENTER: MONITORING AND TREATMENT ALGORITHMS AT REFERRAL AND DURING FOLLOW-UP

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Introduction: IBD is associated with substantial disability and impairs quality of life. Optimal management of IBD requires harmonized monitoring processes and treatment pathways. We aimed to retrospectively analyze quality of care indicators (QIs) including patient assessment strategy, monitoring, treatment decisions and outcomes at referral and during follow-up in the McGill University Health Center (MUHC) IBD Center.
Aims and Methods: We reviewed out- and inpatient records of consecutive patients seen at the MUHC IBD center between June and December 2016. Demographic variables, outpatient visits, inpatient stays including IBD related surgery, laboratory, imaging and endoscopy data, current medications and/or changes in medications, and vaccination profile were captured.
Results: 1357 patients (46.8% male, 64.4% Crohn's disease (CD), age at diagnosis: 29.8 years, age at referral: 39.3 years, duration of disease: 14.1 years) were included. At referral 49.5% of CD patients had ileocolonic, 45% complicated behavior (B2 or B3) and 23.7% perianal disease. 47.2% and 41.7% of UC patients had extensive and moderate to severe disease, respectively. Patients

were objectively re-evaluated at referral: 68.4% underwent ileocolonoscopy, 15.7% upper GI endoscopy, 15.6% of CD patients had abdomino-pelvic MRI or CT and 23.6% abdominal US. CBC, CRP and FCAL were measured in 89.9%, 81.9% and 16.5%, respectively. Medical therapy was changed in 53.6% (active disease: 75.6%, remission: 24.4%), and 22.5% of patients started biological therapy at around referral. 12.4% of patients required hospitalization while 6% surgery at referral. During follow-up, in June-December 2016, 41.1% of patients were receiving biological therapy and 15.1% of patients were steroid dependent. An objective patient monitoring strategy was applied at the IBD center: ileocolonoscopy/colonoscopy was performed in 79% within 2 years before, and in 32% within 6 months from index visit. Biomarkers (CRP: 78%, FCAL: 37.6%) *C. difficile* or stool culture (18% and 17.9%) and therapeutic drug monitoring (16.3%) were performed frequently. Treatment was changed in 18%. Need for surgery (4%) and hospitalization (8%) were low, while 16.8% of patients required an IBD-related ER visit within 6 months after index visit.
Conclusion: Our data support that tight monitoring was applied at the MUHC IBD center with a high emphasis on objective patient (re) evaluation, and accelerated treatment strategy at referral or during follow-up.
Disclosure: Nothing to disclose

P0938 BENEFITS OF IMPLEMENTING A RAPID ACCESS CLINIC IN A HIGH VOLUME INFLAMMATORY BOWEL DISEASE CENTER: ACCESS, RESOURCE UTILIZATION AND OUTCOMES

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Introduction: IBD impacts on a patient's physical health, social functioning and quality of life, contributing to the health-economic burden associated with the disease, especially in emergency situations. We aimed to prospectively measure the impact of the implementation of a rapid access clinic (RAC) at a tertiary IBD center.
Aims and Methods: Consecutive patients from the McGill University Health Center who accessed the RAC via email were prospectively included, between June 2017 and January 2018. Time to medical appointment, resource utilization (laboratory, imaging and endoscopy), need for change in medical therapy, unplanned emergency (ER) visits or admissions 30 to 90 days after consulting the RAC were collected.
Results: 173 patients (61% female, mean age: 38 years, CD: 64%, L3: 50.9%, B2-3: 34.6%, UCE3: 53.8%, biological therapy: 67.3%, previous surgery: 21%) were included. 85% of requests were considered appropriate for a RAC appointment. 65.9% of patients presented with a clinical flare. Patients were seen at the IBD clinic a median of 3 days (mean 4.7) after the request. Laboratory assessment including FCAL (52%) and CRP (80%) was performed as appropriate. Fast-track endoscopy (colonoscopy or sigmoideoscopy) was performed in 32 and 11 patients (19.8% and 6.6%), and 13 patients (7.8%) had abdominal/pelvic CT. Treatment was modified in 78 patients (48.8%). Admission was initiated in 5 patients during RAC visit. A total of 8 (4.6%) and 3 (1.7%) patients required an ER visit within 30 and 90 days after the RAC appointment, of which 2 and 1 patients had non-IBD reason for presenting at ER.
Conclusion: Implementation of a RAC improved healthcare delivery by avoiding unnecessary ER visits and optimizing resource utilization.
Disclosure: Nothing to disclose

P0939 FECAL CALPROTECTIN AS A SURROGATE MARKER FOR PREDICTING RELAPSE IN ADULTS WITH ULCERATIVE COLITIS: A META- ANALYSIS

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Introduction: The clinical course of ulcerative colitis (UC) is featured by remission and relapse, which remains unpredictable. Recent research revealed that fecal calprotectin (FC) could predict clinical relapse for UC in patients with remission, but this role of FC has not been applied to clinical practice.
Aims and Methods: We carried out a comprehensive electronic search of PUBMED, WEB OF SCIENCE, EMBASE and the Cochrane Library to identify all eligible studies. Diagnostic accuracy including pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR) and pooled area under the receiver operating characteristic (AUROC) was calculated using a random effects model. Sources of heterogeneity were detected by subgroup analysis. Potential factors correlated to DOR were tested by meta regression.
Results: 14 articles enrolling a total of 1043 participants were finally included for final calculation. Pooled sensitivity, specificity, PLR, NLR were 0.73 (95% CI: 0.67–0.77), 0.77(95% CI: 0.74–0.80), 3.32 (95% CI: 2.30–4.79) and 0.40(95% CI: 0.32–0.51) respectively. The area under the summary receiver-operating characteristic (sROC) curve was 0.81 and the diagnostic odds ratio was 9.29 (95% CI: 5.71–15.12). FC was more diagnostically accurate in studies using Bühlmann as FC assay (DOR = 15.08; 95% CI: 6.84–33.25) and studies with longer follow-up time (DOR = 9.61; 95% CI: 5.52–16.72) or a lager cut-off value (DOR = 11.64; 95% CI: 4.93–16.72). There was no significant correlation between any of the covariates and the DOR in the univariate meta-regression analysis.
Conclusion: Our study confirms the diagnostic utility of FC for the detection of UC relapse in adults. Due to its simplicity and noninvasiveness, measuring FC levels at clinical remission appears to be a reliable and reproducible indicator to predict UC relapse.
Disclosure: Nothing to disclose

P0940 GASTROINTESTINAL SYMPTOMS ARE COMMON IN U.S. PATIENTS WITH MODERATE-SEVERE PSORIASIS

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Introduction: Patients with moderate-to-severe plaque psoriasis (PsO) are at increased risk of developing inflammatory bowel disease (IBD). A survey was conducted to evaluate the prevalence of gastrointestinal symptoms in PsO patients.
Aims and Methods: An electronic survey was available to U.S. PsO patients with data collected from Jan-Feb. 2017. Patients with moderate-to-severe plaque PsO and healthy controls (HC), with common co-morbidities allowed in both groups qualified for inclusion in the survey. Psoriasis patients were further categorized as those without recent exposure to biologic therapy (PsO-) vs those with recent (within 4 months) biologic exposure (PsO+). GI symptoms and signs, including frequency and severity, were compared across groups. CalproQuest (CPQ) scores, which have recently been proposed as a tool to identify patients with elevated fecal calprotectin levels and increased risk for IBD, were also calculated. Patients with inflammatory bowel disease (IBD), inflammatory bowel syndrome (IBS), or other gastrointestinal (GI) diagnoses with symptoms that overlap with IBD were excluded.
Results: Overall, 915 patients with self-reported moderate-severe PsO and 1,411 healthy controls participated. Demographics were generally comparable between

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	Psoriasis patients (PsO-)	Psoriasis patients + recent treatment* (PsO+)	Healthy controls (HC)
Number of pts	465	450	1411
GI signs & symptoms			
Belly Pain	20.6% (96) p = 0.002 vs HC p = 0.002 vs PsO+	36.9%(166) p = 0.002 vs HC	10.5%(148)
Full/Bloated	37.2% (173) p = 0.002 vs HC p = 0.002 vs PsO+	48.4% (218) p = 0.002 vs HC	25.3% (357)
Diarrhea	16.3% (76) p = 0.023 vs HC p = 0.002 vs PsO+	29.3% (132) p = 0.002 vs HC	12.2% (172)
Mucous in stool	4.5% (21) p = 0.020 vs HC p = 0.317 vs PsO+	6.0% (27) p = 0.002 vs HC	2.4% (34)
Blood in stool	4.3% (20) p = 0.004 vs HC p = 0.390 vs PsO+	5.6% (25) p = 0.002 vs HC	1.9% (27)

Data reported in % (n), *recent treatment = within 4 months of biologic, p-values are comparisons between psoriasis groups and healthy controls.

[Table 1]

groups. GI symptoms and signs were significantly more prevalent in the PsO- and PsO+ groups vs the HC group. Pain, fullness/bloating, and diarrhea were more frequent in PsO+ vs PsO- groups (Table 1). A significantly greater percentage of PsO- and PsO+ patients had positive CPQ scores vs HCs, with the greatest percentage of positive CPQ scores in the PsO+ group: 9.5% in PsO-, 20.2% in PsO+ vs 5.7% in HC, p = 0.005.

Conclusion: GI symptoms and signs are common in patients with moderate-to-severe PsO, more so than in healthy controls. This suggests that physicians caring for patients with PsO may consider assessing for GI symptoms and signs, and monitoring for their progression with treatment of PsO to identify patients potentially at risk for developing IBD.

Disclosure: This study was supported by Janssen Research & Development, LLC.

P0941 THE ACCURACY OF A HOME PERFORMED FAECAL CALPROTECTIN TEST IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Endoscopic examination is a golden standard in evaluation of mucosal healing, which should be the main goal in the treatment of paediatric patients with inflammatory bowel disease (IBD). However, due to clear invasiveness, biomarkers, especially faecal calprotectin (FC), have become standard part of remission assessment.

Aims and Methods: The aim of the study was to compare accuracy for detection of endoscopic activity using a recently developed FC home test to standard ELISA assay (FC-ELISA). Finally, 102 consecutive observations from 89 paediatric patients with IBD (62 Crohn's disease (CD) and 27 Ulcerative colitis (UC)) were included in prospective observation study. We parallelly performed home FC test based on a smartphone image evaluation from lateral flow device (FC-IBDoc, Buhlmann Laboratories AG, Switzerland) analysed by physician and FC-ELISA in IBD patients indicated for endoscopic evaluation. We defined mucosal healing by endoscopic scores, in patients witch CD by SES-CD $<=2$ (n = 44), in patients with UC by UCEIS $<=4$ (n = 27) and in patients with CD after ileocecal resection (ICR) by Rutgeert's score i0 and i1 without signs of colon involvement (n = 19). Due to multiple observations from one subject the associations between mucosal healing and FC were assessed using generalized linear mixed model and linear mixed model. The sensitivity and specificity of FC-IBDoc and FC-ELISA for respective scores were analysed using ROC curve with cross-validated area under curve (AUC), optimal cut-off values were found. The AUCs were compared using DeLong test and regression models were compared using ANOVA.

Results: We found an association of the mucosal healing scores of the entire group both with FC-ELISA (p = 0.002) and FC-IBDoc (p = 0.012). The AUC for FC-ELISA was 0.883 (95% CI 0.807–0.960) with optimal cut-off at 136.5 ug/g, the AUC for FC-IBDoc was 0.792 (95% CI 0.688–0.895) with optimal cut-off at 48 ug/g. The accuracy of FC-ELISA was better than FC-IBDoc when tested by Delong test (p = 0.033). Similarly, the regression mix-model constructed using FC-ELISA as predictor was significantly better than the model using FC-IBDoc. We did not find any association with FC, neither tested by FC-ELISA nor by FC-IBDoc, and mucosal healing among subset of patients assessed by SES-CD, UCEIS nor Rutgeert's score. When assessing inflammation intensity using linear mix-model for subsets of observations evaluated by SES-CD we found association with FC-ELISA ($\beta = 2.35$,95% CI 0.98–3.81), but not with FC-IBDoc. We found association of UCEIS both with FC-ELISA and FC-IBDoc ($\beta = 0.62$, 95% CI 0.37–0.85, resp. $\beta = 0.46$,95% CI 0.19–0.74). FC-ELISA and FC-IBDoc was associated with Rutgeert's score in subgroup of CD patients after ICR ($\beta = 0.46$, 95% CI 0.21–0.70, resp. $\beta = 0.30$, 95% CI 0.10–0.53).

Conclusion: The standard ELISA assay for FC evaluation seems to be a more reliable predictor of mucosal healing than the FC home test in paediatric IBD patients. The cut-off values for both tests were highly incongruous. The FC-IBDoc could not be used for prediction of the inflammation intensity defined by SES-CD.

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P0942 DOES FAECAL MICROBIAL DYSBIOSIS CORRELATES WITH DISEASE ACTIVITY MEASURES, FAECAL CALPROTECTIN AND SYMPTOM SCORES IN ADULT PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) which primarily consists of Crohn's disease (CD) and Ulcerative Colitis (UC) has a chronic relapsing nature. Therefore, it is of importance to detect, predict and treat a relapse as soon as possible in order to decrease the inflammation and avoid further intestinal damage. There is increasing evidence substantiating that intestinal microbial dysbiosis in IBD plays a role in the pathogenesis and progression hereof. Dysbiosis is poorly understood and therefore not yet considered in clinical use for optimizing treatment of IBD.

Aims and Methods: The aim was to characterize the microbiome in IBD in a consecutive cohort, and correlate dysbiosis index and other findings to conventional disease activity measures in understanding and interpreting the microbiome in IBD.

During 1 year, 120 consecutive IBD patients in any IBD therapy were enrolled in the web-outpatient clinic at North Zealand University Hospital, Capital Region of Denmark to monitor on Constant.care.dk. Patients were randomized to home-monitoring every 3rd month or on demand (monitoring after patients choice) on Constant care © and CalproSmart™ app. All home-monitoring data were visualized to the patients in a traffic light manner: Harvey-Bradshaw Index (HBI) for CD or Simple Clinical Colitis Activity Index (SCCAI) for UC and faecal calprotectin (FC) using CalproSmart™ Self Test Kit (Calpro AS, Norway).

The microbial dysbiosis index (DI); 1–5 normo-dysbiosis, GA-map™ (Genetic Analysis AS, Norway)[1] was correlated to disease activity indices and FC. Polymerase chain reaction (PCR) of faecal bacteria's 16S rRNA, Illumina was additionally analysed and subsequent bioinformatic analyses were performed.

Patients were asked to send faecal samples for both microbiome analyses longitudinally every time they were scoring themselves on the apps.

Results: Eighty four IBD patients consented to send faecal samples for microbiome analysis. 64 (76%) send longitudinal samples, 14 (17%) handed in only one sample each and 6 (7%) did not send any samples at all. Out of the 78 patients that sent faecal samples – 11 (14%) were diagnosed with CD (n = 36 samples), 63 (81%) with UC (n = 230) and 4 (5%) with IBDU (n = 22). Median (IQR) for the following variables FC, SCCAI, HBI and DI were respectively: 82 (28–455), 1 (0–2), 3 (1–9), 3 (2–4). Spearman correlations between FC and DI: 0.24 ($p < 0.01$), DI and SCCAI: 0.17 (p = 0.01), DI and HBI: 0.25 (p = 0.17). Based on Illumina microbial data 3 clusters (PCoA) according to FC values categorized as; remission (0–200 mg/kg), moderate activity (200–600 mg/kg) and severe activity (>600mg/kg) showed a trend towards separation in these 3 groups, ANOSIM R = 0.15, p = 0.001. No clear clusters were observed in regards to HBI and SCCAI.

Conclusion: Disease activity measures FC and SCCAI showed relatively small but significant correlations with DI-Dysbiosis Index. Illumina microbial data showed a trend in separating FC in mild, moderate and severe inflammation. Further bioinformatic analyses are awaiting on the individual longitudinal data in relation to disease course and changes in disease activity.

Disclosure: The study was financially supported by Ferring International, Switzerland and Non-financial supported by Calpro AS, Norway and Genetic Analysis AS, Oslo, Norway

Reference

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P0943 DIAGNOSTIC YIELD IN THE VISUALIZATION OF CAPSULE ENDOSCOPY BY A TRAINED NURSE

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Introduction: Capsule endoscopy (CE) allows a complete, painless and noninvasive exploration of the small bowel (SB), eliminates insufflation inconveniences and the need of sedation permitting the patient the possibility to return to daily activities after its intake. During the last years, endoscopy nurses have gained autonomy and acquired new roles for diagnostic purposes that were previously only reserved to the medical field. The implementation of CE has given nurses a broad field to develop in an autonomous and secure way.

Aims and Methods: We aimed to compare the diagnostic precision of a nurse with a specific endoscopic training to a gastroenterologist trained in visualization of the small bowel by capsule endoscopy.

Validation and reliability study of diagnostic procedures in witch were included all patients that were evaluated in a clinical setting at the Hospital Clínic of Barcelona with a CE for the study of the SB, for the period of June 2016 to October 2017.

Capsules were visualized blindly by a capsule endoscopy trained gastroenterologist and a nurse.

Results: 103 patients were included, average age of 54.28% ± 18.5. 44.7% was male, and 55.3% female. The most common indication for CE was anemia in 52.4% of cases. SB cleansing was excellent, good of fair in a 6.8%, 76.7% and 16.5% respectively.

The average time for visualization for the gastroenterologist and the nurse was 15.54 ± 7.05 y 16.12 ± 6.77 min, respectively with no significant differences.

The gastroenterologist and the nurse detected a total of 532 and 644 lesions respectively, which were significant in 129 (24.25%) and 135 (20.96%) (p = ns), and no significant were 403 (75.75%) y 509 (79.04%) ($p < 0.001$), respectively.

There was a good and statistical significant correlation between both explorers for the detection of significant and no significant findings ($R = 1$; $p < 0.001$).
The sensibility for a nurse was of 96.62% for any lesions, 100% for significant lesions and 95.53% for non-significant lesions.
This nurse, acquires sensibility and a positive predictive value (PPV) for the detection of lesions in the SB by CE, being of 100% for significant lesions, and uses a similar amount of time as a CE trained gastroenterologist.
Conclusion: A specialized nurse, trained and familiarized with the pathology of the small bowel, can detect the same amount of significant lesions as a trained gastroenterologist for the exploration of CE. The nurse can also detect more non-significant lesions that usually lack of clinical relevance.
Disclosure: Nothing to disclose

P0944 HOW TO PREDICT THE RESPONSE TO THERAPY IN CROHN'S DISEASE? – WHEN CONTRAST-ENHANCED ULTRASOUND CAN MAKE A DIFFERENCE

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Introduction: Contrast-enhanced ultrasonography (CEUS) in Crohn's Disease (CD) allows the detection and quantification of transmural vascularization.
Aims and Methods: The aim of this study was to evaluate the CEUS as a predictor of response to immunosuppressive treatment in CD.
A retrospective study was carried out with inclusion of patients with ileal CD, undergoing ileocolonoscopy and start immunosuppressive therapy, both with an interval < 8 days in relation to the CEUS. Demographic, endoscopic, clinical and analytical data were analyzed at the time of CEUS evaluation.
After assessing an area of interest in the bowel wall, the time-intensity curve was determined and quantitative parameters were recorded. Subsequent therapeutic changes, complications of the disease, surgery and need for hospitalization in the first 6 months were considered as failure to therapy.
Results: Twenty-eight CD patients were included. Significant endoscopic inflammatory activity (SES-CD≥7) was identified in 14 patients (50%).
The increase in brightness intensity, in relation to baseline, in patients with significant endoscopic activity was higher than in patients without significant endoscopic activity, 14.2x vs 4.7x, $p = 0.002$.
Ten patients did not respond to the therapy (35.7%). In relation to the increase in brightness intensity, a median was higher in the group of non-responders compared to the group of responders, 15.9x vs 4.8x, $p < 0.001$.
The area on the ROC curve of the increase in brightness intensity for prediction of therapeutic failure was 0.939. For values > 7.68x the baseline, the sensitivity, specificity, positive and negative predictive value was 100%, 83.3%, 76.9% and 100%, respectively.
There was no association between median C-reactive protein or fecal calprotectin and endoscopic activity ($p = 0.301$ and $p = 0.237$) and therapeutic response ($p = 0.065$ and $p = 0.440$).
Conclusion: The CEUS proved to be a useful, non-invasive, superior to the analytical parameters in detection of ileal inflammatory activity and prediction, with an excellent accuracy the treatment failure in CD.
Disclosure: Nothing to disclose

P0945 THERAPEUTIC DRUG MONITORING OF ADALIMUMAB: A COMPARATIVE STUDY OF A NEW POINT-OF-CARE QUANTITATIVE TEST WITH THREE ESTABLISHED ELISA ASSAYS

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Introduction: The need for therapeutic drug monitoring (TDM) in the treatment of inflammatory bowel disease (IBD) patients under biologics, namely adalimumab (ADA), is unquestionable. Several ELISA-based methodologies are already available in the market. A new point-of-care device (POC-ADA) was recently launched for monitoring serum ADA levels.
Aims and Methods: The aim of this study was to validate the first point of care for TDM of serum ADA levels available in the market by comparing it with three well- established methods. Sera from 199 IBD patients undergoing ADA therapy were quantified by two commercial ELISA, one in-house ELISA and a point of care rapid test. Moreover, donor's serum samples were spiked with known concentrations of ADA and the percentage of recovery of each assay was evaluated.
Results: Regarding the clinical samples, the Intraclass Correlation Coefficients (ICC) of the POC-ADA assay vs. the three ELISA-based established methods was 0.530, 0.761 and 0.864, respectively POC_ADA/ELISA A, POC_ADA/in-house ELISA and POC-ADA/Elisa B. When using different cutoffs for a qualitative comparison, POC_ADA showed an accuracy between 73–89% and the kappa statistics revealed mostly a good agreement (0.492 and 0.682). Spiked samples showed an excellent ICC between theoretical and measured concentrations for all the assays 0.927, 0.984, 0.982 and 0.989 and a good recovery 111%, 113%, 86%, 110%, respectively ELISA A, ELISA B, POC-ADA and in-house ELISA.
Conclusion: The new and first POC-ADA rapid test, which is able to deliver results within 15 min, can be safely used to replace the commonly used ELISA-based ADA quantification kits. This new assay is perfect for immediate concentration adjusted dosing avoiding delays cause by ELISA assays with a turnaround time of approximately 8h.
Disclosure: FM served as speaker and received honoraria from Merck Sharp & Dohme, Abbvie, Vifor, Falk, Laboratorios Vitoria, Ferring, Hospira and Biogen.

P0946 FECAL CALPROTECTIN AND FECAL IMMUNOCHEMICAL TEST HAVE DIFFERENT ASSOCIATIONS WITH ENDOSCOPIC ACTIVITY IN ULCERATIVE COLITIS

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Introduction: Fecal calprotectin (Fcal) and fecal immunochemical test (FIT) are known to be a useful predictor of endoscopic activity in ulcerative colitis (UC). The aim of this study is to confirm the correlation between ulcerative colitis endoscopic index of severity (UCEIS) and the two tests in addition to the existing Mayo endoscopic subscore (MES).
Aims and Methods: A total of 130 results, obtained in simultaneous examination with endoscopy and two tests, were retrospectively evaluated for 110 patients with UC. The efficacy of two tests for evaluation of endoscopic activity was compared. Endoscopic activity were assessed using the MES and UCEIS.
Results: Both Fcal and FIT results were significantly correlated with MES and UCEIS ($p < 0.001$ and $p < 0.001$). But Fcal showed a more accurate statistical correlation than FIT in both MES ($r = 0.688$ versus 0.662) and UCEIS ($r = 708$ versus 0.683). In the mucosal healing state, the sensitivity of FIT was more accurate than that of Fcal (sensitivity to MES 0; FIT 97% versus Fcal 71%, sensitivity to UCEIS 0 or 1; FIT 93% versus Fcal 64%).
Conclusion: Both Fcal and FIT were well correlated with endoscopic activity in UC. Fcal was more accurate than FIT in endoscopic activity and FIT was more sensitive to mucosal healing.
Disclosure: Nothing to disclose

P0947 AN OPEN-LABEL PROSPECTIVE STUDY OF THE SOLUBLE SERUM MARKER ST2 (IL-33 RECEPTOR) IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS TREATED WITH GOLIMUMAB: CLINICAL, ENDOSCOPIC AND HISTOLOGICAL RESULTS OF THE EVOLUTION STUDY

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Introduction: Suppressor of Tumorigenicity 2 (ST2) is an IL33 receptor detected in mucosa and serum of IBD patients and associated with inflammatory burden[1]. Golimumab (GLM) is effective for induction and maintenance of response in patients with moderate to severe ulcerative colitis (UC)[2]. Non-invasive serum biomarkers to assess intestinal inflammation and predict clinical response to therapeutic regimens are needed and may assist current IBD patient care.
Aims and Methods: This was an open-label uncontrolled multicenter prospective study. Primary objective was to evaluate the correlation of serum soluble ST2 levels with endoscopic and histological activity in subjects with moderate to severe active UC treated with GLM. All subjects were evaluated for clinical, endoscopic and histologic activity at screening, week 6 (W6) and week 16 (W16). Endoscopic and histologic activity were scored with the Mayo endoscopy score and Geboes score, respectively. Biomarker samples (ST2 and fecal calprotectin, FC) were collected at baseline and subsequent visits. All study data were analyzed using descriptive statistics. Statistical tests were two-tailed and considering a significance level of 0.05.
Results: A total of 38 patients were treated with GLM, 34 (89.5%) completed through W6 (full analysis set, FAS), and 29 (76.3%) completed through W16. Mean age (range) was 34.6 (19–65) years; 15 (44.1%) were male. At baseline, 94.1% had moderately active disease (Mayo score 6–10) and 5.9% (N = 2) severe disease; 27 (79.4%) were treated with immunosuppressants and 16 (47.1%) were taking glucocorticoids. At W6, 47.1% of patients were in clinical response and 14.7% in clinical remission; 62.1% and 37.9% at W16, respectively. At W6, ST2 levels were significantly correlated with endoscopic activity ($r_s = 0.451$, 95% CI: 0.133–0.685, $p = 0.0074$) but not with histological activity ($r_s = 0.252$, 95% CI: −0.094–0.544, $p = 0.1506$). At W16 no correlations were significant. For patients with endoscopically active (n = 20) *vs.* inactive (n = 14) UC at W6, ST2 levels were different at baseline: mean (SD) levels were 25.0 ± 12.5 *vs.* 17.2 ± 6.8 ng/mL ($p = 0.0259$). Changes from baseline to W6 were also different between patients with endoscopically active *vs.* inactive UC at W6: ST2 increase of 2.4 ± 7.8 *vs.* decrease of −3.5 ± 6.9 ng/mL ($p = 0.0290$), respectively. The best cut-off for ST2 level at W6 to discriminate between endoscopically active *vs.* inactive UC at W6 was 16.9 ng/mL, with specificity = 71% and sensitivity = 85% (AUC = 0.800, $p = 0.0001$). ST2 did not correlate with FC at any timepoint (baseline, W6, W16).
Conclusion: This exploratory study shows that ST2 may be a surrogate biomarker of UC disease activity and therapeutic response.
Disclosure: Patrícia Machado is an employee of MSD Portugal and George Philip of Merck & Co., Inc., Kenilworth, NJ, USA. Isabel Redondo was an employee of MSD Portugal at the time the study was conducted.

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P0948 CONTRAST-ENHANCED BOWEL ULTRASOUND IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is a chronic inflammatory disease of the bowel that necessitates thorough disease activity monitoring to provide an optimal treatment strategy. Colonoscopy is considered to be a gold standard method for mucosal healing assessment, although the method is invasive and not the most comfortable for a patient. Contrast-enhanced ultrasound (CEUS) is a promising non-invasive method of bowel wall evaluation.
Aims and Methods: Our aim was to estimate relation between endoscopic activity of UC and quantitative CEUS parameters. During a period from November 2016 to March 2018 45 patients with known UC were recruited into our study. Abdominal CEUS of the bowel (contrast agent – sulfur hexafluoride) with a linear transducer was performed in each patient. The acquired video-loops were processed on a computer work-station with an application Philips QLab. Region of interest including all the layers of the bowel was chosen. The application delivered a time-intensity-curve (TIC) as well as a fitted curve and TIC parameters. The latter were compared with endoscopic activity (Schroeder score) in a bowel segment examined with CEUS. Statistical analysis was carried out using Statistica 8.0 software.
Results: 39 patients were taken for the final analysis, in 7 patients the quality of CEUS data turned out to be inappropriate for quantitative analysis. 4 patients had endoscopic remission (Schroeder 0), 13 had mild disease (Schroeder 1), 15 – moderate disease (Schroeder 2), 7 – severe disease (Schroeder 3). Statistical analysis revealed a significant correlation between volume parameters (area under TIC, peak intensity) and endoscopic activity (Pearson correlation coefficient – 0.6 for AUC and 0.531 for PI, $p < 0.05$).
Conclusion: Quantitative parameters of bowel wall contrast enhancement significantly correlate with endoscopic activity in UC, therefore CEUS is a promising non-invasive tool for disease activity monitoring in patients with UC. Although further large studies are needed to recommend the method for a routine use.
Disclosure: Nothing to disclose

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P0949 CUTTING EDGE TECHNOLOGIES TO PREDICT TREATMENT RESPONDER AND NON-RESPONDER IN IBD PATIENTS

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Introduction: As it has been shown so far, ''-omics'' alone cannot help solving the dilemma of IBD. Physiological intermolecular modulation spectroscopy (PIMS), a cutting-edge technology is able to reconcile these data with the clinic. PIMS is a label free technology through which dynamic molecular resonance of entire proteins and macromolecular assemblies in a given organ of an individual is recorded, on real time, as the temperature within the sample rises from −37 to 37°C. It discriminates the responders from non-responders to a given treatment.
Aims and Methods: In a transversal clinical study, protein extracts of peripheral blood mononuclear cells (PBMC) of 47 outpatients (female = 16, mean age = 40.8 ± 16.4 years & men = 31, mean age = 41.5 ± 18.6) diagnosed with UC or CD (UC = 20, CD = 27) and treated with anti-TNFα, were subjected to PIMS analysis. Patient's data were blinded. One µg of total protein from each patient's PBMC was challenged with 10ng of infliximab. After determination of base line the samples were frozen at −37°C. Dynamic changes in macromolecular interaction were registered from −37 to 37°C. Three CD patients from each group of responder and non-responder were subjected to Nematic protein Organization technique (NPOT) technology in order to identify the pharmacologically active interactome behind.
Results: PIMS discriminated responder from non-responder profiles as follow: responder to infliximab CD 58% (n = 15) versus 42% (n = 12) non-responder as well as in UC, 65% (n = 13) versus 35% (n = 7) non-responder. This prediction matched with 98% accuracy with corresponding clinical results with only two miss matches in CD. NPOT revealed the presence of proteins ITGA2B, TLN1, FLNA, HSN and SAMHD1 beside the TNF alpha receptor in responder groups whereas only FLNA and SAMHD1 were found in non-responder group.
Conclusion:
1. PIMS in a blinded transversal study is able to stratify patients into two distinct groups of responders and non-responders to infliximab.
2. NPOT revealed the candidate protein interactors needed for benefic effects of infliximab. This could be of a high value for development of biomarkers.
Disclosure: Nothing to disclose

P0950 SATISFACTION OF DEEP NURSE ADMINISTERED PROPOFOL SEDATION VERSUS MIDAZOLAM AND FENTANYL DURING COLONOSCOPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE, RANDOMIZED CLINICAL TRIAL

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Introduction: Activity in chronic inflammatory bowel disease (IBD), (Crohn's disease and ulcerative colitis) is monitored endoscopically to adjust ongoing pharmacologic treatment in order to achieve defined therapeutic targets such

as mucosal healing. However, many patients opt out of endoscopic evaluation. Bowel preparation, pain, anxiety, embarrassment, and logistics are factors affecting adherence.
Aims and Methods: The aim of this study was to investigate the influence of deep sedation on the attitude towards colonoscopic monitoring in patients with IBD. A prospective, randomized clinical trial of deep nurse administered propofol sedation (NAPS) versus moderate midazolam and fentanyl sedation. Patients provided a satisfaction score prior to discharge. Patient aged > 17 years with a strong suspicion or established diagnosis of IBD and scheduled colonoscopy were eligible for the study. Exclusion criteria: ASA class > II, pregnancy, non-compliant with fasting, a history of complicated anaesthesia or inability to complete satisfaction survey.
Results: A total of 126 patients were randomized to deep (n = 62) or moderate sedation (n = 64). The deep sedation group was sedated significantly more to their liking (p = 0.001), experienced less pain (5 = no pain, 1 worst pain) (4.97 vs 3.42, p = < 0.001), and rated the current experience better than prior sedations and higher than the moderate sedation group, (4.30 vs 3.65, p = < 0.001). Of note, the deep sedation group were more likely to accept frequent endoscopies (4.33 vs 3.55, p = < 0.001), and scored higher on Overall Satisfaction score (4.94 vs 4.04, p = < 0.001) than the moderate sedation group. The results were consistent within a week after the procedure.
Conclusion: Patients with IBD significantly favor deep sedation over moderate sedation. Pain and previous experience with moderate or deep sedation are important contributing factors. Availability of deep propofol sedation may facilitate patient adherence to endoscopy-based monitoring programmes, including drug adjustment and cancer surveillance.
Disclosure: Nothing to disclose

P0951 LOW HAEMOGLOBIN DENSITY (LHD%) AS A NEW BIOMARKER FOR THE DETECTION OF IRON DEFICIENCY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: In the absence of a feasible, non-invasive gold standard, iron deficiency anaemia (IDA) is best measured by the use of multiple indicators. However, the choice of an appropriate single iron biomarker to replace the multiple-criteria model for IDA screening at the population level continues to be debated. Recently, low haemoglobin density (LHD%) from Coulter counters has been suggested as a useful tool to detect iron deficiency.[1] Its diagnostic performance in a population of patients with inflammatory bowel disease (IBD) has not yet been evaluated. Using the mathematical sigmoid transformation LHD% = $100\times\sqrt{}$(1-(1/(1 + e (1.8 (30-MCHC))))), this study investigated the reliability of LHD% for the assessment of iron status in iron deficiency anaemia (IDA), anaemia of chronic inflammation (ACI) and mixed IDA/ACI.
Aims and Methods: The study population consisted of 88 patients with IBD (mean age 39.09 ±13.12 years, 78.4% female) who consecutively attended the Interdisciplinary Crohn Colitis Centre Rhein-Main, Frankfurt/Main for routine evaluation between October 2014 and September 2016. In addition to LHD%, blood count, transferrin saturation (TSAT), serum ferritin (SF), and C-reactive protein (CRP) were determined by routine assays. Patients with anaemia were classified as having IDA if active inflammation (CRp < 5mg/L) was absent, TSAT < 20% and ferritin level < 30μg/L; patients were classified as having ACI if active inflammation was present (CRP ≥5mg/L), TSAT < 20% and ferritin level ≥100μg/L; patients were classified as having IDA/ACI if active inflammation was present, TSAT < 20% and ferritin level >100μg/L.[2] Receiver operator characteristic (ROC) curves were constructed to evaluate the diagnostic performance of LHD%.
Results: In ferropoenic IBD patients, applying a cut-off of 3.7%, LHD% values were not statistically different in patients with IDA compared to the IDA/ACI group (17.80 vs. 23.52%; p = 0.834). Significant differences were not observed between patients with ACI (LHD 12.52%) compared with the IDA/ACI group (LHD 23.55%, p = 0.268). ROC analysis for LHD% in the detection of iron deficiency showed the following: Area under the curve 0.927; cut off 3.7%, sensitivity 86%, specificity 85%. Haematological and biochemical parameters of the patients are shown in Table 1.
Conclusion: These results clearly demonstrate that LHD% is a reliable biomarker for the detection of iron deficiency in IBD patients with anaemia regardless of whether inflammation is present. Our findings indicate that LHD can provide added value in diagnosing iron deficiency in anaemic IBD patients.
Disclosure: Nothing to disclose

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P0952 MONITORING OF SURROGATE MARKERS OF ATHEROSCLEROIS IN A PROSPECTIVE COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Recent epidemiological studies report an increased risk of ischemic vascular disease in patients with inflammatory bowel disease (IBD). In a previous study (1) we have shown increased expression of surrogate markers of early atherosclerosis (ATS), such as aortic stiffness and intima media thickness (IMT) in a homogeneous cohort of IBD patients, in spite of absence of traditional risk factors for ATS, suggesting a role for chronic inflammation.
Aims and Methods: The aim of this study was to assess prospectively modifications of IMT and arterial stiffness in a longitudinal study on the same cohort, in relation to therapy and disease characteristics. A total of 39 patients with IBD (14 ulcerative colitis and 25 Crohn's disease) underwent a second clinical, biohumoral and instrumental assessment after a mean period of 4.8 ± 0.3 years. Carotid IMT was evaluated by using high resolution B-mode ultrasonography. Arterial stiffness was assessed by measurement of carotid-femoral Pulse Wave Velocity (cf-PWV) and Augmentation Index (AIx).
Results: We found a statistically significant increase in body mass index (22.44 kg/ m^2 at baseline vs 23.39 kg/ m^2 at last follow-up visit, p = 0.043), white blood cell count (7339.05/mmc at baseline vs 8291.28 mmc at follow-up, p = 0.015) and total cholesterol (160.79 mg/dl at baseline vs 172.08 mg/dl at follow-up, p = 0.028); while a statistically significant reduction in glycemia (88.69 mg/dl at baseline vs 83.90 mg/dl at follow-up, p = 0.019 was observed. No statistically significant variation was observed with respect to the values of the AIx and carotid IMT; while an average increase in cf-PWV values was observed (8.67 m/s at baseline vs. 9.19 m/s at follow-up, p = 0.129), but without reaching statistical significance. As far as concerns the other hemodynamic parameters, we found a trend in improvement of PAD (diastolic arterial pressure) and PAM (mean arterial pressure): respectively 75.31 mmHg at baseline vs 71.15 mmHg at follow-up, p = 0.064; 89.51 mmHg at baseline vs 85.13 at follow-up, p = 0.062). No statistically significant difference was found for PAS (systolic blood pressure). On logistic regression analysis, the only variable that was able to influence the worsening of cf-PWV is the duration disease (p = 0.048).
Conclusion: In our prospective cohort of IBD patients there was no significant increase in the expression of surrogate markers of ATS, except cf-PWV which did increase over time. Disease duration was the only variable, among those evaluated, able to predict the worsening of cf-PWV. ATS in IBD is a progressive complication, however progression is slow and the timing of surveillance measures is yet to be established.
Disclosure: Nothing to disclose

Abstract No: P0951

	ID (n = 29)	Functional ID (n = 5)	IDA (n = 33)	ACI (n = 13)	Mix (IDA/ACI) (n = 8)	IBD remission (n = 38)	Healthy controls (n = 49)
Hb (g/dL)	13.60 (10.90–15.10)	12.70 (12.50–13.00)	11.00 (7.40–13.30)	11.30 (9.50–12.70)	11.15 (9.80–12.70)	14.05 (12.40–16.80)	13.90 (12.10–16.80)
ESR	10.00 (1.00–31.00)	24.00 (21.00–58.00)	20.00 (2.00–79.00)	24.00 (2.00–61.00)	35.00 (12.00–89.00)	2.00 (2.00–18.00)	3.00 (2.00–22.00)
CRP (mg/L)	2.70 (1.00–17.50)	10.20 (1.80–14.30)	2.70 (1.00–24.40)	12.40 (1.40–181.00)	30.10 (1.60–78.80)	1.30 (1.00–4.90)	1.00 (1.00–4.40)
Ferritin (μg/L)	16.90 (5.00–29.10)	33.30 (32.50–40.20)	13.90 (5.00–28.40)	285.00 (115.00–1028.00)	52.80 (30.50–73.10)	93.20 (33.00–378.00)	86.10 (17.60–298.00)
TSAT%	12.20 (4.54–32.70)	16.80 (12.00–19.10)	5.68 (2.50–21.90)	15.00 (2.44–25.60)	8.48 (4.90–20.00)	25.00 (16.20–67.30)	29.50 (15.40–50.40)
MCHC (g/dL)	33.20 (31.60–35.50)	32.50 (32.10–34.30)	31.90 (28.60–34.00)	32.30 (30.40–34.30)	31.65 (29.90–35.50)	34.20 (32.70–36.10)	34.40 (33.00–35.80)
LHD%	5.61 (0.71–23.06)	10.48 (2.09–14.94)	17.80 (2.73–96.20)	12.52 (2.09–57.22)	23.55 (4.28–73.82)	2.28 (0.41–8.77)	1.91 (0.54–6.71)

[Table 1: Haematological and biochemical parameters]

P0953 LONG-TERM OUTCOME OF TRANSMURAL HEALING VERSUS MUCOSAL HEALING IN CROHN'S DISEASE: THE TIME FOR A NEW TARGET

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Introduction: While mucosal healing (MH) has been proved to predict clinical outcomes in Crohn's disease (CD), little is known about the long-term outcome of transmural healing (TH).
Aims and Methods: The aim of this study was to prospectively assess the one-year clinical outcomes of CD patients achieving TH after 2 years of treatment with biologics, comparing to patients reaching MH alone or no healing (NH). We performed a 1-year observational longitudinal study, evaluating steroid-free clinical remission (CR), clinical relapse, rate of hospitalization and surgery in all CD patients treated with biologics for 2 years, who were classified in accordance with clinical, endoscopic and sonographic findings in 3 groups: TH, MH and NH.
Results: Among 218 patients who completed a 2-year treatment period with biologics, 68 subjects (31.2%) presented TH, 60 patients (27.5%) MH alone, while 90 patients (41.3%) did not achieve any healing (NH). At the end of the study, TH was associated with higher rate of steroid-free CR, lower rates of clinical relapse, hospitalizations and surgeries at 1-year respect to MH and NH ($p < 0.001$). Furthermore, TH was associated with a longer time until clinical relapse (HR 0.87, $p = 0.01$), hospitalization (HR 0.88, $p = 0.002$) and surgery (HR 0.94, $p = 0.008$) than MH. Also among patients withdrawing biologics, TH predicted better clinical outcomes at 1-year than MH ($p < 0.01$).
Conclusion: TH is the most ambitious and powerful endpoint associated with complete improvement of all clinical outcomes, even more than MH. Additionally, TH was associated with better long-term clinical outcomes than MH also after biologic withdrawal.
Disclosure: Nothing to disclose

P0954 ADVANCED ENDOSCOPY FOR SURVEILLANCE OF COLONIC INFLAMMATORY BOWEL DISEASE: SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Considering the high risk of dysplasia and cancer in inflammatory bowel disease (IBD), surveillance is advocated. However, international guidelines do not reach a uniform recommendation on how to perform surveillance.
Aims and Methods: We performed a systematic review with meta-analysis to assess the best endoscopic surveillance strategy in colonic IBD. The systematic review was performed in PubMed/MEDLINE, EMBASE, SCOPUS and Cochrane databases to identify studies comparing white light endoscopy (WLE) and advanced endoscopy (AdvE) in the detection of dysplasia or neoplasia in colonic IBD. A sub-analysis between dye-spray chromoendoscopy (DCE), narrow-band imaging (NBI), I-SCAN, full-spectrum endoscopy (FUSE) and auto-fluorescence imaging (AFI) was also performed. Another sub-analysis explored the role of random vs targeted biopsies in the detection of dysplastic lesions in IBD. Pooling was performed using diagnostic fixed or random-effect model according with heterogeneity.
Results: Twenty-seven studies (6167 IBD patients with 2024 dysplastic lesions) met the inclusion criteria. There was no publication bias. AdvE showed a higher likelihood of detecting dysplastic lesions than WLE (19.3% vs 8.5%, OR = 2.036), with an incremental yield (IY) of 10.8%. DCE (OR = 2.605) and AFI (OR = 3.055) had higher likelihood of detecting adenomas than WLE; otherwise, I-SCAN (OR = 1.096), NBI (OR = 0.650) and FUSE (OR = 1.118) were not superior to WLE. Dysplasia was found in 1256/7267 targeted biopsies (17.3%) and in 363/110040 random biopsies (0.33%) (OR = 66.559, IY = 16.9%).
Conclusion: AdvE, especially DCE and AFI, was associated with higher likelihood of discovering dysplastic lesions than WLE. Chromoendoscopy with targeted biopsies should be the preferred endoscopic technique for IBD surveillance.
Disclosure: Nothing to disclose

P0955 ROLE OF SERUM PROCALCITONIN FOR DIAGNOSIS OF CYTOMEGALOVIRUS REACTIVATION IN EXACERBATION OF ULCERATIVE COLITIS PATIENTS

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Introduction: Serum procalcitonin (PCT) is an excellent marker of infectious conditions. We evaluated serum PCT as diagnostic marker for CMV reactivation in exacerbation of ulcerative colitis patients.
Aims and Methods: We retrospectively analyzed clinical data from 47 patients with exacerbation in UC for whom serum procalcitonin and CMV study were measured between January 2017 and December 2017. Diagnosis of CMV reactivation was either CMV IgM, CMV antigenemia, blood CMV PCR, tissue CMV PCR or CMV immunohistochemical stain were positive. Other infectious conditions were excluded.
Results: Positive CMV reactivation among them were observed in 28 patients (59.6%). There was no difference in the sex, steroid, immunomodulator, anti-TNF agents, and disease extension between the two groups. The mean serum PCT levels in positive CMV reactivation and negative CMV reactivation were 0.127 ± 0.29 mg/mL and 1.510 ± 3.53 ng/mL, respectively ($p = 0.10$). Also, there was no difference in the white blood cell, neutrophil, lymphocyte, hemoglobin, platelet, ESR, CRP, albumin and Fecal calprotectin between two groups.
Conclusion: Serum PCT was not correlated with CMV reactivation in exacerbation of ulcerative colitis patients.
Disclosure: Nothing to disclose

P0956 SYSTEMATIC REVIEW: PREDICTING THE DEVELOPMENT OF PSYCHOLOGICAL MORBIDITY IN INFLAMMATORY BOWEL DISEASE

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Introduction: Psychological morbidity (anxiety and/or depression) in inflammatory bowel disease (IBD) is common (reported prevalence of up to 50% in patients with IBD) and has significant personal and economic costs to society. Prediction of psychological morbidity in IBD may allow for early intervention, but predictive factors are unclear.
Aims and Methods: To undertake a systematic literature review to determine predictors of the development of psychological morbidity in patients with IBD. Electronic searches for English-language articles were performed using keywords for "psychological morbidity" according to DMS-IV, "prediction" and "IBD" in the MEDLINE, PsychInfo and Web of Science databases for studied published from 1997 to February 2018. Studies were included if they had both baseline data (T1) and follow data (T2) to allow differentiation between factors *associated with* and those *predictive of* psychological morbidity.
Results: 1129 studies were identified, of which seven met the inclusion criteria. Five of these focused on predicting depression with only two studies additionally examining anxiety. The median age of patients was 37 years (range 11.8–48) and on average 59% of participants were female (SD 18.2). Longitudinal follow-up periods varied considerably (median 12 months (range 6–60)). Statistical methods were inconsistent across studies and included regression models, cross-lagged panel models and ANCOVAs. Physical factors predicting psychological morbidity included: female gender (OR 1.7; 95% CI 1.61–2.71); additional comorbidity (≥1 chronic illness alongside IBD) (OR 4.31; 95% CI 2.28–6.57); surgical intervention (OR 1.9; 95% CI 1.15–3.13) and immunosuppressant use (OR 1.56; 95% CI 1.03–2.38). Predictive psychological factors included: parental stress (r-change = 0.03, $F(1,58) = 35.6$, $p < 0.05$); attachment anxiety ($r = 0.61$, $P \leq 0.001$); psychological thriving ($r = -0.37$, $p < 0.01$) and gratitude ($r = -0.43$, $p < 0.01$). Factors with an inverse relationship to the development of morbidity were protective, for example higher levels of gratitude reduced the likelihood of developing psychological morbidity.
Conclusion: Psychological morbidity in IBD may be predicted by disease-related and psychological factors, potentially allowing earlier intervention and reducing personal and economic costs. Further longitudinal data from large IBD cohorts are required to determine additional predictive factors rather than associations. Development and validation of a predictive tool for the development of psychological morbidity in IBD would benefit patients and health care professionals.
Disclosure: Nothing to disclose

P0958 ULTRASONOGRAPHIC FINDINGS ASSOCIATED WITH A HIGHER RISK OF SURGERY IN PATIENTS WITH STRICTURING CROHN'S DISEASE

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Introduction: In Stricturing Crohn's Disease (SCD) strictures have traditionally been classified as inflammatory or fibrotic: the first have been thought to respond to medical treatment and the latter have usually been associated with the need for surgery[1]. Recent papers establish that in most cases these strictures appear to have mixed characteristics[2], and that even in inflammatory strictures medical treatment doesn't always avoid the risk of critical stenosis of the bowel lumen, thus resulting in surgery too. In our study we tried to identify ultrasonographic findings in SCD that may associate with a higher risk of surgery and allow us to make early choices regarding treatment election in this specific cohort of patients.
Aims and Methods: We conducted a case-control study at our institution, selecting 70 patients diagnosed with SCD that underwent ultrasonography (US) during follow up from 2013 to 2017 and then divided them into groups depending

on the need for surgery: surgery group and control group. Main target was evaluating ultranosographic findings associated with a higher risk of surgery, US features analyzed are described in results. We used Student's T and Chi^2 tests for quantitative and qualitative variables comparison respectively, and performed multivariable analysis using logistic regression. We considered statistical significance a p value of <0.05.

Results: Out of 70 patients, 24 needed surgery because of obstructive symptoms (34.29%), while 46 remained surgery-free at the time of the analysis (65.71%). Baseline characteristics of both groups can be found in table 1. Median time from US to surgery was 71.5 days (IQ range [12–300]). Ileocolic resection was performed in 16 patients (66.6%) while the rest underwent ileocolic plus other kind of bowel resection (8 patients, 33.3%). When comparing US findings, the following ones reached statistical significance: stricture doppler activity (control group: mean 0.86 SD 0.34 vs surgery group: mean 2.08 SD 0.88, $p < 0.001$), presence of fistulas (enteromesenteric: $chi^2 = 4.23$, $p = 0.04$; enteroenteric: $chi^2 = 9.13$, $p = 0.003$) and presence of abscess ($chi^2 = 8.46$, $p = 0.004$). When performing multivariable analysis, these data appear to have clinical significance regarding risk of subsequent surgery but they didn't reach statistical significance probably due to lack of sample size. Data obtained applying logistic regression are: doppler activity (OR = 1.14 IC95% [0.79–1.64], $p = 0.46$), enteroenteric fistula (OR = 5.43, IC95% [0.7–40] $p = 0.09$), associated abscess (OR = 7.9, IC95% [0.5–112], $p = 0.69$). Bowel wall thickness, presence of pre-stenotic dilation and involvement of mesenteric fat did not show clinical or statistical significant association with the risk of surgery ($p = 0.20$, $p = 0.517$ and $p = 0.25$, respectively).

Conclusion: In our experience, transmural complications detected in a follow-up US of patients with SCD are associated with a higher risk of surgery and should be taken into account when deciding the best choice of treatment, wether it is a possible therapeutic escalation of medical therapy or early surgical resection. These data must be validated in prospective studies that confirm our findings.

Characteristic	Surgery group (n = 24)	Control group (n = 46)
Sex, n: male (%), female (%)	10 (41.7%), 14 (58.3%)	26 (56.5%), 20 (43.5%)
Age at diagnosis of CD: mean (SD)	34.33 (15.1)	37,09 (16.2)
Smoking, n: smokers (%), non smokers (%), ex smokers (%)	12 (50%), 8 (33.3%), 4 (16.7%)	4 (8.8%), 39 (84.7%), 3 (6.5%)
Stricture location according to Montreal, L: n (%)	L1: 15 (62.6%), L3: 8 (33.3%), L4: 1 (4.1%)	L1: 33 (71.7%), L2: 3 (6.5%), L3: 7 (15.2%), L4: 1 (2.1%)
Number of strictures (n, %)	1 (11, 45.83%), 2 (9, 37.5%), 3 (3, 12.5%), 4 (1, 4.1%)	1 (22, 47.82%), 2 (19, 41.3%), 3 (5, 6.5%)
Associated fistula (n, %)	17 (70.8%)	9 (19.56%)
Associated abscess (n, %)	6 (25%)	3 (6.5 %)
AntiTNF treatment: n (%)	17 (70.83%)	8 (17.39%)

[Baseline characteristics of the study group.]

Disclosure: Nothing to disclose

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P0959 NBI FINDINGS IN MICROSCOPIC COLITIS AND UTILITY OF NBI GUIDANCE ON YIELD OF COLONIC BIOPSIES FOR ITS DIAGNOSIS

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Introduction: Microscopic colitis (MC) is an important cause of chronic diarrhoea in adults. Histopathology is the gold standard for diagnosis but colonic biopsy has a variable yield. Endoscopically, the mucosa is normal, often leading to delayed diagnosis As the mucosa appear normal on endoscopy in most cases, there is no specific area to target for biopsy.

Aims and Methods: The aim of the current study was to evaluate the ileocolonic mucosa in patients with suspected MC with narrow band imaging (NBI) and to describe the narrow band imaging findings (NBI), in patients with microscopic colitis. We also aimed to study the utility of NBI guided biopsy for improving the diagnostic yield of colonic biopsies by comparing yield of NBI-guided biopsy with the yield of white light colonoscopy-guided biopsy for the diagnosis of microscopic colitis.

Materials and methods: We prospectively recruited patients aged more than 18 years with suspected microscopic colitis during the period July 2016 to December 2017. Patients with malignancy, coeliac disease, small intestinal bacterial overgrowth, inflammatory bowel disease, gastrointestinal tuberculosis and severe comorbidities were excluded. Patients underwent blood investigations, imaging including contrast enhanced computed tomography abdomen (if indicated), stool analysis and hydrogen breath tests using glucose,lactose and lactulose. All patients underwent colonoscopy with ileal intubation if possible. Patients underwent both HDWLE and NBI during the same setting by the same observer. NBI finding were recorded in a predefined format. Four pieces of biopsies were taken during white light examination (WLE) from caecum/ascending colon and four pieces from descending colon/sigmoid colon. Additional four pieces of biopsies were taken during NBI examination from same colonic segments during NBI examination Each set of biopsies was collected in separate containers and labelled for further histopathological processing and examination by an expert gastrointestinal histopathologist. The diagnosis of MC was made using statements of the European Microscopic Colitis Group 2012.

Results: A total of 53 patients suspected to have microscopic colitis were enrolled in the study, and a final diagnosis of MC was established in 43 [mean age – 45.83(±15.92), males – 27]. Out of 43 cases with MC, 25(58.1%) patients had collagenous colitis (CC), 14 (32.5%) had lymphocytic colitis (LC) and 4(9.4%) had mixed picture fulfilling criteria for both. The WLE findings were normal mucosa in all patients. NBI showed type 1 pit pattern in all patients with MC. Vascular pattern was regular pattern in all patients. Mucosal pattern was honey comb type in all patients. A patternof focal area of abnormal vascularity with focally obscure pit pattern was found to be more common in cases than controls [35(81.39%); 5(12.5%) ($p = 0.052$). In the group of CC, NBI guided biopsy yielded the diagnosis in 88% (22 out of 25 patients) whereas white light guided biopsy yielded the diagnosis in all 25 cases (100%) ($p = 0.24$). In the group of lymphocytic colitis, NBI guided biopsy yielded the diagnosis in 92% (13 out of 14 patients) whereas white light guided biopsy yielded the diagnosis in all 14 cases (100%) ($p = 0.89$).

Conclusion: This prospective studydescribes the NBI findings of colon in patients with MC and describes a unique sign of focal area of abnormal vascularity with focally obscure pit pattern to be more common in MC. However, there was no significant difference in yield of NBI-guided biopsy compared to white light colonoscopy-guided biopsy for the diagnosis of MC.

Disclosure: Nothing to disclose

P0960 THE PREVALENCE OF INFLAMMATORY BOWEL DISEASE IN PATIENTS WITH HIDRADENITIS SUPPURATIVA

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Introduction: Hidradenitis suppurativa (HS) is an inflammatory, recurrent skin disease of hair follicle, that mainly presents in axillary, inguinal and anogenital regions. Clinically, the condition can imitate the cutaneous Crohn's disease and it can co-exist with inflammatory bowel diseases (IBD). HS and IBD have many similarities in clinical appearance, pathogenesis and etiology.

Aims and Methods: The purpose of our study was to determine the prevalence and characteristics of inflammatory bowel disease in patients diagnosed with hidradenitis suppurativa by comparing clinical signs, endoscopy, histology and laboratory results.

Thirty-nine patients (64% male; mean age: 35,77; median: 34) were seen with diagnosed hidradenitis suppurativa, whom underwent screening colonoscopy. By the endoscopic and histological results, we made two patient-groups (HS and HS+IBD) and compare the epidemiological, clinical, laboratory data.

Results: The prevalence of IBD was 17,9% among HS patients (n = 7; Crohn's disease: 6; colitis ulcerosa:1). The average time between HS and CD diagnosis was one year. In 'HS+IBD' group, CRP levels were not significantly higher (mean: 36,37 mg/l; median: 27) but we found higher ASCA IgG levels (mean: 15,48; median:10). In HS group, body mass index (BMI) was higher than 30kg/m^2 in all cases. In 'HS+IDB' group, all patients have lower BMI. In the two patient-groups, we could not find any difference in smoking habits and NOD2 polymorphism.

Conclusion: Based on our data, the appearance of IBD correlated with younger age, lower body mass index, severe HS activity, penetrating form. In the future, it may be justified to screen HS patients for IBD.

Disclosure: Nothing to disclose

P0961 BASELINE ALBUMIN LEVEL IS NOT A SIGNIFICANT PREDICTOR OF TOFACITINIB EFFICACY IN PATIENTS WITH ULCERATIVE COLITIS: RESULTS OF MULTIVARIATE EXPOSURE-RESPONSE ANALYSIS

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Introduction: Serum albumin concentration has been shown to be inversely related to drug clearance for biologic therapies used to treat inflammatory bowel disease.[1–3] Lower albumin levels may be linked to higher drug clearance rates and poorer clinical outcomes for some biologics.[4] Albumin levels as a predictor of efficacy in patients (pts) receiving tofacitinib is uncertain.

Aims and Methods: Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). We evaluated the effect of baseline albumin (BALB) on tofacitinib pharmacokinetics (PK) and efficacy. Four randomised placebo-controlled studies of tofacitinib in pts with moderate to severe UC were included in PK analyses: one Phase (P) 2 study (A3921063, NCT00787202)[5] and three P3 studies (OCTAVE Induction 1 & 2, NCT01465763 & NCT01458951; and OCTAVE Sustain, NCT01458574).[6] The base PK model was one-compartmental disposition with covariates for BALB, evaluated as a potential predictor for apparent oral clearance (CL/F). The effect of BALB related to efficacy endpoints in P3 induction and maintenance studies was evaluated in a multivariate analysis.

Results: 1096 pts were included in the PK analysis: 641 males and 455 females; the majority (81.3%) were white; median age: 40 years. Mean (standard deviation) BALB was 4.18 g/dL (0.39), range 2.1–5.4 g/dL. In the population PK (popPK) model, BALB was evaluated as a predictor of individual CL/F, showing no statistically significant correlation, so was not included in the final popPK model. BALB concentration was evaluated as a covariate in exposure-response (ER) efficacy analyses, and was shown by stepwise covariate modelling to be non-significant, so was not included in the final ER model. Primary endpoints for induction and maintenance studies were remission based on central read at Weeks 8 and 52, respectively. Multivariate analysis showed no statistically significant correlation between BALB and efficacy endpoints in ER analysis after accounting for other significant predictors of efficacy such as baseline Mayo score.

Conclusion: In contrast to biologic therapies,[1–3] tofacitinib clearance was not related to albumin concentration. As shown in multivariate analyses, BALB had no effect on induction or maintenance efficacy endpoints, and therefore may not be informative to tofacitinib dosing decisions.

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P0962 EFFICACY AND SAFETY OF GASTRO-RESISTANT PHOSPHATIDYLCHOLINE (LT-02) FOR MAINTENANCE OF REMISSION IN PATIENTS WITH ULCERATIVE COLITIS INITIALLY REFRACTORY TO MESALAZINE: A RANDOMISED, DOUBLE-BLIND, DOUBLE-DUMMY PLACEBO-CONTROLLED STUDY (PCG-4)

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Introduction: Preceding PCG 2 was a prospective, double-blind, randomised, phase 3 induction study to compare the efficacy and safety of two different dosing regimen of LT-02 (LT-02 0.8 g QID, LT-02 1.6 g BID) with placebo for 12 weeks for induction of remission in patients with mild-to-moderately active ulcerative colitis refractory to 5-ASA. Present PCG-4 was aimed to investigate the maintenance profile of LT-02.

Aims and Methods: This was a prospective, double-blind, double-dummy multicenter trial to compare the efficacy and safety over 48 weeks of LT-02 1.6 g BID versus placebo and mesalazine 0.5 g TID in a randomization ratio of 2:1:1 for maintenance of remission in patients with UC who had achieved either deep remission (total mDAI score $\leq$1, with 0 points in rectal bleeding and stool frequency-subscores) or remission (total mDAI score $\leq$2, no subscore $>$1) during PCG-2. Primary endpoint was the

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	LT-02 1.6 g BID (N = 75)	Placebo (N = 37)	Mesalazine 0,5 g TID (N = 38)
Primary Endpoint			
Number (%) of patients relapse-free and not a treatment failure after 48 weeks	37(49.3%)	16 (43.2%)	19 (50.0%)
Subgroup analyses: Number (%) of patients relapse-free and not a treatment failure after 48 weeks:			
by Criterion of Deep Remission at baseline of PCG-4 fulfilled [n/N (%)]:			
Yes	24/43 (55.8%)	9/24 (45.8%)	12/22 (54.8%)
No	13/32 (40.6%)	5/13 (38.5%)	7/16 (43.8)
by Localization of disease at baseline of PCG-2 [n/N (%)]:			
Left-sided	22/43 (51.2%)	9/20 (45.0%)	14/25 (56.0%)
Extended	15/32 (46.9%)	7/17 (41.2%)	5/13 (38.5%)
Secondary endpoints:			
Time in Study, in days: Mean (SD)	231.7 (134.7)	183.4 (144.2)	214.4 (136.8)
Time to Clinical Relapse or Discontinuation, in days: Median [95% CI] ; HR [95% CI (LT-02 vs PCO)]	338 [172; —] ; 1.371	167 [52; —]	343 [101; —]
Change from baseline of Histological Index: Mean (SD)	0.5 (0.85)	0.5 (1.01)	0.6 (1.04)

[Primary & secondary efficacy endpoints]

percentage of patients being relapse-free with relapse defined as a rectal bleeding score of ≥1 and a mucosal appearance score of ≥2 of the mDAI scores and not a treatment failure defined as premature withdrawal (whatever the reason) after 48 weeks.
Results: Due to premature recruitment stop of PCG-2 only 150 patients of 400 targeted patients were included (Table). Both the primary and secondary efficacy endpoints showed no significant differences across treatment groups (Full Analysis Set).
Numbers of AEs, SAEs and ADRs were comparable for patients in the three treatment groups. Tolerability of LT-02 was assessed as very good or good by the majority of patients.
Conclusion: Although the study failed to prove superiority of LT-02 treatment vs. placebo for maintenance of remission in UC, there was a numerical trend towards superior efficacy of LT-02 compared to placebo and a marked prolongation of the time to clinical relapse.
Disclosure: Employed by Dr. Falk Pharma GmbH

P0963 REFLECT: A FRENCH NATIONWIDE PROSPECTIVE STUDY OF CT-P13 -INFLIXIMAB BIOSIMILAR USE IN REAL LIFE

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Introduction: CT-P13 is the first monoclonal antibody biosimilar to infliximab (IFX) approved in France. Reflect trial has been set up to evaluate in real life the use of the CT-P13 biosimilar after its introduction in a French sanitary cooperation group (UNIHA) created at the initiative of university hospitals which support the generation of real-world data.
Aims and Methods: Reflect is a multicenter, prospective, observational study, which aimed to describe in real-life the treatment effectiveness and the characteristics of patient (pts) treated with CT-P13. Inclusion criteria were pts (≥ 6 yrs-old) with Crohn's Disease (CD), Ulcerative Colitis (UC), rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis, treated with CT-P13. Both IFX naive pts (IFXn) and pts having switched from IFX originator to CT-P13 (IFXs) were enrolled. Preliminary results in pts suffering from CD or UC using descriptive statistical analyses from inclusion are reported here. Descriptive analyses were performed.
Results: Between October 2016 and December 2017, among the 627 pts included in the study, 282 pts had an inflammatory bowel disease (IBD) and were analyzed. At baseline, they were 176 CD (51.1% males; mean age: 37.0 ± 13.9 years; median time since diagnosis: 5.7 years) and 106 UC (55.7%; 40.7 ± 17.8 years; 5.5 years). For CD patients colonic/ileocolonic localization was noted in 23.6%/ 45.3%, and 37.3% had perianal disease. For UC patients, left-sided colitis/extensive colitis was noted in 27.7%/57.4%. Almost all pts have been already treated with CT-P13 before inclusion (90.8% of CD and 90.0% of UC); the median treatment duration was 5.6 and 7.4 months, respectively. Previous treatments with biotherapies other than infliximab were taken by 42.9%of CD and 45.5% of UC pts. A minority of pts (12.4% of CD and 9.1% of UC) switched from the originator infliximab to CT-P13. At inclusion, the median Mayo Score for UC were 2 and 1 in IFXn and IFXs pts respectively and the median Harvey-Bradshaw Index (HBI) for CD were 2 and 1 in IFXn and IFXs pts respectively. At 6 and 12 month follow-up, 59.8% and 77.8% of CD pts and 48.7% and 69.2% of UC pts were in remission. In IFXn pts the median change from baseline to 6 and 12 months were 0 and – 2 for mayo score and 0 and -1 for the HBI respectively. Except for the HBI at 6 months, there was no change in the IFXs pts in both UC and CD scores at 6 and 12 months. The safety results are showed in table 1.

	Safety population (N)	n (%)	Number of AE(s)
Pts with at least one adverse event (AE)			
UC pts	106	16 (15.1%)	33
CD pts	176	33 (18.8%)	69
Pts with at least one serious AE			
UC pts	106	4 (3.8%)	7
CD pts	176	10 (5.7%)	14
Pts with at least one allergic infusion reaction†			
UC pts	106	1 (0.9%)	1
CD pts	176	3 (1.7%)	4
Pts with at least one infection‡			
UC pts	106	–	–
CD pts	176	1 (0.6%)	1

[Safety results]
† Including acute and delayed hypersensitivity reactions.
‡ Including severe infections, tuberculosis, opportunistic infections, hepatitis.
Conclusion: Preliminary results from this prospective cohort suggest that patients treated with CT-P13 maintained elevated rates of remission in CD and UC pts at 12 months. No new safety concerns were identified.

Disclosure: This research was sponsored by Pfizer. YB and SN received remuneration for their services as a member of the Steering Committee for ReFLECT. YB has received consulting fees from Abbvie, Biogaran, Boehringer Ingelheim, Ferring, Hospira, Janssen, MSD, Norgine, Pfizer, Roche, Sanofi, Shire, Takeda, UCB, lecture fees from Abbvie, Ferring, Janssen, Mayoli Spindler, MSD, Norgine and Takeda and received research grant support from Pfizer and Takeda. SN has received fees from Takeda, Pfizer, Abbvie, MSD, Tillots, Ferring, Novartis, Norgine, Janssen, HAC pharma.

P0964 REAL-LIFE EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB AS INDUCTION THERAPY FOR KOREAN IBD PATIENTS IN WHOM ANTI-TNF TREATMENT FAILED: THE FIRST ASIAN PROSPECTIVE COHORT STUDY

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Introduction: Vedolizumab (VDZ) is a gut-selective monoclonal antibody blocking α4β7 integrin, which can be effective for patients with inflammatory bowel disease (IBD). Although several studies have reported the real-world experiences of VDZ in Western patients, no study has been reported in Asian IBD patients.
Aims and Methods: We aimed to investigate the clinical effectiveness and safety of VDZ as an induction therapy for Korean patients with Crohn's disease (CD) or ulcerative colitis (UC), who were previously failed to anti-tumor necrosis factor (TNF) therapy. Between August 2017 and April 2018, a total of 34 patients with CD (n = 21) or UC (n = 13) received an induction therapy with VDZ at the Asan Medical Center, Seoul, Korea and were prospectively enrolled in the ASAN VDZ registry. Of those, patients who received three doses of VDZ (week 0, 2, and 6) and were evaluated at week 14 were analyzed. The co-primary outcomes were corticosteroid-free clinical remission (both for CD and UC) and endoscopic remission/ response (for UC) at week 14. The secondary outcomes were corticosteroid-free clinical response, clinical remission/ response, and safety (both for CD and UC).
Results: A total of 23 patients were enrolled (CD, 13 [56.5%]; male, 16 [69.6%]; median age, 38 years [range, 19–52]; median disease duration, 8.5 years [range, 0.7–23.3]). Thirteen patients (56.5%) previously had experienced failures to one anti-TNF agent and 10 patients to two anti-TNF agents (43.5%). Corticosteroid-free clinical remission rates in CD and UC patients were 22.2% and 10%, respectively (Table 1). In patients with UC, endoscopic remission and response rates were 10% and 20%, respectively (Table 1). Corticosteroid-free clinical response rates were 44.4% for CD patients and 30% for UC patients, respectively (Table 1). Clinical remission/ response rates were 33.3%/ 55.6% for CD patients and 10%/ 40% for UC patients, respectively (Table 1). In patients with CD, median Harvey-Bradshaw index, leukocyte count, C-reactive protein level, and fecal calprotectin level were not significantly decreased at week 14 compared with the baseline values (p=0.28, P=0.17, P=0.79, and P=0.43, respectively). In patients with UC, median partial Mayo score was significantly decreased (p = 0.003). However, median leukocyte count, C-reactive protein level, and fecal calprotectin level were not significantly decreased (p=0.38, P = 0.75, and p=0.08, respectively). Nasopharyngitis (30.4%) was the most common adverse events. IBD exacerbation was observed in 4 patients (17.4%) with IBD-related admissions in 2 patients (8.7%).
Conclusion: In Korean IBD patients with prior failures to anti-TNF therapy, VDZ induction therapy may be effective with acceptable safety profile. Further long-term follow-up studies with larger number of patients are required to prove the effectiveness and safety of VDZ.
Disclosure: Nothing to disclose

P0965 IMPROVEMENT IN PHYSICIAN'S GLOBAL ASSESSMENT WITHIN 2 WEEKS IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH TOFACITINIB

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). OCTAVE Induction 1 & 2 (NCT01465763 & NCT01458951) were identical, randomised, double-blind, placebo-controlled Phase 3 trials in adult patients with moderately to severely active UC who had failed, or were intolerant to, steroids, immunomodulators or tumour necrosis factor inhibitors.[1] Rapid onset of tofacitinib efficacy with

significant improvements in patient-reported symptoms (Mayo stool frequency and rectal bleeding subscores) was observed within 3 days.[2]

Aims and Methods: The Mayo score is a combination of four subscores including the Physician's Global Assessment (PGA), which comprises the daily record of abdominal discomfort, and other observations such as physical findings and the patient's performance status. Here, we evaluate the time course of improvement in PGA in patients with UC following induction therapy with tofacitinib. PGA subscores of patients who received placebo or tofacitinib 10 mg twice daily (BID) for 8 weeks in the OCTAVE Induction 1 & 2 trials were collected at baseline, and at Weeks 2, 4 and 8 of the blinded treatment period. Comparisons between groups were made using stratified Cochran-Mantel-Haenszel chi-square test.

Results: A total of 905 patients received tofacitinib 10 mg BID (mean age 41.2 years; 59.2% male) and 234 patients received placebo (mean age 41.1 years; 56.4% male). At baseline, the mean total Mayo score in both placebo and tofacitinib groups was 9.0; the mean partial Mayo score (total Mayo score excluding endoscopic subscore) in both treatment groups was 6.4. By Week 2, 10.3% of patients treated with tofacitinib, compared with 3.4% of placebo-treated patients, achieved a PGA subscore of 0 ($p < 0.01$). Similarly, by Week 2, significantly more patients treated with tofacitinib vs placebo achieved a PGA subscore of 0 or 1 (41.3% vs 27.4%; $p < 0.0001$). A greater proportion of tofacitinib-treated patients had a reduction of $\geq$1 PGA point from baseline compared with placebo patients at Week 2 (52% vs 37.6%; $p < 0.0001$). From Week 2 to Week 8, differences between tofacitinib-treated and placebo-treated patients increased for all three PGA subscores analysed ($p < 0.01$ for all comparisons).

Conclusion: In these two randomised trials in patients with UC, treatment with tofacitinib was associated with a significant improvement in the PGA subscores within 2 weeks and continuing through to Week 8. This coincided with an improvement in patient-related outcomes (stool frequency and bleeding).

Table. Summary of PGA subscores in OCTAVE Induction 1 & 2

	Placebo N = 234	Tofacitinib 10 mg BID N = 905	Difference from placebo, % (95% CI)
PGA subscore of 0, n (%)			
Week 2	8 (3.4)	93 (10.3)	6.9 (3.8, 9.9)**
Week 4	18 (7.7)	149 (16.5)	8.8 (4.6, 13.0)**
Week 8	20 (8.5)	188 (20.8)	12.2 (7.8, 16.7)***
PGA subscore of 0 or 1, n (%)			
Week 2	64 (27.4)	374 (41.3)	14.0 (7.4, 20.5)***
Week 4	87 (37.2)	511 (56.5)	19.3 (12.3, 26.3)***
Week 8	73 (31.2)	507 (56.0)	24.8 (18.1, 31.6)***
Reduction of $\geq$1 point from baseline PGA, n (%)			
Week 2	88 (37.6)	471 (52.0)	14.4 (7.4, 21.4)***
Week 4	121 (51.7)	615 (68.0)	16.2 (9.2, 23.3)***
Week 8	95 (40.6)	575 (63.5)	22.9 (15.9, 30.0)***

**$p < 0.01$; ***$p < 0.0001$ vs placebo based on Cochran-Mantel-Haenszel chi-square test; Data are full *analysis* set.

BID, twice daily; CI, confidence interval; N, number of evaluable patients; n, number of patients; PGA, Physician's Global Assessment.

[Table]

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P0966 IMMUNOLOGICAL CROSS-REACTIVITY OF ANTI-DRUG ANTIBODIES TO ADALIMUMAB AND ABP 501

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Introduction: ABP 501 (AMGEVITA®; adalimumab) is an approved biosimilar to adalimumab (Humira®), a fully human recombinant monoclonal antibody. Amgen validated separate assays to independently detect ADAs against ABP 501 and adalimumab; this testing strategy was applied to both binding and neutralizing ADA detection to evaluate immunogenicity of ABP 501 compared to adalimumab. The goal of the present analyses is to assess the extent of ADA cross-reactivity between the biosimilar and reference product (RP) among patients with rheumatoid arthritis and psoriasis in two pivotal Phase 3 studies.

Aims and Methods: All protocol-defined antibody samples collected from drug-exposed subjects, irrespective of treatment group, were tested for binding antibodies against ABP 501 and adalimumab RP using a validated electrochemiluminescence-based assay. Binding ADA magnitude was expressed as signal-to-noise (S/N), defined as the mean signal of the study sample divided by the mean signal of the negative control analysed on the same plate. Samples positive for binding ADAs were then tested in a TNFα-target binding assay for neutralizing activity. Neutralizing antibody titre was reported as the highest dilution that tested positive in the assay. Validated assay parameters for both binding and neutralizing assays such as assay cut point, sensitivity, precision, and drug tolerance for each assay were highly similar. Correlation of binding and neutralizing antibody results (S/N or titre) between ABP 501 or and adalimumab RP assays was evaluated using the Pearson's correlation coefficient. Concordance of antibody results (positive/negative) was evaluated using the kappa statistic.

Results: Irrespective of treatment group, the binding ADA results for ABP 501 and adalimumab RP assays correlated well, with a Pearson correlation coefficient >0.950 and concordance measure of (kappa $>$ 0.860). In a small subset of samples that were not concordant, the distribution of sample reactivity was detected equally across assays. The magnitude of ADAs was at or near the assay cut point, indicating low probability of clinical impact. Furthermore, neutralizing antibody titre results correlated well between ABP 501 and adalimumab RP assays with a Pearson correlation coefficient $>$ 0.780 and strong concordance (kappa $>$ 0.884).

Conclusion: No meaningful differences were observed in the detection of binding and neutralizing ADAs in the different ADA assays, providing evidence of high similarity between ABP 501 and adalimumab RP.

Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

P0967 DEEP REMISSION AND MUCOSAL HEALING IN IBD PATIENTS UNDER IMMUNOSUPPRESSION WITH AZATHIOPRINE AND 6-MERCAPTOPURINE

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Introduction: Mucosal healing and deep remission (DR) are therapeutic targets in inflammatory bowel disease (IBD).

Aims and Methods: We aimed to characterize DR in patients with Crohn's Disease (CD) and Ulcerative Colitis (UC) under monotherapy with immunomodulators.

Out of a total of 432 patients observed in 2017–2018, 45 were under azathioprine or 6-mercaptopurine monotherapy for a period $\geq$3–6 months. Patients who underwent surgery, patients previously treated with anti-TNF and patients who started anti-TNF were excluded. DR was defined by: clinical remission (CR) in patients without endoscopically documented ulcers / erosions. Imaging activity was also evaluated in patients with CD.

Results: Mean age was 37.9 ± 12.4 years and 53.3% were men. Of the 45 studied patients, 33 had CD (76.8%) and 12 UC (23.2%). In the group with CD Montreal Classification was evaluated (A2-90.9%, L1-39.4%, B1-78.8%), and in this group the prevalence of perianal disease and penetrating phenotype was 27.3% and 12.1%, respectively. In UC 75.0% had extensive colitis-E3. The mean age of diagnosis was 28.9 ± 11.0 years and the mean duration of the disease was 8.9 ± 6.8 years. The majority of patients were under azathioprine (93.3%). Mean duration of treatment was 5.15 ± 3.98 years.

CR was obtained in 37 patients (CD-89.7%, CU-66.7%) and DR in 25 (DC-57.6%, CU-50.0%). Age of diagnosis, early onset and duration of immunomodulatory treatment were not associated with DR. In CD, ileal disease, penetrating phenotype, and perianal disease showed no significant association with DR. The need for topical/oral corticosteroids after initiation of treatment was significantly associated with lower mucosal healing rates ($p = 0.033$).

Conclusion: Despite the high rate of clinical remission under immunomodulator in monotherapy, about half of the patients did not achieved deep remission. The need for corticoid was associated with a lower probability of mucosal healing.

Disclosure: Nothing to disclose

P0968 HIGH-DOSE VITAMIN D DOES NOT PREVENT POSTOPERATIVE ENDOSCOPIC AND CLINICAL RECURRENCE IN CROHN'S DISEASE

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Introduction: Vitamin D deficiency is common in Crohn's disease (CD). Preclinical experiments and one clinical trial suggested anti-inflammatory effects of vitamin D in CD. We studied the anti-inflammatory effect of vitamin D in a prospective placebo controlled clinical trial in patients with CD undergoing an ileocolonic resection with ileocolonic anastomosis.

Aims and Methods: This was a prospective randomized, placebo-controlled trial in 17 centres in Belgium and the Netherlands. CD patients were randomized to receive weekly 25.000 IU vitamin D or placebo for 6 months following their first or second ileocolonic resection. All other CD medication was stopped. The primary endpoint was endoscopic recurrence defined as a modified Rutgeerts score $\geq$i2b at 26 weeks (>5 aphthous ulcerations in the neoterminal ileum, with or without anastomotic lesions); secondary endpoints included clinical recurrence (Crohn's disease activity index (CDAI) $\geq$ 220), quality of life (SF-36, IBD-Q and EQ-5D), safety and differential outcomes by baseline vitamin D serum concentrations. All endoscopies were centrally read and adjudicated by 2 expert blinded endoscopists (GD and PB).

Results: 143 patients were randomized (72 to vitamin D and 71 to placebo); baseline patient characteristics were comparable between the two groups (mean age (±SD) 34 (±12) vs 37 (±15) years, and 38% vs 40% male, respectively). Serum 25-OHvitamin D levels increased from median (IQR) 42 (27–56) nmol/L to 87 (73–105) nmol/L in the intervention group at week 26 ($p = <0.00001$), and remained unchanged at 43 (29–64) nmol/L in patients on placebo throughout the whole study. No difference was seen in the incidence of endoscopic recurrence at 26 weeks between the two groups (Table 1). In addition, the cumulative clinical recurrence rates at week 26 were comparable (Table 1). Quality of life as measured by SF-36, IBD-Q and EQ-5D improved slightly over time in both groups but was not significantly different between the two groups. Adverse events were uncommon in either group; adverse events with an incidence >5% included abscess formation in both groups and wound infection in the placebo group, and were related to the prior surgery. Outcome was not affected by baseline serum vitamin D level, season of inclusion, or ethnicity.

Conclusion: High-dose vitamin D treatment did not reduce the incidence of postoperative endoscopic and clinical recurrence in Crohn's disease patients, despite normalization of serum 25(OH)D concentrations. Hence vitamin D deficiency might merely be a consequence of disease activity rather than a causal explanation in the pathophysiology of Crohn's disease.

	Vitamin D	Placebo	p-value
Rutgeerts $\geq$ i2b	58%	66%	0.37
Rutgeerts $\geq$ i2a	87%	82%	0.22
CDAI $\geq$ 220	18%	18%	0.93

[Table 1. Endoscopic and clinical recurrence rates at week 26]

Disclosure: ClinicalTrials.gov ID NCT02010762, funding by IOIBD and BROAD

P0969 EVALUATING THE LONG TERM SAFETY AND EFFICACY OF ENDOSCOPIC DILATION TREATMENT OF PRIMARY AND SECONDARY DIGESTIVE STRICTURES IN CROHN'S DISEASE

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Introduction: Stenosing lesions in Crohn's disease respond poorly to medical treatments alone. In the face of this problem, bowel-sparing techniques have been developed, including endoscopic dilation, as an alternative to definitive surgery. There is still insufficient evidence regarding the long term success rate, for all phenotypes taken together, and insufficient knowledge of the predictive factors for the success of endoscopic dilation. The aim of our study was to assess efficacy and safety in strictures in Crohn's disease. The secondary objective was to highlight factors predicting the success of this procedure.

Aims and Methods: We conducted a single-centre retrospective cohort study including all patients managed endoscopically, between January 2000 and November 2016, with dilation of digestive strictures in the context of Crohn's disease (all phenotypes taken together). The technical and clinical success was assessed, as was the complication rate. Surgical management after endoscopic management was considered as a failure

Results: 104 patients were included in the course of this study, of whom 56 (53.8%) were men. Of the total number of patients, 43% presented a phenotype considered to be severe (fistulising lesions, ano-perineal lesions...). Median follow-up was of 61 months, or a little over 5 years. A total of 145 dilations were performed on 104 strictures, and 113 concerned secondary anastomotic strictures (77.9%). Technical success was obtained in 117 dilations (92.9%), and only one immediate complication, of the haemorrhagic type, was identified in the course of the endoscopy. There were 10 delayed complications (6.9%), represented by 6 perforations, 2 haemorrhagic events and 2 cases of bacteriaemia with febrile episodes. During our follow-up, 71 patients (68.2%) were treated only endoscopically. Of these patients, 52 (71.2%) required only one dilation session. The remaining 33 patients (31.7%) had surgery within a median delay of 13 months in relation to the first dilation. The presence of another stricture ($p = 0.03$) or a long stricture ($p = 0.02$) were factors predicting the need for surgery in a multivariate analysis. Early clinical success was a protective factor ($p = 0.0005$).

Conclusion: Endoscopic dilation appears to be an effective long term alternative in the management of Crohn's strictures, whether they are primary or secondary in nature and this, for all phenotypes taken together. This procedure allowed two thirds of the patients with stenosing lesions to avoid the need for surgery.

Disclosure: Nothing to disclose

P0970 ESTABLISHING PK EQUIVALENCE BETWEEN ADALIMUMAB AND ABP 501 IN THE PRESENCE OF ANTI-DRUG ANTIBODIES USING POPULATION PK MODELLING

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Introduction: Adalimumab (HUMIRA®) and its approved biosimilar ABP 501 (AMGEVITA® ; adalimumab) exhibit nonlinear pharmacokinetics (PK) following a single subcutaneous (SC) dose in healthy volunteers possibly due to target mediated disposition or development of anti-drug antibodies (ADAs). The presence of nonlinear PK leads to low and variable drug levels posing a challenge in assessing PK equivalence of these two agents. To address this we used a population PK modeling approach to assess PK equivalence.

Aims and Methods: A one-compartment linear PK model with first-order absorption was selected to characterize the ABP 501 and adalimumab PK in healthy subjects. The model was parameterized in terms of apparent systemic clearance and apparent central volume of distribution for subjects with or without ADAs. Body weight, albumin and ADA status were evaluated for their potential impact on adalimumab or ABP 501 PK. For subjects who developed ADAs, the model evaluated the inclusion of additional antibody mitigated clearance mechanisms using Michaelis-Menten (MM) type of saturable clearance or time-dependent changes in linear clearance. The effect of treatment on PK parameters was evaluated by comparisons of the empirical Bayes' estimates of the individual PK model parameters.

Results: In healthy subjects without ADAs, the ABP 501 and adalimumab PK after SC administration was linear and adequately described by a one-compartment model with first order absorption and linear clearance from the central compartment. Inclusion of an additive time dependent linear clearance for subjects with ADAs was superior to a model incorporating an additive MM saturable clearance for subjects with ADAs. Graphical and statistical comparisons of empirical Bayes' estimates by treatment demonstrated no difference in any PK model parameters by treatment. The population and inter-individual variability estimates of clearance and volume were 0.399 (33.6%) L/d and 8.94 (23.5%) L, for a 72.7 kg subject (median body weight). The time to onset and magnitude of the additive ADA-related linear clearance was 33.7 (54.4%) days and 1.15 (52.6%) L/d. Diagnostic plots demonstrated good concordance between observed and population or individual predicted concentrations without any bias. Visual predictive checks demonstrated the model described well the variable PK following a single dose of ABP 501 or adalimumab. The model described the PK of each individual well and was used to estimate accurately each individual's area under the concentration curve (time 0 to infinity) for all 203 subjects who completed the study.

Conclusion: The present population PK modeling confirms PK similarity of ABP 501 to adalimumab.

Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

P0971 TIME COURSE OF THE INCIDENCE AND MAGNITUDE OF ANTI-DRUG ANTIBODIES TO ADALIMUMAB AND ABP 501 AND AMONG PATIENTS ON CONCOMITANT IMMUNOMODULATORY THERAPY

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Introduction: Immunomodulatory therapy with agents such as methotrexate and corticosteroids can impact the development of anti-drug antibodies (ADAs) to monoclonal antibodies such as adalimumab used to treat inflammatory bowel disease. ABP 501 (AMJEVITA®; adalimumab) is an approved biosimilar to adalimumab. Here we report results from a Phase 3 study in patients with rheumatoid arthritis (RA) comparing the incidence of ADAs and the relative magnitude of the ADA response between ABP 501 and adalimumab reference product (RP) on background methotrexate (MTX).
Aims and Methods: We analysed data from a randomized, double-blind, 26 week, 1:1 active-controlled study designed to show clinical equivalence between ABP 501 40 mg and adalimumab 40 mg subcutaneously every two weeks among adalimumab-naive adult patients with moderate to severe RA who had an inadequate response to MTX. Patients were required to receive a stable dose of MTX (range 7.5 to 25 mg/week) for the duration of the study. Patients were also allowed to remain on oral corticosteroids at a dose of ≤10 mg/day of prednisone, or equivalent. Validated electrochemiluminescent assays were developed and used for detection of binding ADAs. ADA magnitude was expressed as signal-to-noise (S/N), defined as the mean signal of the study sample divided by the mean signal of the negative control analysed on the same plate. Samples positive for binding ADAs were then tested in a TNFα-target binding assay for neutralizing activity. Neutralizing antibody titre was reported as the highest dilution that tested positive in the assay.
Results: For the ABP 501 and adalimumab (RP) groups, 5 (1.9%) and 6 (2.3%) patients, respectively, tested positive for pre-existing binding antibodies and no patients tested positive for pre-existing neutralizing antibodies. Overall, 201 (38.2%) of all patients tested positive for binding antibodies at weeks 4, 12, or 26, with similar percentages in each treatment group (ABP 501, n = 101, 38.3%; adalimumab, n = 100, 38.2%) across all time points. A total of 53 (10.1%) of all randomized patients tested positive for neutralizing antibodies at weeks 4, 12, or 26, which was also similar in each treatment group (ABP 501, n = 24, 9.1%; adalimumab, n = 29, 11.1%). The rate of seroconversion over time for both treatment groups was similar, progressively increasing throughout the study. For subjects testing ADA positive, the magnitude of both the binding and neutralizing ADAs across the treatment groups were evenly distributed, with similar median S/N or titre values at each time point.
Conclusion: Similar immunogenicity rates were observed and relative magnitude of the ADAs was similar between the ABP 501 and adalimumab RP treated patients.
Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

P0972 INJECTION SITE REACTIONS AND INJECTION SITE PAIN FOR THE ADALIMUMAB BIOSIMILAR ABP 501: RESULTS FROM TWO DOUBLE-BLIND RANDOMIZED CONTROLLED STUDIES

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Introduction: Adalimumab (40 mg/0.8 mL strength) is a commonly used, subcutaneously administered anti-TNF therapy for inflammatory bowel disease. Clinical studies of adalimumab in rheumatoid arthritis (RA) have documented that the injection site reactions (erythema, itching, haemorrhage, pain or swelling) were the most common adverse events and that the immediate post administration pain from the injection to be 3.7 cm on a 10 cm visual analogue scale (VAS). ABP 501 (AMGEVITA®; adalimumab) was recently approved in the EU as the first biosimilar to adalimumab, a fully human recombinant monoclonal antibody. Formulation excipients of a biosimilar can differ provided there is no impact to product quality. ABP 501 is therefore formulated with different set of excipients that do not include citrate as that is known to cause pain or stinging.
Aims and Methods: To compare injection site pain and injection site reactions between ABP 501 and adalimumab, two randomized, double-blind, active-controlled clinical trials were conducted; one in patients with moderate to severe RA (n = 526) and the other in patients with moderate to severe plaque psoriasis (PsO; n = 350). The details of the two study designs and their efficacy, safety, and immunogenicity results have been previously reported. In both studies, injection site pain perception was assessed at baseline and at weeks 4, 8, and 12 using a 100 mm horizontal VAS measured within 5 minutes after injection.
Results: In the RA study 9 injection site reactions treatment-emergent adverse events (TEAEs) occurred in 6 of 264 subjects (2.3%) in the ABP 501 group and 39 events occurred in 13 of 262 subjects (5.0%) in the adalimumab reference product (RP) group. In the PsO study 4 injection site reactions TEAEs occurred in 3 of 174 subjects (1.7%) in the ABP 501 group and 26 events occurred in 9 of 173 subjects (5.2%) in the adalimumab RP group through week 16. In the RA study, mean injection site pain perception scores were lower in the ABP 501 group (range: 10.0–10.7 mm) vs. the adalimumab RP group (range: 16.1–21.4 mm) at each evaluated visit. In the PsO study, mean injection site pain perception scores were also lower in the ABP 501 group (range: 3.3–4.5 mm) compared with the adalimumab RP group (range: 12.4–19.3 mm) at each of the four time-points.
Conclusion: These results confirm that in addition to having clinically equivalent efficacy, the frequency of injection site reactions and perception of injection site pain were lower with ABP 501 compared with adalimumab RP. Results are attributed to the different excipients in the ABP 501 formulation.
Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

P0973 DEVELOPMENT OF ANTI-DRUG ANTIBODIES AMONG THOSE TREATED WITH ADALIMUMAB AND ABP 501 AND ITS IMPACT ON SERUM DRUG CONCENTRATION IN RANDOMISED

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Introduction: Sustained clinical response to biologic therapies is predicated on adequate drug exposure, which can, in turn, be impacted by development of binding anti-drug antibodies (ADAs).
Aims and Methods: To compare serum trough concentrations of adalimumab and ABP 501, an approved biosimilar and correlate them with incidence of immunogenicity. We descriptively analyzed serum drug trough concentration data and the binding anti-drug antibodies from baseline to primary analysis time point in two randomized controlled trials comparing ABP 501 with adalimumab. The first was a 52-week study among patients with moderate-to-severe plaque psoriasis (PsO); the second was a 26-week study among patients with moderate-to-severe rheumatoid arthritis (RA) on background therapy with methotrexate.
Results: The proportion of subjects with binding ADA positive results increased from 29.0% to 57.0% from week 4 to week 16 (time of primary analysis in the plaque psoriasis study) and 18.1% to 33.5% from week 4 to week 24 (time of primary analysis) in the RA study. Mean serum trough concentrations of ABP 501 and adalimumab was lower among those who tested positive for binding in all time points. However, trough concentration over the duration of the study remained similar between the two treatment arms in binding ADA negative and binding ADA positive subgroups in both studies.

	Mean (standard deviation) trough serum drug concentration (ug/mL)				
	Rheumatoid Arthritis			Plaque Psoriasis	
Treatment group	Week 4	Week 12	Week 24	Week 4	Week 16
ADA negative subgroup					
ABP 501	4.13 (1.48)	7.28 (2.75)	8.18 (3.41)	6.67 (2.23)	8.21 (3.11)
Adalimumab	4.07 (1.45)	7.05 (2.80)	7.92 (3.06)	6.85 (2.14)	8.62 (3.31)
ADA positive subgroup					
ABP 501	2.90 (1.77)	3.75 (3.18)	3.81 (3.79)	4.62 (2.16)	5.04 (2.25)
Adalimumab	2.82 (1.70)	3.45 (3.07)	3.59 (3.50)	3.03 (3.05)	3.59 (3.59)

[Serum trough concentrations of ABP 501 and adalimumab in ADA negative and positive subgroups]
Conclusion: The formation of binding ADAs in both studies impacted the exposure of both ABP 501 and adalimumab over time. The degree of decline in drug exposure over time was similar between ABP 501 and adalimumab arms in both studies regardless of the ADA status.
Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

P0974 EARLY DOSE OPTIMIZATION IN NONRESPONDERS TO GOLIMUMAB INDUCTION TREATMENT FOR ULCERATIVE COLITIS IS SUPPORTED BY PHARMACOKINETIC DATA THROUGH 1 YEAR

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Introduction: In the PURSUIT-M study, ulcerative colitis (UC) patients who were nonresponders to golimumab (GLM) induction treatment at Wk6 (by full Mayo score) were given GLM 100mg q4wk from Wk6 through Wk60. We previously showed that, compared with Wk6-Responders, Wk6-Nonresponders have lower GLM trough levels (TLs) at Wk6, and that Wk6-Nonresponders on the 100mg maintenance dose (at Wk6 and Wk10) achieved TLs at Wk14 that were similar to the TLs at Wk14 in Wk6-Responders on the 50mg dose (1). At Wk14, 28% of the Wk6-Nonresponders became responders (by partial Mayo score) after receiving 100mg at Wk6 and Wk10 (2). Here, we report on GLM TLs in the PURSUIT-M trial, in responders and nonresponders to induction treatment, through Wk50.
Aims and Methods: GLM TLs were measured at Wk 6, 10, 14, 18, 26, 34, 42 and 50. To eliminate artefactual changes in median values due to dropouts/missing data, only patients with TLs available at all the timepoints were included in this post-hoc analysis. Also, subgroups based on body weight (BW) < 80kg and

≥80kg were examined: Wk6-Responders with BW < 80kg on 50mg (n = 42), Wk6-Responders with BW < 80kg on 100mg (n = 42), Wk6-Responders with BW≥80kg on 100mg (n = 18), and Wk6-Nonresponders with BW < 80kg on 100mg (n = 62). The 80kg cutpoint was selected based on the maintenance doses currently approved in the EU: either 50mg for BW < 80kg, or 100mg for BW≥80kg.
Results: At Wk14 (steady-state), Wk6-Nonresponders with BW < 80kg on 100mg and Wk6-Responders with BW < 80kg on 50mg had the same median TL (0.98 μg/mL). At Wk26, 42, and 50, the IQ ranges of GLM TL were largely overlapping in these same two subgroups (Table). At each time point, the highest median TLs were observed in Wk6-Responders with BW < 80kg on 100mg, a posology that is not approved in the EU label of GLM for UC.
Conclusion: Based on TLs observed at steady state then followed over 1 year, these data suggest that patients with initial nonresponse to GLM induction who weigh < 80kg may require the GLM 100mg maintenance dose to achieve TLs similar to the TLs in induction responders receiving the maintenance doses currently approved in EU (either 50mg for BW < 80kg, or 100mg for BW≥80kg).

Serum golimumab trough concentrations (μg/ml) at selected timepoints during 1 year of maintenance, based on Clinical Response status, body weight and maintenance dose: Subjects with TLs at all timepoints

	Week-6 Responders,[a] BW < 80 kg, on 50 mg maintenance N = 42	Week-6 Responders,[a] BW < 80 kg, on 100 mg maintenance N = 42	Week-6 Responders,[a] BW ≥80 kg, on 100 mg maintenance N = 18	Week-6 Nonresponders,[a] BW < 80 kg, on 100 mg maintenance N = 62
Week 6 (post-induction)				
Median	2.40	2.54	1.59	1.32
IQ range	(1.34; 4.32)	(1.17; 4.25)	(0.88; 4.76)	(0.60; 2.38)
Week 14 (steady-state)				
Median	0.98	1.75	1.15	0.98
IQ range	(0.50; 1.37)	(1.31; 2.15)	(0.66; 2.24)	(0.53; 1.53)
Week 26				
Median	0.92	1.70	1.01	1.11
IQ range	(0.64; 1.27)	(1.08; 2.30)	(0.59; 1.49)	(0.68; 1.62)
Week 42				
Median	0.80	1.77	1.27	1.15
IQ range	(0.40; 1.23)	(1.27; 2.92)	(0.88; 1.57)	(0.76; 1.91)
Week 50				
Median	0.79	1.74	1.07	1.33
IQ range	(0.55; 1.33)	(1.23; 2.75)	(0.81; 1.42)	(0.67; 1.83)

[a]Responder status at Week 6 based on achieving a Clinical Response (defined as: Decrease [from the Week-0 full Mayo score] of ≥30% and >3 points, with either a rectal bleeding subscore of 0 or 1 or a decrease in the rectal bleeding subscore of ≥1). TL = trough level, BW = body weight, N = number of patients with TL data available at all the timepoints, IQ range = interquartile range

[Table]
Disclosure: G. Philip is an employee of Merck & Co., Inc., Kenilworth, NJ, USA and may hold stock and/or stock options in the company. C. Marano and J. Adedokun are employees of Janssen Research & Development, LLC, Spring House, PA, USA and may hold stock and/or stock options in the company. R. Melsheimer is an employee of Janssen Biologics BV, Leiden, Netherlands and may hold stock and/or stock options in the company. F. Cornillie is an employee of MSD Switzerland and may hold stock and/or stock options in the company.

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P0975 REAL-WORLD DATA ON THE USE OF 5 AMINOSALICYLIC ACID (5ASA) IN NON-FISTULATING, NON-STRICTURING CROHN'S DISEASE IN AN IBD TERTIARY CENTRE

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Introduction: Historical studies showed 5ASAs to be effective in Crohn's disease. However, more recently, several meta-analysis of trial data have now shown no improvement over placebo. The latest ECCO guidelines published in 2016 advises against the use of 5ASA in Crohn's disease.
Aims and Methods: Our retrospective study aims to assess our current practice. Using the IBD registry, we identified every patient diagnosed with Crohn's disease between 2009 and 2017. We included patients with L1/L2/L3 B1 Montreal classification as these patients are more likely to be treated with 5ASAs. Our patients are then subdivided into Group I: small bowel Crohn's (L1/L3 B1) and Group II: colonic Crohn's (L2 B1).
Results: Between 2009 and 2017, we had 453 patients diagnosed with Crohn's disease, 139 were in Group I and 49 in Group II.
In our Group I, 35% were prescribed 5ASA within first year of diagnosis (n = 49). 27 patients were L1 B1 and 22 patients were L3 B1. 18 patients were given 5ASAs as monotherapy. When looking at the prescriber, 16 were consultants, 14 were registrars and there was no documentation for the rest. In 24 patients, the prescriber clearly documented awareness of diagnosis of ileal/ileocolonic Crohn's disease. 13 patients are still on 5ASAs today. Only 2 were discontinued after a discussion about the lack of evidence in CD.
In Group II, 76% were prescribed 5ASAs (n = 19); 10 as monotherapy. In 14 patients, the prescriber documented awareness of diagnosis of colonic Crohn's. 6 patients remain on 5ASAs today, 3 were lost to follow-up and 10 stopped 5ASAs for various reasons including 1 for nephrotoxicity
Conclusion: This retrospective study assess current practice in an IBD tertiary centre. 5ASAs are still being used in this unit. There is awareness of the lack of evidence for using it but there remain patients on it. We recommend a discussion on the potential side effects and the lack of evidence for its use with every patient who remain on 5ASAs. It should be an alternative option in patients where steroids are contraindicated or intolerant.
Disclosure: Nothing to disclose

P0976 PERSISTENCE OF BIOLOGIC THERAPY AND MAPPING OF SEQUENTIAL BIOLOGIC USE: RESULTS OF A SINGLE CENTRE COHORT WITH 841 PATIENTS TREATED OVER 18 YEARS

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Introduction: Biologic therapy has revolutionised the treatment of IBD in the last 20 years. There is limited data on the patient journey through multiple lines of biologics and mapping this to outcomes. We aimed to establish the prevalence of biologic use in a single tertiary IBD centre and assess outcomes defined by biologic persistence.
Aims and Methods: Retrospective review of electronic health records (TrakCare) was performed on all patients who have received infliximab (IFX), adalimumab (ADA), vedolizumab (VEDO) or ustekinumab (UST) in Edinburgh from January 1999 to October 2017. We collected data for demographics, phenotyping details and duration of treatment. Kaplan-Meier survival curves and log-rank analyses were used to compare time to either discontinuation or resectional surgery.
Results: 841 patients were identified who have had biologic therapy for IBD. Median interval from diagnosis to biologic was 4.9 years (IQR 1.3–11.0). The multiple combinations of biologics used is displayed in Figure 1. 665 CD patients (79.7% of total) were treated with biologics; 486 received IFX (73.1%), 169 ADA (25.4%) and 10 VEDO (1.6%) as first line therapy. Second-line therapy was required in 238 patients and consisted of ADA 189 (79.4%), IFX 25 (10.9%), VEDO 18 (7.6%) and UST 6 (2.5%). Third-line therapy was required in 57 patients, VEDO 41 (74.5%) and UST 14 (25.5%). 3 (0.5%) patients received fourth-line therapy with UST. In the CD cohort persistence of treatment on ADA was longer than IFX when used as first-line treatment; median 2373 vs 1430 days (p = 0.0189).
Conclusion: Multiple sequential biologic use is becoming increasingly common and this will accelerate with the increasing use of anti-integrin and anti-IL12/IL23 therapies. Mapping the sequence of biologic use and linking this to outcomes is a priority for IBD research.
Disclosure: Nothing to disclose

P0977 UNDETECTABLE FAECAL ANTI-TNF CONCENTRATIONS AFTER SUBCUTANEOUS ADMINISTRATION IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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Introduction: Faecal loss of antibodies against anti-tumor necrosis factor (TNF) is a possible cause for primary non-response to anti-TNF agents in patients with severe ulcerative colitis (UC) ADDIN EN.CITE ADDIN EN.CITE.DATA [1]. For the intravenously administered infliximab, faecal loss has been demonstrated in the first days after start of treatment. The highest faecal infliximab concentrations were approximately 50-fold lower compared to infliximab serum concentrations. Evidence is lacking about faecal antibody loss with other anti-TNF agents.
Aims and Methods: The aim of this study was to investigate faecal loss of golimumab (GLM), a subcutaneously (sc) administered anti-TNF agent, in patients with moderate to severe UC. GLM concentrations were measured in serum and faeces using an ELISA developed by Sanquin Laboratories (lower limit of quantification (LLOQ) 0.005 μg/mL). First, this ELISA developed for GLM serum measurements was validated for the measurement of GLM in faeces. Homogenized faecal samples (0.95–1.05 g) of moderate to severe UC patients naive to biological therapy were spiked with GLM to obtain three different concentrations (QC-1: 5 μg/ml, QC-2: 0.5 μg/ml and QC-3: 0.05 μg/ml) and stored at −80 °C immediately. Second, faecal samples of patients with moderate to severe UC (endoscopic Mayo score ≥2) starting GLM treatment, (200 mg (day 1) and 100 mg (day 14) sc) followed by maintenance treatment according to the registered label, were prospectively collected at day 1 and 4–6 days after the first GLM injection and stored at −20 °C. Simultaneously, serum samples for the measurement of GLM serum concentrations were collected.
Results: For the assay validation, faecal samples of three anti-TNF naive patients with moderate-to-severe colitis were collected. The median [interquartile range (IQR)] faecal GLM concentrations of samples spiked with QC-1, QC-2 and QC-3 were 3.5 μg/ml [IQR 3.4–3.6 μg/ml], 0.3 μg/ml [IQR 0.3–0.4 μg/ml] and 0.05 μg/ml [IQR 0.04–0.05] respectively. For the clinical validation of faecal loss of GLM, faecal and serum samples of 12 UC patients were collected. The median serum GLM concentrations at day 1 and day 4–6 were 4.9 μg/ml [IQR 2.8–10.3 μg/ml] and 11.5 μg/ml [IQR 8.9–12.8], respectively. In all faecal samples collected at these time points, faecal GLM concentrations were below the LLOQ.
Conclusion: We validated the assay for measurement of GLM in a homogenized fecal matrix. With a hypothetical serum/faeces ratio of 50 for infliximab, faecal GLM concentrations should have been above the LLOQ in a real-life clinical setting. However, no GLM could be detected in faeces of treated UC patients. This may be explained by the fact that maximum serum drug concentrations after sc administration are much lower compared to intravenous administration. Moreover, the variation in bioavailability after sc administration is significantly greater than for iv agents. Furthermore, degradation of GLM in the gut may also play a role. Additional studies are needed to explore these phenomena.
Disclosure: Nothing to disclose

Reference

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P0978 EFFECTIVENESS AND SAFETY OF THE SWITCH FROM REMICADE® TO CT-P13 IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Switching from Remicade® to CT-P13 could be cost-saving strategy in inflammatory bowel disease (IBD) patients
Aims and Methods: We aimed to evaluate the clinical outcomes in patients with IBD after switching from Remicade® to CT-P13 in comparison with patients who maintain Remicade®.
Adult patients under Remicade® (as first biologic treatment) due to active IBD that were in clinical remission [defined by Harvey-Bradshaw index (HBI) in CD or Partial Mayo score (PMS) in UC] with standard dosage at study entry were included. The switch cohort (SC) was comprised with patients that made the switch from Remicade® to CT-P13 and the "non-switch" cohort (NC) was comprised with patients kept under Remicade®. SC came from centres that made the switch in a generalized way to all their patients, and the NC from centres that did not switch any patient from Remicade® to CT-P13. The follow-up started when the switch was made, in the SC, and in March 2015 (when the switch strategy started in most of the centres) in the NC.
Results: 476 patients were included: 199 (42%) in the SC and 277(58%) in the NS (table 1). The switch to CT-P13 was volunteered in only 25% of cases. Median follow-up was 18 months in the SC and 23 months in the NC ($p < 0.01$). 24 out of 277 patients relapsed in the NC after a median follow-up of 23 months; the incidence of relapse was 5% per patient-years. The cumulative incidence of relapse was 2% at 6 months and 10% at 24 months in this group. 38 out of 199 patients relapsed in the SC after a median of 18 months; the incidence rate of relapse was 14% per patient-years. The cumulative incidence of relapse was 5% at 6 months and 28% at 24 months. In the multivariate analysis, to have been switched to CT-P13, adjusted by duration of Remicade® treatment before entry, was associated with a higher risk of relapse ($HR = 3.5$, 95% CI = 2–6).13% of patients had adverse events in the NS and 6% in the SC ($p < 0.05$).
Conclusion: In this large real-life population of IBD patients in remission, switching from Remicade®to CT-P13 was associated with a higher risk of relapse (in comparison with those maintaining the infliximab originator). Nocebo effect might have influenced this result. Switching fromRemicade®to CT-P13 was safe.

	Switch cohort (N = 199)	Non-switch cohort (N = 277)	p
Female gender, n (%)	107 (54)	111 (40)	<0.01
Crohn's disease, n (%)	142 (71)	211 (76)	N.S
Ileal, n (%)	44 (31)	84 (40)	N.S
Colonic, n (%)	44 (31)	42 (20)	N.S
Ileocolonic, n (%)	54 (38)	85 (40)	N.S
Upper GI tract, n (%)	11 (5.5)	15 (5.4)	N.S
Inflammatory phenotype, n (%)	84 (59)	115 (54)	N.S
Stricturing phenotype, n (%)	22 (16)	31 (15)	N.S
Fistulizing phenotype, n (%)	36 (25)	65 (31)	N.S
Perianal, n (%)	76 (38)	81 (29)	<0.05
Ulcerative colitis, n (%)	57 (29)	66 (24)	N.S
Pancolitis, n (%)	32 (56)	38 (58)	N.S
Left-sided colitis, n (%)	19 (33)	25 (38)	N.S
Extraintestinal manifestations, n (%)	51 (25.6)	64 (23)	N.S
Surgery, n (%)	51 (25.6)	96 (34.7)	<0.05
Concommitant treatments			
Azathioprine, n (%)	90 (45)	112(40.4)	N.S
Mercaptopurine, n (%)	3 (1.5)	7 (2.5)	N.S
Methotrexate, n (%)	13 (6.5)	12 (4.3)	N.S

[Table 1. Characteristics of the study population]
Disclosure: M. Chaparro has served as a speaker, or has received research or education funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma. J.P. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Pfizer, Kern Pharma, Biogen, Takeda, Janssen, Roche, Celgene, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Vifor Pharma. J Hinojosa has served as a speaker, a consultant and advisory member for, and has received research funding from MSD, Abbvie, Ferring, Faes Farma, Shire Pharmaceuticals, Chiesi, Otsuka Pharmaceutical, Pfizer – Hospira, Kern Pharma, UCB Pharma, Vifor Fharma, Janssen, Takeda and Dr. Falk Pharma. Montserrat Rivero has

served as a speaker, a consultant and advisory member for Merck Sharp and Dohme, Abbvie and Janssen. Dr. Bermejo has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Takeda and Janssen. Manuel Van Domselar has received funding for attending congresses from Kern Pharma and MSD

P0979 NEED FOR ADALIMUMAB DOSE OPTIMIZATION IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS

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Introduction: During treatment with adalimumab (ADA), a variable proportion of Crohn's disease (CD) and ulcerative colitis (UC) patients with loss of efficacy need dose optimization to regain response. A meta-analysis showed that the mean percentage of CD patients who needed ADA dose optimization was 24.4% per patient-year.[1] Conversely, real-life need for ADA optimization in UC is not well known. No studies have directly compared the need for ADA dose optimization in CD and UC in the same real-life clinical setting.

Aims and Methods: The aim of the study was to compare the need for and timing of ADA dose optimization in two cohorts of patients with luminal CD or UC. In this single centre, observational, cohort study, dose optimization was determined by two senior staff specialized in IBD. CD patients with active perianal disease were excluded. We compared the rates of patients-months on ADA who needed dose optimization in the cohorts of CD or UC patients. We also compared the interval between ADA first induction dose and the first escalated ADA dose. Escalation-free survival was estimated by the Kaplan-Meier method. We also evaluated the rate of de-escalation.

Results: We included 43 patients with CD (mean age 43 years; 56% female) and 43 patients with UC (mean age 50 years; 42% female). Forty-eight% CD patients vs 51% UC patients ($p = 0.92$) were receiving an immunomodulator at baseline. After a median follow-up of 22.8 months (interquartile range [IQR] 9–49 months) and 13.9 months (IQR 5–31 months) for CD or UC patients, respectively ($p = 0.14$), 24 CD patients (56%) vs 28 UC patients (65%) required ADA optimization. In 88% of cases, ADA was escalated to 40 mg weekly. The rate of patient-month who needed ADA dose optimization was 2.5% vs 8.1% ($p < 0.001$) for CD and UC, respectively. In patients who underwent ADA optimization, median time between the first ADA induction dose and the first escalated dose was 11.8 (IQR 6–33) months vs 3.3 (IQR 2–10) months ($p = 0.001$) for CD and UC, respectively. Survival curves showed that patients with UC had an increased probability of needing ADA dose optimization when compared with CD (hazard ratio [HR] 2.51; 95% confidence interval [CI] 1.37–4.61; $p < 0.001$). Twelve CD patients (50%) vs 9 UC patients (32%) were able to de-escalate dose. Survival curves showed that patients with CD had an increased probability of ADA de-escalation when compared with UC patients (HR 2.32; 95% CI 1.10–5.59; $p = 0.030$). Median time to de-escalation was 3.8 months (IQR 3–13) vs 8.9 months (IQR 3–30) for CD and UC patients, respectively ($p = 0.12$). In the multivariate analysis, UC patients (HR 1.84; 95% CI 1.04–3.52; $p = 0.04$) and short-term non-response (HR 3.92; 95% CI 1.79–8.59; $p = 0.001$) were associated with a higher rate of ADA optimization.

Conclusion: In clinical practice, the rate of patient-month who needed ADA dose optimization is higher in UC when compared with luminal CD. Patients with UC required optimization of ADA dosing earlier and also had lower ADA escalation-free survival. The probability of dose de-escalation was also significantly higher in CD patients.

Disclosure: Nothing to disclose

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P0980 ANALYSIS OF NON-MELANOMA SKIN CANCER IN THE ULCERATIVE COLITIS PROGRAMME FOR TOFACITINIB

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Introduction: Tofacitinib is an oral, small-molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). We present an integrated analysis of non-melanoma skin cancer (NMSC) events in the tofacitinib Phase (P) 3 programme for patients (pts) with moderate to severe UC.

Aims and Methods: NMSC events were evaluated from 3 randomised placebo (PBO)-controlled studies (2 identical 8-week induction studies [OCTAVE Induction 1 & 2; NCT01465763, NCT01458951], a 52-week maintenance study [OCTAVE Sustain, NCT01458574]) and an ongoing, open-label extension study (OCTAVE Open, NCT01470612).[1,2] Pts were analysed as 3 cohorts: Induction (P3 induction studies); Maintenance (P3 maintenance study); Overall (pts receiving >1 dose of tofacitinib 5 or 10 mg twice daily [BID] in the P3 programme). An independent, blinded adjudication committee reviewed all potential NMSC. Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) for NMSC were evaluated. Cox proportional hazards model was used for risk factor analysis. Data shown are as of 16 December 2016.

Results: 1124 pts were evaluated for NMSC, with 1648 PY of tofacitinib exposure and up to 4.4 years of treatment. NMSC was reported in 2 Induction pts receiving 10 mg BID, 1 PBO Maintenance pt (IR 0.97) and 3 Maintenance pts receiving 10 mg BID (IR 1.91) (Table). In the Overall Cohort, NMSC was reported in 11 pts (IR 0.67), including 7 pts with squamous cell carcinoma (SCC) and 6 pts with basal cell carcinoma (BCC); 2 pts had both SCC and BCC. No NMSC was metastatic or led to study discontinuation. Of all tofacitinib-treated pts with NMSC, 6 had prior NMSC history, 10 had prior use of thiopurines and 10 had prior tumour necrosis factor inhibitor (TNFi) failure. In the Overall Cohort, higher IRs were observed for subgroups aged ≥ 65 years vs < 65 years, and for subgroups with prior TNFi failure or prior immunosuppressant treatment, vs those without. Cox regression selected prior NMSC (hazard ratio [HR] [95% CI] 64.07 [19.27, 213.03]; $p < 0.0001$) and prior TNFi failure (HR [95% CI] 9.56 [1.21, 75.22]; $p = 0.0320$) as significant risk factors.

Conclusion: NMSC occurred infrequently with tofacitinib treatment in the UC clinical programme. NMSC IRs were similar to those reported for tofacitinib in other indications, including rheumatoid arthritis[3] and for biologic UC treatments.[4] Cox regression analysis selected prior NMSC diagnosis and TNFi failure

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Table. Incidence rates for all NMSC events for Induction, Maintenance and Overall Cohorts, and univariate subgroup analyses for the Overall Cohort

All NMSC

	Induction Cohort		Maintenance Cohort			Overall Cohort
	Placebo N = 234	Tofacitinib 10 mg BID N = 905	Placebo N = 198	Tofacitinib 5 mg BID N = 198	Tofacitinib 10 mg BID N = 196	Tofacitinib All N = 1124
Exposure (PY)	N/A	N/A	103.20	148.77	156.80	1647.76
Number (%) of patients with events	0 (0)	2 (0.2)	1 (0.5)	0 (0)	3 (1.5)	11 (1.0)
IR (95% CI)	N/A	N/A	0.97 (0.02, 5.40)	0.00 (0.00, 2.48)	1.91 (0.39, 5.59)	0.67 (0.33, 1.19)
Overall Cohort, Tofacitinib All, N = 1124						
Baseline characteristic	**Univariate subgroup analysis**		**N**	**n (%)**	**IR (95% CI)**	
Age	< 65 years		1048	7 (0.7)	0.46 (0.18, 0.94)	
	≥65 years		76	4 (5.3)	3.35 (0.91, 8.59)	
Prior TNFi failure	Yes		583	10 (1.7)	1.26 (0.60, 2.31)	
	No		541	1 (0.2)	0.12 (0.00, 0.65)	
Prior immunosuppressant treatment	Yes		838	11 (1.3)	0.88 (0.44, 1.58)	
	No		286	0 (0.0)	0.00 (0.00, 0.92)	

BID, twice daily; CI, confidence interval; IR, incidence rate for unique patients with events per 100 PY; N, number of patients randomised and treated; n, number of patients with event; N/A, not available; NMSC, non-melanoma skin cancer; PY, patient-years; TNFi, tumour necrosis factor inhibitor.

[Table]

as significant risk factors for NMSC.

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P0981 LONG-TERM SAFETY IN THE OPEN-LABEL PERIOD OF A PHASE 2A STUDY OF BRAZIKUMAB, AN ANTIBODY AGAINST INTERLEUKIN-23

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Introduction: Brazikumab (MEDI2070), a human monoclonal antibody that is an anti-p19 subunit inhibitor of interleukin-23, was shown to be effective over 8 weeks of treatment for patients with moderate-to-severe active Crohn's disease.[1] Here, we report the long-term safety and tolerability of brazikumab.

Aims and Methods: The Phase 2a study (NCT01714726) consisted of a 12-week double-blind induction period with randomisation to intravenous brazikumab (700 mg) or placebo, followed by the open-label (OL) period where all patients were administered subcutaneous brazikumab (210 mg) every 4 weeks. Patients were aged 18–65 years, had a ≥6-month history of moderate-to-severe active Crohn's disease, had failed or were intolerant to ≥1 anti-TNFα agent, successfully completed the double-blind period and signed consent for inclusion in the OL period. Adverse events (AEs) and vital signs were recorded every 4 weeks until patients discontinued or completed the study at 100 weeks.

Results: 104 patients entered (n = 52 from placebo to brazikumab and n = 52 from brazikumab to brazikumab) and 57 (54.8%) patients completed the OL period. 87 (83.7%) patients experienced ≥1 treatment-emergent AE (TEAE); 12 (11.5%) experienced ≥1 TEAE leading to permanent discontinuation of study drug and 20 (19.2%) experienced ≥1 serious AE (SAE). The most common TEAEs were headache (22.1%), nasopharyngitis (22.1%), abdominal pain (18.3%) and Crohn's disease (16.3%) [Table]. Half of the SAEs observed were gastrointestinal disorders associated with Crohn's disease. Five SAEs of infection were reported, none of which were opportunistic, such as herpes zoster or tuberculosis; all resolved and the investigational product was permanently discontinued for only one patient. No cases of cancer were reported. The AE profile was similar between patients who completed a previous 12-week course of either placebo or brazikumab treatment.

Conclusion: In this 100-week OL period, brazikumab was well tolerated in patients with moderate-to-severe active Crohn's disease, warranting future studies in larger patient populations.

Treatment-emergent adverse events occurring in ≥5% of patients, n (%)	Total (N = 104)
Headache	23 (22.1)
Nasopharyngitis	23 (22.1)
Abdominal pain	19 (18.3)
Crohn's disease	17 (16.3)
Diarrhoea	14 (13.5)
Influenza	13 (12.5)
Nausea	11 (10.6)
Vomiting	11 (10.6)
Anaemia	10 (9.6)
Arthralgia	10 (9.6)
Pyrexia	9 (8.7)
Upper respiratory tract infection	9 (8.7)
Urinary tract infection	8 (7.7)
Bronchitis	7 (6.7)
Gastroenteritis	7 (6.7)
Asthenia	6 (5.8)

[Table]

Disclosure: BES has served as a consultant for 4D Pharma, AbbVie, Allergan Sales, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Capella Bioscience, Celgene, Eli Lilly and Company, EnGene, Ferring Pharmaceuticals, Gilead, Janssen, Lyndra, MedImmune, Oppilan Pharma, Otsuka, Palatin Technologies, Pfizer, Progenity, Rheos, Seres Therapeutics, Synergy Pharmaceuticals, Takeda, Target PharmaSoluations, Theravance Biopharma R&D, TiGenix and Vivelix Pharmaceuticals; has served on an advisory board for Allergan Sales, Celgene, Eli Lilly and Company, Janssen, Pfizer and Synergy Pharmaceuticals; and has received honoraria from Takeda and WebMD. RAG is an employee of MedImmune. CG is an employee of and owns stock for Allergan plc. SD has served as speaker, consultant and advisory board member for AbbVie, Allergan plc, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Ferring Pharmaceuticals, Hospira, Johnson & Johnson, Merck, MSD, Mundipharma, Pfizer, Sandoz, Takeda, TiGenix, UCB Pharma and Vifor Pharma.

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P0982 CLINICAL DECISION SUPPORT IMPROVES QUALITY OF CARE IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: The growing burden of inflammatory bowel diseases (IBD) has the potential to have a negative impact on the delivery of quality health care. Decision support tools (DST) may facilitate shared decision making (SDM) and improve quality of care by increasing patients' participation in their management.

Aims and Methods: This study aimed to assess the effectiveness of a clinical DST on improving quality of care in ulcerative colitis (UC).

A prospective quality improvement intervention was conducted at two metropolitan hospitals in two states (Victoria and Queensland) in Australia using a DST on a tablet-based app to assess UC symptoms, psychological wellbeing and IBD preventive care. Participants included adult patients aged ≥18 years with mild-to-moderate UC (Simple Clinical Colitis Activity Index ≤15), attending IBD outpatient clinics. Patient management was compared using an interrupted time-series study design to assess the effectiveness of a DST in improving clinical quality indicators pre- and post- use of the DST. The primary outcome was the percentage of process indicators used for UC care. The thirteen process indicators assessed were derived from ECCO guidelines and incorporated management of: disease activity; psychological wellbeing, and; preventive care. Secondary outcomes included: usability [based on the systems usability scale (SUS)] and acceptability of the DST and SDM (based on the decisional conflict scale) following clinic review.

Results: 100 patients with mild-to-moderate UC were invited to and agreed to participate. 50 patients were managed pre-intervention in outpatient clinics using standard care [median age 54 (range 23–81); 48% male)] and 50 patients used the DST for clinical management [median age 45 (range 19–78); 54% female] over an 18-week period. ***Primary outcome:*** A significant increase in the use of process indicators overall was observed following use of the DST [27% vs 94% ($p < 0.001$)], as well as specifically those for psychological wellbeing (15% vs 91%; $p < 0.001$), preventive care (22% vs 94%; $p < 0.001$) and disease activity management (52% vs 94%; $p < 0.001$). ***Secondary outcomes:*** The DST was found to be usable (SUS score = 82). The majority of patients deemed the DST to be acceptable with 91% of patients demonstrated interest in using the DST for outpatient management. SDM was greater in the post-intervention group, with a mean decision conflict score of 18.0, compared to a mean decision conflict score

of 33.5 in the pre-intervention group (p = 0.002), indicating less decisional conflict (and greater SDM) by patients in management decisions in the post-intervention group.
Conclusion: Implementing an evidence-based DST in the outpatient setting significantly improves quality of care, as measured by an increased use of process indicators. The DST improved the quality of the delivery of the psychological and preventive health aspects of care which may be neglected during routine IBD care. DSTs therefore have the potential to minimize errors of omission via a standardized approach to care.
Disclosure: Nothing to disclose

P0983 USTEKINUMAB IMPROVES PRODUCTIVITY AND REDUCES WORK LIMITATION OF PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE: RESULTS FROM THREE PHASE 3 CLINICAL TRIALS

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Introduction: UNITI-1 & 2 and IM-UNITI are Phase 3 multicenter, randomized, double-blind, placebo-controlled studies to evaluate the safety and efficacy of ustekinumab (UST) in adults with moderately to severely active Crohn's disease (CD).
Aims and Methods: To assess the effect of UST on improving work productivity with 8 weeks of induction therapy and maintaining improvement over the next 44-week period in patients with active CD. Patients with moderately to severely active CD [defined by a CD Activity Index (CDAI) score of 220–450] who had an inadequate response or intolerance to TNF inhibitors (UNITI-1, N = 741) or conventional therapy (UNITI-2, N = 639) were randomized in a 1:1:1 ratio to receive placebo or UST 6mg/kg intravenously (IV) or UST 130mg subcutaneously (SC) at week 0. Patients who had a clinical response to UST at week 8 (defined as having a reduction in CDAI score ≥100 points, or CDAI score < 150 if baseline CDAI score ≤248) were re-randomized to receive placebo or UST (SC) 90mg q12w or q8w through week 44 (IM-UNITI, N = 388). The impact of CD on productivity at work, school or home was measured using a visual analog scale (VAS) ranging from 0–10 (0 = no impact at all and 10 = very much impact). Of patients who were working two weeks prior to each visit, presenteeism (productivity loss on the job) was assessed using the Work Limitation Questionnaire (WLQ). The WLQ has 4 domains (time management, and physical, mental-interpersonal and output demands) with each domain score ranging from 0–100 and higher scores indicating greater work limitations. Productivity VAS and WLQ outcomes were collected and compared between treatment groups at baseline, week 8 (induction), and 22 and 44 weeks after induction (maintenance).
Results: At induction baseline, mean productivity VAS values ranged from 6.3–6.8, indicating significant impact of CD on productivity, and were comparable across treatment groups. At Week 8, patients in both UST dose groups had statistically significantly greater improvement in productivity VAS score vs. the placebo group in both UNITI-1 and UNITI-2 (all comparisons, $p < 0.05$). The reduction in productivity VAS score from baseline in the UST dose groups combined was −1.6 (23.2% improvement) in UNITI-1 and -2.1 (33.3% improvement) in UNITI-2, compared to placebo (−0.8 [11.9% improvement] in UNITI-1 and -1.1 [17.7% improvement] in UNITI-2, p-values < 0.01). Overall, percent improvement from baseline was numerically greater for UST-treated vs. placebo patients in 3 out of 4 WLQ domain scores at Week 8: time management (24.1% vs. 17.6% in UNIT-1, and 35.1% vs. 27.3% in UNIT-2), physical demand (21.2% vs. 11.9% in UNIT-1, and 25.6% vs. 21.9% in UNIT-2), output demand (21.4% vs. 20.1% in UNIT-1, and 38.3% vs. 21.0% in UNIT-2) and mental-interpersonal demand (19.5% vs. 20.3%in UNIT-1, and 33.7% vs. 24.5% in UNIT-2). Improvements in productivity VAS and WLQ scores were better maintained in the UST groups vs. the placebo group in the IM-UNITI study through Week 44.
Conclusion: UST treatment improves productivity and reduces work limitations in patients with moderate to severe CD.
Disclosure: This study was supported by Janssen Research & Development, LLC.

P0984 SWITCH OF INFLIXIMAB ORIGINATOR TO BIOSIMILAR CT-P13 IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS IN A LARGE GERMAN IBD CENTER. A ONE YEAR, RANDOMIZED AND PROSPECTIVE TRIAL

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Introduction: The infliximab biosimilar CT-P13 has been approved by the EMA for the treatment of ulcerative colitis (UC) and Crohn's disease (CD) based on extrapolation of data from rheumatology trials. Since then, several un-controlled and controlled studies have later-on shown that CT-P13 could be safe and effective for IBD patients who switched from originator to biosimilar or who received CT-P13 as first infliximab, although in the pivotal trial (1) a trend to disease worsening after swichting was observed in CD patients. In addition, no randomized long-term data from single-centre cohorts were presented that prospectively analysed efficacy and safety in IBD-patients who switched from originator to biosimilar infliximab.
Aims and Methods: We performed an independent, prospective and randomized, double-blinded trial in patients of the IBD center Munich with CD and UC who had responded to originator infliximab for at least 3 months. We provided each elegible patient with individualized information about biosimilars and the possibility of switching from originator infliximab to CT-P13. Between June and September 2015, 200 (68%) of the elegible patients consented to the blinded switch. After randomization, patients were either switched to CT-P13 or maintained on originator infliximab and prospectively observed.
Primary endpoint was a combination of clinical remission at 52 weeks and the ability to continue the study drug throughout 52 weeks.
Clinical remission was evaluated at weeks 0, 24 and 52 for UC using the modified Rachmilewitz Clinical Activity Index (CAI) and CD using the Crohn's disease activity score (CDAI). Study infliximab was discontinued, if loss of response or side effects occurred.
Results: Of 200 patients participating, 111 (55.5%) patients were switched to CT-P13 and 89 (44.5%) were maintained on the originator in a double-blinded mode (uneven numbers are due to the simplified randomization process). Mean age, sex, type of IBD and remission rates at study start were equally distributed in both study groups: 46.8% vs. 47.2% women, mean age 37 vs. 40 years, 62.2% vs. 58.4% patients with CD, and 82.9% vs. 80.9% remission rates at start in the CT-P13 group vs. the originator group, respectively. Discontinuation of the study due to loss of response or side effects occurred in 25.2% (n = 28) of patients in the CT-P13 group and 18.0% (n = 16) in the originator group (p = 0.219). Among those patients who could continue study therapy throughout 52 weeks, remissions was achieved in 83.1% of the patients (n = 69) in the CT-P13 group and 89.0% (n = 65) in the originator group (p = 0.290). Hence, the primary endpoint (clinical remission and continuation of study drug at 52 weeks) was achieved in 62.2% of the patients (n = 69) in the CT-P13 group and 73.0% (n = 65) in the originator group (p = 0.104).
Conclusion: After switching from the originator infliximab to the biosimilar CT-P13, 11% more patients lost response or had to stop therapy due to side effects as compared to those patients who remained on the originator infliximab. Although this difference did not reach significance level, our finding is in accordance with the results of the other double blinded switch-trial, the NOR-SWITCH study, in which a similar outcome was observed in IBD without reaching significance level. In both studies larger numbers might have shown significant differences. We conclude that switching from the originator infliximab should not be enforced, until results of larger long-term switch-trials in CD and UC are available, especially since in most European countries all infliximab products are sold at the same price, now.
Disclosure: Thomas Ochsenkühn has received lecture fees, unrestricted travel grants and honoraria for advice from Abbvie, Biogen, Celltrion, Janssen, MSD, Mundiphama, Sandoz, Shields, Shire, Stada, and Takeda. Fabian Schnitzler has received honoraria from Abbvie and MSD.

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P0985 RATIONALE AND PHASE 2 CLINICAL TRIAL DESIGN FOR PRV-6527, AN ORAL INHIBITOR OF THE CSF1RECEPTOR KINASE (CSF-1R) FOR CROHN'S DISEASE

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Introduction: Bone marrow-derived myeloid antigen presenting cells, such as macrophages (Mø) and myeloid dendritic cells (mDCs) have been increasingly linked to pathogenesis of Crohn's disease (CD). Monocytes (Mo) recruited to the intestinal lamina propria differentiate into an inflammatory Mø/mDC phenotype, which then expresses high levels of TNFα, IL-12 and IL-23 upon activation by enteric bacteria, inducing proliferation of Th1 T cells. Colony stimulating factor (CSF-1) is prominent among the several factors that support Mo/Mø/mDC survival, proliferation, and differentiation. PRV-6527, also known as JNJ-40346527, is an oral small molecule inhibitor of CSF-1R, in development by Provention Bio to target inflammatory Mo/Mø/mDC for the interception and treatment of CD.
Aims and Methods: To demonstrate that preclinical and biomarker data support the clinical study of PRV-6527, whose objectives are to assess the safety, tolerability and clinical efficacy of the CSF-1R inhibitor PRV-6527 in Crohn's disease, as well as to determine blood and tissue pharmacodynamics and pathway gene signatures in biopsy tissue. Colitis was induced in C.B-17 SCID mice by i.p. injection of $4x10^5$ $CD45^+RB^{high}$ T cells harvested from Balb/C donor spleens.

Mice were treated orally with 15 mg/kg PRV-6527, a selective inhibitor of CSF-1 receptor kinase, either prophylactically or therapeutically through termination on day 42. Murine anti-TNFα monoclonal antibody (CNTO5048) was administered therapeutically at 3 mg/kg i.p. as positive control. RNAseq analysis of murine colonic mucosa was performed, and gene expression profiles were compared to publicly available profiles from healthy and CD mucosal biopsies (Rutgeerts GSE16879). The PRINCE (PRovention INvestigation in Crohn's DiseasE) Phase 2 study (EudraCT Number: 2017-003017-25) is a randomized, double-blind, placebo-controlled, parallel-group, multicenter study in adult subjects with moderately to severely active CD. The study hypothesis is that PRV-6527, a CSF-1R inhibitor, will be superior to placebo in treating subjects with moderate to severe active CD over 12 weeks, as measured by the change from baseline in the Crohn's Disease Activity Index (CDAI) score. Approximately 80 subjects are planned to be enrolled. Proof of mechanism will be assessed in secondary endpoints, including mucosal changes on endoscopy and histology and the presence of inflammatory myeloid cells by immunohistochemistry and gene signature in mucosal biopsies.

Results: A CSF-1 gene signature was elevated in the inflamed mucosa in CD and remained elevated in anti-TNF-non-responder patients. Inhibition of the CSF-1 receptor by PRV-6527 significantly reduced histological disease scores by ~60% in established murine colitis. Recruitment of $CD3^+$ T cells was reduced and $F4/80^+$ mononuclear cells were decreased to levels similar to control. RNAseq analysis demonstrated significant concordance of disease pathways between human CD and the mouse model. Treatment of mice with either PRV-6527 or CNTO5048 impacted those pathways in a manner comparable to patients who respond to infliximab.

Conclusion: Pre-clinical and human biomarker data support the study of PRV-6527, a CSF-1R inhibitor, in CD and the promise for an oral therapy with the potential for benefit in anti-TNF non-responders. Furthermore, these PD and biomarker data could be useful for patient stratification for future clinical studies or for tailored therapy in CD patients.

Disclosure: Authors 1, 4, 5 and 6 employees of Provention Bio Authors 2 and 3 employees of Janssen R&D

P0986 LONG-TERM FOLLOW-UP OF PATIENTS WITH SEVERE, STEROID-RESISTANT ULCERATIVE COLITIS WHO RECEIVED INDUCTION THERAPY WITH CYCLOSPORINE AND WERE MAINTAINED WITH VEDOLIZUMAB

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Introduction: Vedolizumab is an anti-integrin monoclonal antibody approved for use in moderate to severe ulcerative colitis (UC). However, concurrent use of calcineurin inhibitors was not studied in the original clinical trials. We have previously described the 10 and 26 week outcomes of the first prospective study bridging cyclosporine to vedolizumab in patients with severe, steroid-resistant UC (ECCO and DDW 2018). Here we present the longer term follow-up on these patients.

Aims and Methods: This is follow-up of a prospective study of 17 UC patients treated with cyclosporine in conjunction with vedolizumab at the Military Medical Academy in Belgrade, Serbia. UC patients, not responding to IV steroids for 3 days were treated with IV cyclosporine at doses of 2 mg/kg titrated to goal trough level of 300–400. At day 8 after IV cyclosporine was started (defined as week 0), those who responded were prescribed vedolizumab 300 mg IV. After vedolizumab was administered, cyclosporine was continued orally at double the IV dose and discontinued after 8 weeks of cyclosporine use. Vedolizumab was additionally dosed at 300 mg at weeks 2 and 6, followed by 300 mg IV every 8 weeks. Patients were followed up to 52 weeks. Demographics and disease information were reviewed. Clinical and endoscopic response and remission were the primary endpoints.

Results: Seventeen patients (mean age 40 (range 20–67 yrs)); mean disease duration 4.9 ± 4 yrs with severe, steroid-resistant UC were treated with cyclosporine. Fifteen (79%) patients (9/15 male) initially responded to IV cyclosporine (median cyclosporine dose 200 mg (100–300) IV and 400 mg (200–600) oral. At initial follow-up at week 10, ten (67%) patients achieved a Mayo score of ≤1 (decrease from 3 at admission). At week 26, 14/15 patients were in clinical remission. One patient was referred to surgery due to recurrence of symptoms. At week 52 of follow-up, eleven of 14 (79%) patients continued to be in clinical and endoscopic remission. The remaining 3 patients (21%) had a clinical response to treatment but continued to have endoscopically active disease. No adverse effects were reported from either cyclosporine or vedolizumab during the duration of the study.

Conclusion: In the first prospective study bridging cyclosporine to vedolizumab in steroid-refractory severe UC patients, the clinical outcomes at 10 weeks were predictive of those at 52 weeks. At one year follow-up, patients continued to be responsive to treatment, with the majority maintaining clinical and endoscopic remission.

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P0987 PROBIOTICS CAN IMPROVE THE INFLIXIMAB RESPONSE FOR PATIENTS WITH CROHN'S DISEASE

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Introduction: Even though the biological agents (BAs) are used, there are still not less CD cases who are not responsive to BAs. Thus we hypothesize that "can probiotics benefit CD patients who are not responsive to BAs"?

Aims and Methods: To distinguish the gut microbiota differences between response and non-response to infliximab (IFX), and observe the effect of probiotics on improving the response rates, for patients with CD. The faeces and peripheral blood from 38 cases of CD treated with IFX were collected. According to the response to IFX, they were divided into Response Group (Group 1, $n = 29$) and Non-response Group (Group 2, $n = 9$; cases have been exclusive when opportunistic infections or IFX doses deficiency were merged). The gut microbiota was sequenced by 16SrDNA, and the concentrations of fecal calprotectin (FCP) were detected by ELISA. The peripheral blood antibodies (ATI) and trough level (TLI) of IFX were detected, and the frequencies of $CD8^+CD28^+$T and $CD8^+CD28^-$T cells were detected through flow cytometry (FCM). A triplet live bacteria tablet, consisting of *Streptococcus faecalis*, *Clostridium butyricum*, and *Bacillus mesentericus* (SCB), was prescribed for the patients of non-response for 16 weeks. All the above-mentioned factors were compared between the two groups, as well as between pre-treatment and post-treatment for the non-response group.

Results: I. Gut microbiota: The species of bacteria in Response Group and Non-response group were 659 and 560, respectively. Surprisingly, a novel bacteria, the *Alistipes*, was found to be the most dominant bacterial between the two groups.
II. FCP, TLI and ATI: The concentrations of FCP in Non-response Group were significantly higher than those of the Response Group. Nine patients (100%) in the Non-response Group were ATI-positive whereas only 2 (6.90%) were positive in the Response Group. The TLIs of the Response Group were significantly higher than those of the Non-response Group.
III. $CD8^+$T lymphocyte subsets: The percentages of peripheral blood $CD8^+CD28^+$T lymphocytes of non-response group were significantly lower than those of Response Group. The frequencies of $CD8^+CD28^-$T cells in the Non-response group were significantly higher than those of the response group.
IV. Probiotics treatment: Five of 9 (55.56%) non-responders expressed *Alistipes*, and FCP decreased but TLIs increased for the non-responders after SCB treatment. Seven of the 9 (77.78%) non-responders were transferred to clinical response, and 6 (66.67%) were ATI-negative. The frequencies of $CD8^+CD28^+$T lymphocytes increased and $CD8^+CD28^-$T lymphocytes decreased for the non-responders. The overall response rate increased from 76.32% (29/38) to 94.74% (36/38) ($p = 0.047$).
V. Predicting efficiency of *Alistipes*: *Alistipes* significantly correlated with anyone of IFX response, clinical response, FCP, TLI, ATI, $CD8^+CD28^+$T and $CD8^+CD28^-$T lymphocytes *Alistipes* was proved to be powerful to predict the IFX non-response, with an area under curve (AUC) of 0.914, 100% in specificity, and 82.8% in sensitivity.

Conclusion: Decrease in diversity, especially in *Bacillus* and *Clostridium*, is the vital characteristic of CD patients with IFX non-response. Lower *Alistipes*, TLI, and $CD8^+CD28^+$T lymphocytes, as well as higher $CD8^+CD28^-$T lymphocytes and surveillance factors (FCP and ATI), are associated with IFX non-response. The triplet live bacteria tablet, SCB, is brilliant to equilibrate the general immunity balance ($CD8^+CD28^+/CD8^+CD28^-$T lymphocytes) and thus to improve the IFX response rates. The novel bacteria, *Alistipes*, can predict the IFX non-response with high efficiency.

Disclosure: Nothing to disclose

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P0988 ETROLIZUMAB TREATMENT MODULATES MADCAM-1 LEVELS IN SERUM IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Etrolizumab, a monoclonal antibody to the β7 integrin, inhibits both α4β7:mucosal addressin cell adhesion molecule 1 (MAdCAM-1)-mediated lymphocyte trafficking to the gut mucosa and αEβ7:E-cadherin-mediated lymphocyte retention. In patients with ulcerative colitis (UC) from the Phase 2 EUCALYPTUS trial (NCT01336465), treatment with etrolizumab resulted in a reduction in serum levels of soluble (s) MAdCAM-1 compared with placebo; this reduction in sMAdCAM-1 paralleled a reduction in free β7 receptors in the peripheral blood, with complete receptor occupancy (RO) observed at day 5 after the first dose in both dose cohorts (100 mg and 300 mg).[1,2] Pharmacodynamic (PD) activity in patients with Crohn's disease has yet to be evaluated.

Aims and Methods: The effect of etrolizumab treatment on serum levels of sMAdCAM-1 (PD biomarker) and β7 RO in patients with moderate to severe Crohn's disease were evaluated in a substudy of cohort 1 of the Phase 3 BERGAMOT trial (NCT02394028). Patients were randomly assigned to receive subcutaneously administered etrolizumab 105 mg once every 4 weeks, etrolizumab 210 mg at weeks 0, 2, 4, 8, and 12 or placebo during a 14-week induction period. Biomarker and pharmacokinetic (PK)/PD analysis was conducted using serum and whole blood samples obtained at baseline and weeks 1 (days 3, 4 or 5), 2, 4, 10 and 14 from patients who enrolled in the PK/PD substudy. Measurements of serum sMAdCAM-1 were performed using a validated assay on the Gyrolab xP immunoassay platform. Whole blood samples were evaluated by flow cytometry within 24-48 hours of collection to assess β7 expression, β7 occupancy and enumeration of peripheral blood lymphocyte subsets using previously established methods.
Results: This preliminary analysis included 64 patients with Crohn's disease (etrolizumab 105 mg, n = 29; etrolizumab 210 mg, n = 24; placebo, n = 11). Patients treated with etrolizumab showed a sustained decline in sMAdCAM-1 from baseline (week 1: group median decline of ~40%, weeks 4 through 14: group median decline of ~80%) with minimal (< 10%) changes from baseline observed in the placebo arm (**Table**). β7 integrin receptors on "$\beta7^{high}$ intestinal homing" $CD3^+$ T cells were rapidly and completely occupied in etrolizumab-treated patients as indicated by a near 100% decrease in $CD3^+$ T cells with "available" β7 receptors. Similar RO results were observed with CD4 T, CD8 T and CD19 B lymphocytes. There were no dose-related differences observed in sMAdCAM-1 reduction and RO.

	sMAdCAM-1 (median % change ± MAD from baseline)	Intestinal homing CD3+ T cells with "available" β7 (median % change ± MAD from baseline)
Etrolizumab 105 mg		
Week 1	−37.2 ± 7.5	−100.0 ± 0.0
Week 4	−78.5 ± 4.1	−99.8 ± 0.2
Etrolizumab 210 mg		
Week 1	−38.0 ± 8.1	−100.0 ± 0.0
Week 4	−78.1 ± 2.0	−100.0 ± 0.0
Placebo		
Week 1	−7.8 ± 6.2	23.5 ± 25.6
Week 4	−4.9 ± 10.1	24.7 ± 32.8

Week 1 = days 3, 4 or 5 after first dose. MAD, median absolute deviation.

[Table 1. Absolute Change From Baseline of Serum sMAdCAM-1 and β7 "Available" Intestinal Homing $CD3^+$ T Cells After Etrolizumab Treatment]
Conclusion: In this preliminary analysis, sMAdCAM-1 was reduced following etrolizumab treatment in patients with Crohn's disease. Full β7 RO was achieved with both doses of etrolizumab. Overall, results were similar to those reported in UC[1] and confirm the expected pharmacologic profile of etrolizumab.
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P0989 EARLY INITIATION OF ADALIMUMAB SIGNIFICANTLY DIMINISHES ENDOSCOPIC POST-OPERATIVE CROHN'S DISEASE RECURRENCE, AND IS SUPERIOR TO IMMUNOMODULATORY THERAPY, REGARDLESS OF RISK STRATIFICATION. A RANDOMIZED, CONTROLLED STUDY

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Introduction: A sizable proportion of patients with Crohn's disease (CD) will undergo intestinal resection. Most will experience early post-operative endoscopic and clinical disease recurrence. The superiority of anti-TNF agents over both placebo and immunomodulators in the prevention of post-operative recurrence using a risk-stratified strategy was previously demonstrated.
Aims and Methods: To evaluate the efficacy of an early unstratified approach comparing anti-TNF (adalimumab) with thiopurine (6-mercaptopurine, 6MP) therapy on post-operative CD recurrence, as demonstrated by endoscopy at 24 weeks.
All CD patients undergoing a first ileocecectomy for inflammatory complications were prospectively recruited to the Post Operative Adalimumab Recurrence Trial (POPART). Patients were randomized within 45 days to receive either adalimumab or 6MP. All patients underwent ileocolonoscopy at 24 weeks post operation to asses for endoscopic recurrence as defined by the Rutgeerts score. Endoscopic recurrence was defined as a Rutgeerts score of i2-i4.
Results: Fourty-one patients were recruited to the study. Four patients were lost to follow-up, and two who did not adhere to treatment were excluded from the final analysis. A total of 35 patients completed the study protocol −16 were treated with 6MP and 19 with adalimumab. Mean age 32.2 ± 21.6, 62.9% males, 54.3% non-smokers. Follow-up endoscopy was performed at week 24. Baseline clinical parameters and smoking status were comparable between treatment arms (43.8% vs. 38.9% respectively, p = 0.774).
Endoscopic recurrence at week 24 was significantly lower in the adalimumab vs. the 6MP arm: 21.1% vs 56.2%, p = 0.03. Other clinical and biologic indices at week 12 and 24 were comparable (Table 1).
Table 1. Clinical and endoscopic parameters of Crohn's disease patients at post ileocecectomy weeks 12 and 24 according to medical therapy
Conclusion: Early treatment of post-operative CD patients with adalimumab is significantly superior to 6MP, regardless of risk stratification. Endoscopy is superior to clinical and biochemical indices, in early risk stratification of patients.
Disclosure: Nothing to disclose

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	12 weeks			24 weeks		
Clinical parameter	6-MP n = 16	Adalimumab n = 19	Pv	6-MP n = 16	Adalimumab n = 19	Pv
BMI (kg/m2)	18.6 ± 8.0	24.1 ± 3.5	0.01	19.0 ± 7.8	22.4 ± 7.0	0.11
CRP (mg/dl)	6.9 ± 14.0	2.4 ± 3.6	0.20	4.6 ± 6.9	2.4 ± 2.1	0.21
Calprotectin (mg/kg)	256.1 ± 228.1	255.5 ± 27.3.0	0.99	193.8 ± 192.0	391.8 ± 695.1	0.48
CDAI (score)	94.6 ± 58.3	88.0 ± 45.2	0.78	105.8 ± 71.5	71.5 ± 73.0	0.15
IBDQ (score)	181.0 ± 29.4	178.7 ± 32.6	0.83	180.0 ± 28.1	182.1 ± 32.7	0.84
Endoscopic recurrence (≥Ri2) (%)				56.3	21.1	**0.03**

[Table 1.]

P0990 EVALUATING EFFICACY, SAFETY AND PHARMACOKINETICS AFTER SWITCHING FROM INFLIXIMAB ORIGINATOR TO BIOSIMILAR CT-P13: RESULTS FROM A LARGE TERTIARY REFERRAL CENTER

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Introduction: The use of infliximab (IFX) biosimilar CT-P13 has dramatically increased in patients with Crohn's disease (CD) and ulcerative colitis (UC), but doubts about the efficacy and safety of switching from IFX originator to biosimilar still exist with patients and health care professionals.

Aims and Methods: We investigated pharmacokinetics as well as efficacy and safety of a mandatory switch from IFX originator to CT-P13.

In our tertiary referral center, CT-P13 was initiated in a 2 step procedure, with initiation of CT-P13 in IFX naïve patients from November 2015 onwards (controls). In March 2017, all patients receiving IFX originator were electively switched to CT-P13 (cases). Patient reported outcome (PRO2), C-reactive protein (CRP), IFX trough levels (TL, ELISA apDia) and anti-drug-antibodies (ADA, drug sensitive assay apDia) were measured at switch (T0), the next infusion of CT-P13 (T1) and 6 months after switch (T2).

The primary endpoint was IFX discontinuation within 6 months after switch. Secondary endpoints included loss of clinical remission, need for treatment optimization, adverse events, as well as evolution of PRO2, CRP and IFX TL. Clinical remission was defined as a rectal bleeding score of 0 and a stool frequency $\leq$1 for UC, or an abdominal pain score $\leq$1 and liquid stool frequency $\leq$1.5 for CD. Treatment optimization was defined as the need for changes in IFX dosage or introduction of additional disease-modifying drugs.

Results: A total of 401 patients (53% male, median age 25 years, 71% CD, 61% in clinical remission) were enrolled, including 361 cases and 40 controls. Both groups were comparable except for median disease duration (7.0 vs. 1.5 years, $p=0.011$), median duration of IFX treatment (6.0 vs. 0.9 years, $p<0.0001$), concomitant immunosuppressive therapy (6% vs. 20%, $p=0.002$), and median CRP (1.5 vs. 2.3 mg/L, $p=0.032$). IFX discontinuation within 6 months of switch was observed in 4% of cases and 13% of controls ($p=0.04$). The percentage of patients developing loss of clinical remission (22% vs. 29%, $p=0.91$), adverse events (2% vs. 8%, $p=0.052$) and ADA (0.6% vs. 2.5%, $p=0.18$) were similar between both groups. In addition, cases less frequently needed treatment optimization (24.9% vs. 42.5%, $p=0.02$). Table 1 shows the evolution of median PRO2, CRP and IFX TL over time. Although PRO2 increased significantly in cases between T0 and T2, this difference was not statistically different compared to the increase in PRO2 in controls ($p=0.61$). In both groups, CRP and IFX TL remained stable over time.

Conclusion: Compared to continued therapy with biosimilar CT-P13, switching from IFX originator to CT-P13 was not associated with an increased risk of treatment discontinuation, loss of response or adverse events. In addition, no differences in IFX TL or immunogenicity could be identified.

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P0991 ANTI-TNF ALPHA THERAPY IN BIOLOGICS-NAÏVE ULCERATIVE COLITIS PATIENTS IN A PROSPECTIVE "REAL WORLD" STUDY IN GERMANY (BIOCOLITIS-REGISTRY)

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Introduction: The BioColitis Registry (Biological Registry with Ulcerative Colitis-Patients in Germany) of the Competence-Network IBD is a five-year prospective registry of Ulcerative Colitis (UC)-patients with an early disease and/or a newly introduced biological-therapy in Germany. In this sub-analysis of the BioColitis Registry we are showing the 6-months clinical efficacy of anti-TNFs in biologics-naïve UC-patients.

Aims and Methods: Within the framework of this five-year prospective non-interventional study with an every 6-months online documentation and assessment of the clinical course of disease, medication, psychosocial burden and health economics as well as the patient's genetic profile were separately examined. At the end of 2016, nearly 900 UC-patients from 52 gastroenterology practices and hospitals in Germany had been included prospectively into the "BioColitis-Study" with a 5-years follow-up until the end of 2021. The following subgroup-analysis of 183 biologics-naïve UC-patients of 439 newly introduced anti-TNF therapies in UC-patients reports the clinical efficacy at 6-months in the 183 biologics-naïve UC-patients with a newly introduced anti-TNF-therapy as an induction and maintenance therapy. The selection of the respective anti-TNF therapy was made in the IBD-experienced centers on the basis of clinical requirements taking patient's request into account. The primary objective was the steroid-free remission (pMayo <2) at months 6.

Results: 183 anti-TNF-naïve UC-patients with a 6-months follow-up were available for the sub-analysis (average age: 42 years; female: 47%; pancolitis 52%; course of disease: 9.7 years). 76/183 UC-patients were in steroid-free remission at months 6 (41.5%). Along with the steroid-free remission, there are significantly fewer signs of sub-depression/ depression than in the group without a remission (EQ-5D) at months 6 (12.7% vs. 39.6%; $p=0.0001$). The analysis of steroid-free remission at months 6 with the different anti-TNF-antibodies showed the following remission-rates: Adalimumab 28/60 (46.7%), Infliximab 24/74 (32.4%), Golimumab 16/31 (51.6%) and Vedolizumab 8/18 (44.4%) (n.s.). In addition, the patients received 5-ASA in 40.4%, and immunosuppressants in 27.3% at months 6.

Conclusion: About 40% of the investigated anti-TNF-naïve UC-patients were in clinical remission at months 6. These anti-TNF UC-patients, even in steroid-free remission showed an unexpectedly high (co) morbidity with unmet needs e.g. regarding depression, indicating a reduced health state already in these UC-patients without a remission at months 6.

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		T0	T1	T2	p-value*	p-value**
Median (IQR) PRO2	Cases	2 (0–9)	2 (0–9)	2 (0–12)	0.0001	0.61
	Controls	5 (0–11)	5 (0–11)	5 (0–14)	0.30	–
Median (IQR) CRP	Cases	1.4 (0.6–3.5)	1.4 (0.6–3.2)	1.4 (0.7–3.1)	0.39	0.50
	Controls	1.2 (0.4–3.5)	0.9 (0.4–3.2)	1.4 (0.4–4.0)	0.30	–
Median (IQR) TL	Cases	5.5 (3.9–7.7)	5.7 (4.1–8.1)	5.5 (4.0–7.7)	0.59	0.06
	Controls	6.7 (3.9–11.4)	9.0 (4.0–11.0)	6.4 (3.7–11.0)	0.23	

[Table 1]

*Evolution of CRP, IFX TL, PRO2 between T0 and T2 within groups (Wilcoxon ranked sum test).

**Evolution of CRP, IFX TL, PRO2 between T0 and T2 between cases and controls (Mann Whitney U test). CRP: C-reactive protein, IQR: interquartile range; IFX TL: infliximab trough level; PRO2: patient-reported outcome.

P0992 IMMUNOGENICITY AFTER TRANSITION FROM ADALIMUMAB TO ABP 501 IN PATIENTS WITH PLAQUE PSORIASIS

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Introduction: ABP 501 (AMGEVITA®; adalimumab) is the first approved biosimilar to adalimumab (HUMIRA®). Here we report immunogenicity results from a Phase 3 study in patients with moderate to severe plaque psoriasis without concomitant immunosuppressive therapy that undergo a single transition from adalimumab reference product (RP) to ABP 501. In this report we have examined the incidence of anti-drug antibodies (ADAs) and the relative magnitude of the ADA response among patients that transitioned from adalimumab RP to ABP 501.

Aims and Methods: Patients were randomized 1:1 (ABP 501: n = 175; adalimumab RP: n = 175) to receive ABP 501 or adalimumab every 2 weeks for 16 weeks. Eligible subjects who continued treatment beyond week 16 were re-randomized in a blinded fashion such that all subjects initially randomized to ABP 501 continued treatment with ABP 501, and subjects initially randomized to adalimumab RP either continued treatment with adalimumab RP or underwent a single transition to ABP 501 in a 1:1 ratio. The last dose was at week 48; end of study at week 52.

After re-randomization, ADAs were assessed on weeks 20, 32 and 52. A validated electrochemiluminescent assay was used for detection of binding ADAs. Samples positive for binding ADAs were then tested in a TNFα-target binding assay for neutralizing activity. Neutralizing antibody titre was reported as the highest dilution that tested positive in the assay.

Results: The proportion of subjects positive for binding and neutralizing antibodies was comparable from baseline through week 52, regardless of the transition (adalimumab RP/adalimumab RP 74.7% (59/79) binding and 20.3% (16/79) neutralizing; adalimumab RP/ABP 501 74.0% (57/77) binding and 24.7% (19/77) neutralizing). The overall incidence of binding antibodies that formed after the re-randomization at week 16 was comparable from week 16 through end of study [adalimumab RP/adalimumab RP 72.2% (57/79) vs. adalimumab RP/ABP 501 72.7% (56/77)]. To determine the true effect of transition from adalimumab RP to ABP 501, the rate of ADA development was assessed in subjects who were binding ADA negative through week 16. In this subset, the incidence of binding ADA was similar between the transition group [28.6% (8/28)] and those who remained on adalimumab RP [35.5% (11/31)]. None of these subjects that tested ADA negative through week 16 developed neutralizing antibodies after transition through week 52.

Conclusion: Transition from adalimumab RP to ABP 501 was not associated with higher immunogenicity.

Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

P0993 TIME COURSE OF THE INCIDENCE AND MAGNITUDE OF ANTI-DRUG ANTIBODIES TO ABP 501 AND ADALIMUMAB IN PSORIASIS PATIENTS TREATED FOR 16 WEEKS

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Introduction: Adalimumab therapy is associated with appearance of anti-drug antibodies (ADAs). ABP 501 (AMGEVITA®; adalimumab) is an approved biosimilar to adalimumab (HUMIRA®). The goal of the present analysis was to compare the time course of incidence and magnitude of ADAs among patients who are not on immunomodulatory medication.

Aims and Methods: We analysed data from a Phase 3 randomized double blind study by comparing the incidence of ADAs and relative magnitude of the ADA response between ABP 501 and adalimumab reference product (RP) in patients with moderate-to-severe plaque psoriasis. Patients were randomised (1:1) to receive ABP 501 or adalimumab every 2 weeks for 16 weeks. ABP 501 and adalimumab RP were administered at an initial loading dose of 80 mg subcutaneous on Week 1/Day 1, followed by 40 mg subcutaneous every other week (starting at Week 2) for 16 weeks.

ADAs were assessed at baseline, week 4 and week 16. A validated electrochemiluminescent assay was used to detect binding ADAs. Assays were developed for both ABP 501 and adalimumab RP, and each serum sample was tested using both assays irrespective of treatment group. Binding ADA magnitude was expressed as signal-to-noise (S/N), defined as the mean signal of the study sample divided by the mean signal of the negative control analysed on the same plate. Samples positive for binding ADAs were then tested in a TNFα-target binding assay for neutralizing activity. Neutralizing antibody titre was reported as the highest dilution that tested positive in the assay.

Results: For the ABP 501 and adalimumab RP groups, 1/171 (0.6%) and 2/168 (1.2%) patients tested positive for pre-existing binding antibodies and no patients tested positive for pre-existing neutralizing antibodies. Overall, 206 of 347 (59.4%) patients developed positive binding antibodies through week 16 post-baseline, which was similar to the percentages in each treatment group (ABP 501, 55.2% (96/174); adalimumab RP, 63.6% (110/173)). A total of 41/347 (11.8%) of all randomized patients developed positive neutralizing antibodies through week 16 post-baseline, which was also similar to the percentages in each treatment group (ABP 501, 9.8% (17/174); adalimumab RP, 13.9% (24/173)). The rate of seroconversion over time for both treatment groups was similar with exposure. For subjects testing ADA positive, the magnitude of both the binding and neutralizing ADAs across the treatment groups are reported as median S/N or titre values between groups per time point.

Conclusion: No clinically meaningful differences were observed in the incidence and magnitude of binding and neutralizing ADAs between ABP 501 and adalimumab RP-treated patients with plaque psoriasis.

Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

P0994 GUT COLONIZATION WITH EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING ENTEROBACTERIA MIGHT BE ASSOCIATED WITH CIPROFLOXACIN RESISTANCE IN INFLAMMATORY BOWEL DISEASE PATIENTS: PRELIMINARY STUDY RESULTS

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Introduction: Inflammatory bowel disease (IBD) patients are a risk group for antibiotic resistance because of the frequent hospitalizations, immunosuppressive therapy and treatment with antibiotics [1]. Extended spectrum beta-lactamase producing Enterobacteria (ESBL-E) are the most frequently found multidrug resistant microorganisms colonizing the gut of IBD patients. Also previous studies have shown that Ciprofloxacin use in IBD patients is higher comparing to non-IBD patients (27% vs 1%) [2]. There might be a link between these findings.

Aims and Methods: The aim of the study was to determine if there is an association between gut colonization with ESBL-E and Ciprofloxacin resistance in IBD out-patients. A cross-sectional study was conducted analysing all patients with confirmed ulcerative colitis (UC) or Crohn's disease (CD) diagnosis previously hospitalized in two largest tertiary medical care centres in Riga, Latvia during a 5-year period (2013–2017). Patients participated in out-patient interviews, faecal biomaterial was obtained, Enterobacteria were cultured and analyzed for ESBL presence and Ciprofloxacin resistance according to EUCAST guidelines.

Results: A total of 54 patients with confirmed IBD diagnosis – 83.3% (n = 45) UC patients and 16.7% (N = 9) CD patients were enrolled in the study. Patients included 55.6% (n = 30) male and 44.4% (n = 24) female patients with the mean age of 44.74 (SD = 15.82) years. ESBL-E was found in 7.4% (n = 4) of the IBD cases. Ciprofloxacin resistance was found in 14.3% (n = 8) of the IBD cases. More patients with Ciprofloxacin resistance had also gut colonization with ESBL-E (75%; n = 3), whereas most patients without Ciprofloxacin resistance did not have gut colonization with ESBL-E (90%; n = 45) (p = 0.008). ESBL-E strains colonizing the gut included *E. coli* (n = 2), *E. faecium* (n = 1) and *Kl. pneumonia*e (n = 1). Enterobacteria strains resistant to Ciprofloxacin included *E. coli* (n = 6), *E. coli* in combination with *Kl. pneumoniae* (n = 1) and *Vancomycin-resistant enterococcus* (n = 1). The severity of the Ciprofloxacin resistance in 2 cases showed high resistance (MIC > 32) and was found in *E. coli*.

Conclusion: Gut colonization with ESBL-E might be associated with Ciprofloxacin resistance in IBD out-patients, E. coli being the most commonly found and the most resistant strain linking the cases. Ciprofloxacin use should be avoided in IBD patients colonized with ESBL-E, especially ESBL producing E. coli.

Disclosure: Nothing to disclose

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P0995 PREDICTIVE ROLE OF ANTI-TNF TROUGH LEVELS IN THE OUTCOME OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN REMISSION

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Introduction: It has been suggested that the knowledge of serum concentration of the anti-TNF drug could be relevant in the management of inflammatory bowel disease (IBD) patients. However, a consistent clinical benefit of the adjustment of treatment based on drug levels in patients at remission has not been established.

Aims and Methods: The aim was to evaluate whether anti-TNF drug levels in IBD patients in clinical remission may predict their outcome (that is, the risk of disease relapse during the following months).

Unicentre, observational, prospective study. All consecutive Crohn's disease (CD) and ulcerative colitis patients on maintenance therapy with infliximab (IFX) or adalimumab (ADA) and being in clinical remission, were included. At inclusion, anti-TNF drug trough level was measured and, during a 6 months follow-up period from this measurement, the clinical outcome of the patients was evaluated. During the follow-up period, all therapeutic decisions (treatment withdrawal, anti-TNF dose escalation, switch to another anti-TNF or to another biologic,), were based exclusively on standard clinical, analytical and endoscopic parameters. The cut-off to consider therapeutic anti-TNF trough levels, based on our previous study[1], was above 3.4 for IFX and 7.2 μg/mL for ADA.

Results: 102 patients in remission while receiving anti-TNF therapy were included (54% men, mean age at diagnosis 33 years, 80% CD, 65% were on ADA and 34% were on IFX). 45% received concomitant immunosuppressive therapy. 33% were exposed to a previous anti-TNF drug. Sub-therapeutic anti-TNF trough levels were found in 53% of the patients in clinical remission at the inclusion. During the 6 months follow-up period, 11% of the patients relapsed. From the patients with therapeutic drug levels, 6% relapsed, whereas 14% of the patients with sub-therapeutic anti-TNF levels relapsed at the end of follow-up ($P > 0.2$). Also, there were not differences between CD or UC patients, and between patients who received ADA or IFX. Anti-TNF dose was escalated empirically in 13 patients with loss or response, and 8 (61%) of them regain remission: 5/10 patients with sub-therapeutic anti-TNF trough levels (measured just previously to dose escalation) but also 3/3 with therapeutic levels before intensification.

Conclusion: Anti-TNF drug levels in IBD patients in clinical remission do not predict the risk of relapse during the following months. The majority of patients with sub-therapeutic anti-TNF levels remain in remission during follow-up. Therefore, therapeutic strategies based on anti-TNF trough levels in IBD patients in remission need further research.

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P0996 CIPROFLOXACIN RESISTANCE IS HIGHER IN ULCERATIVE COLITIS PATIENTS WITH MORE SEVERE DISEASE ACTIVITY AND MORE EXACERBATIONS: PRELIMINARY STUDY RESULTS

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Introduction: Ulcerative colitis (UC) patients are a risk group for antibiotic resistance because of the frequent hospitalizations, immunosuppressive therapy and treatment with antibiotics [1]. Previous studies have shown that Ciprofloxacin use in UC patients is higher comparing to non-UC patients (27% vs 1%) [2]. In many cases Ciprofloxacin is given as empiric treatment by non-gastroenterologists to UC patients with exacerbations and higher disease activity. This could lead to higher antibiotic resistance and worse outcome in this particular UC phenotype.

Aims and Methods: The aim of the study was to determine if there is an association between Ciprofloxacin resistance and UC disease activity and what are the risk factors attributing to that. A cross-sectional study was conducted analysing all patients with clinically, endoscopically and histologically confirmed UC diagnosis previously hospitalized in two largest tertiary medical care centres in Riga, Latvia during a 5-year period (2013–2017). Patients participated in out-patient interviews regarding their risk factors for Ciprofloxacin resistance, faecal biomaterial was obtained and analysed for Ciprofloxacin resistance according to EUCAST guidelines Version 7.1 and UC disease activity was evaluated according to the full Mayo score (FMS).

Results: A total of 45 patients with confirmed UC diagnosis, 55.6% (n = 25) male and 44,4% (n = 20) female patients with the mean age of 44.74 (SD = 15.82) years, were enrolled in the study. Ciprofloxacin resistance in faecal biomaterial was found in 17,8% (N = 8) of the cases. *E. coli* was the most frequently found bacterial strain resistant to Ciprofloxacin, found in 6 cases alone and in 1 case in combination with *Kl. pneumonia*. In 1 case *Vancomycin-resistant enterococcus* resistant to Ciprofloxacin was found. The severity of the Ciprofloxacin resistance for *E. coli* in 2 cases showed high resistance (MIC > 32). Patients with Ciprofloxacin resistance had more severe disease – moderate or severe disease activity (FMS 6–12) compared to patients without Ciprofloxacin resistance – remission or mild disease activity (FMS 0–5) ($p < 0.001$). Also, the mean FMS was higher in patients with Ciprofloxacin resistance found in their faecal biomaterial – 2 (SD = 1.07), comparing to patients without Ciprofloxacin resistance – 1.1 (SD = 0.52) ($p = 0.001$). Differences in various factors that could attribute to Ciprofloxacin resistance were analysed in these UC patients and revealed no statistically significant differences between UC patients with and without Ciprofloxacin resistance regarding socio-demographic factors like age, gender and international travels; IBD-related factors like UC complications and treatment modalities; and risk factors for Ciprofloxacin resistance like previous hospitalizations, residence in a nursing home, antibiotic treatment, urinary tract infections and invasive manipulations in the past 12 months. The only factor that was different in UC patients with and without Ciprofloxacin resistance was the number of UC exacerbations in the past 12 months. UC patients with Ciprofloxacin resistance had higher number of exacerbations 4,25 (SD = 4.92) comparing to UC patients without Ciprofloxacin resistance 1.23 (SD = 2.46) ($p = 0.011$).

Conclusion: There is a high resistance to Ciprofloxacin in UC patients. More severe disease and more exacerbation in the past 12 months increase the resistance to Ciprofloxacin. Ciprofloxacin use should be avoided in these UC patients., because this may lead to a higher antibiotic resistance and worse outcome in these patients.

Disclosure: Nothing to disclose

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2. Leung, W., et al., Prevalence and predictors of MRSA, ESBL, and VRE colonization in the ambulatory IBD population. *Journal of Crohn's and Colitis*, 2012. 6(7): 743–749.

P0997 TREATMENT PERSISTENCE WITH IMMUNOSUPPRESANT, ANTI-TUMOR NECROSIS FACTOR, AND ANTI-INTEGRIN AGENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE COHORT ANALYSIS IN GERMANY

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Introduction: Real-world treatment of inflammatory bowel disease (IBD) remains challenging. High adverse event (AE) rates and limited effectiveness of treatments in some patients may lead to early therapy discontinuation. The aim of this study was to assess treatment persistence with immunosuppressant (IS), anti-tumor necrosis factor (aTNF) and anti-integrin (aI) agents in patients with IBD.

Aims and Methods: We conducted a retrospective cohort analysis of patients diagnosed with ulcerative colitis (UC) or Crohn's disease (CD) who were newly initiating treatment with IS, aTNF or aI from 01/01/2013-31/12/2015. Patients were identified from a German sickness fund (AOK PLUS), had continuous insurance coverage, and had no evidence of IS, aTNF or aI use for 12 months before the index date (date of newly initiating selected therapy during the study period). Treatment persistence was defined as percentage of patients still on index therapy after 12, 24 and 36 months, censoring for death and end of follow-up period. Patients were considered to have discontinued therapy if there was a drug coverage gap > 60 days. Cox regression analysis was used to identify differences in mean persistence between the 3 treatment groups, adjusting for baseline characteristics.

Results: A total of 1,126 (UC: 450; CD: 676) met the inclusion criteria and constituted the treatment-naïve IBD cohort used for the analysis. Mean age of UC and CD patients was 42.5 and 36.5 years; 47.6% and 60.5% were female. Among UC patients, IS was the most common (85.8%) index therapy, followed by aTNF (13.6%) and aI (0.7%). Among CD patients, IS was the most common (77.7%) index therapy, followed by aTNF (21.2%) and aI (1.2%).

By 12 months, 55.7% of UC and 57.7% of CD patients discontinued their index therapy. Of the 990 patients followed for 24 months (UC: 395; CD: 595), 66.2% of UC and 67.8% of CD discontinued their index therapy. Of the 802 patients followed for 36 months (UC: 325; CD: 477), 73.1% of UC and 74.4% of CD discontinued their index therapy.

Adjusting for baseline characteristics, aTNF was associated with later treatment discontinuation compared with IS (hazard ratio [HR]: 0.364, $p < 0.001$) in UC patients. In CD patients, both aTNF and aI were associated with later treatment discontinuation compared with IS (aTNF HR: 0.562, $p < 0.001$; aI HR: 0.187, $p = 0.018$).

Conclusion: Although some patients performed better than others, persistence with IBD treatment is far from ideal, with more than 50% of patients discontinuing their index therapy by 12 months in this dataset. It also needs to be noted that because of the requirement for 60 days' continuous therapy with the index agent, we could not report the rate of discontinuations occurring early in therapy. As demonstrated in previous studies, IBD treatment discontinuation mainly results from poor effectiveness and/or safety concerns. There is an urgent need for development of more effective and/or safe IBD therapies which should lead to better real-world treatment persistence.
Disclosure: This study was financially suported by Genentech Inc.. Thomas Wilke has received honoraria from several pharmaceutical/consultancy companies e.g. Novo Nordisk, Abbvie; Merck; GSK, BMS, LEO Pharma, Astra Zeneca, Bayer, Boehringer Ingelheim, Pharmerit. Study number: MA39587

P0998 ORALLY-ADMINISTERED EMU OIL ATTENUATES CLINICAL INDICATORS OF DISEASE IN A MOUSE MODEL OF ACUTE CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is a chronic relapsing inflammatory bowel disease, characterised by severe transmural inflammation of the gastrointestinal tract. The aetiology of CD remains unclear and there is no known cure. Emu Oil (EO) is extracted from adipose tissue of the emu; a large flightless bird native to Australia. Previously, we demonstrated that orally-administered EO reduced inflammation and protected the intestine against experimentally-induced ulcerative colitis, colitis-associated colorectal cancer, NSAID-enteropathy and chemotherapy-induced mucositis.
Aims and Methods: To investigate whether orally-administered EO could attenuate disease severity in a trinitrobenzene sulfonic acid (TNBS) mouse model of CD. Female ARC(s) mice ($n = 10$/group) were intra-rectally administered 120µl water or TNBS (3mg). Mice were orally-administered water or EO (80µl or 160µl) daily for five days and were culled on day six. Bodyweight and disease activity index (DAI; four parameters including bodyweight loss, general condition, rectal bleeding and stool consistency) were recorded daily. Burrowing activity and facial grimace parameters were assessed as behavioural measures of disease progression. Colonoscopy was performed to assess disease severity based upon thickening of the colon, changes to vasculature pattern, presence of fibrin, granularity of mucosal surface and stool consistency. Additionally, proximal and distal colonic crypt depth, myeloperoxidase activity (indicative of acute inflammation) and fluorescein isothiocyanate dextran (indicative of intestinal permeability) uptake were quantified. $p < 0.05$ was considered statistically significant.
Results: Compared to normal controls, TNBS decreased bodyweight (days 1, 2 and 4; maximum 4.5% bodyweight reduction; $p < 0.05$) and increased DAI (days 1–6; maximum 11-fold increase; $p < 0.01$). In TNBS-treated mice, 80µl EO significantly reduced DAI scores on days 5 and 6 (maximum 55% reduction) compared to controls ($p < 0.05$), though bodyweight loss remained unchanged. TNBS administration increased mouse grimace scores (11.5-fold; indicative of pain and distress), compared to normal controls; an effect significantly attenuated by both 80µl (11.5-fold decrease) and 160µl (5.4-fold decrease) EO treatment ($p < 0.001$). Colonoscopically-assessed disease severity score was greater in TNBS controls (2.9 ± 0.3; [mean ± SEM]), compared to normal controls (0.1 ± 0.1; $p < 0.001$). Importantly, in TNBS-treated animals, both 80µl and 160µl volumes of EO significantly reduced colonoscopically-assessed disease severity (80µl: 1.7 ± 0.3; 160µl: 2.1 ± 0.3), compared to TNBS controls ($p < 0.01$). TNBS induced compensatory distal colonic crypt lengthening (190.9 ± 8.6) compared to normal controls (161.1 ± 3.9; $p < 0.05$), which remained unaffected following EO administration (80µl: 206.6 ± 10.7; 160µl: 202.4 ± 4.9), compared to TNBS controls ($p > 0.05$). Burrowing activity, proximal colonic crypt depth, myeloperoxidase activity and intestinal permeability remained unchanged across all treatment groups ($p > 0.05$). Moreover, in normal animals, EO treatment did not significantly impact any parameter compared to water-treated controls.
Conclusion: Emu Oil reduced clinical indicators of disease severity, including daily disease activity index, grimace pain scores and colonoscopically-assessed disease parameters in TNBS-treated mice. These findings suggest therapeutic efficacy for Emu Oil as an adjunct to conventional treatment approaches for Crohn's disease.
Disclosure: Nothing to disclose

P0999 LOW GOLIMUMAB TROUGH LEVELS AT WEEK 6 ARE ASSOCIATED WITH POOR CLINICAL, ENDOSCOPIC AND HISTOLOGICAL OUTCOMES IN ULCERATIVE COLITIS PATIENTS: PHARMACOKINETIC RESULTS OF THE EVOLUTION STUDY

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Introduction: Golimumab (GLM) is a fully human anti-TNF effective for induction and maintenance of response and remission in moderate to severe ulcerative colitis (UC) patients[1]. Measurement of anti-TNF serum trough levels (TL) is increasingly used to assist in physician decisions on dose (de) escalation or discontinuation to achieve the treatment target in IBD.
Aims and Methods: This study evaluated the association of GLM TL with clinical, endoscopic and histological disease activity measures and with fecal calprotectin (FC) levels in a multicenter, open label, nonrandomized, prospective study of Portuguese patients with moderate to severe active UC treated with GLM. Subjects were followed for a period of 16 weeks with clinical assessments and data collection at screening, week 6 (W6) and week 16 (W16). GLM TLs and FC were measured at both W6 and W16. GLM TLs were assayed with an ELISA kit[2]. All study data were summarized using descriptive statistics. Statistical tests were two-tailed and considering a significance level of 0.05.
Results: A total of 38 patients were treated, 34 (89.5%) completed through W6 (full analysis set, FAS) and 29 (76.3%) completed through W16. Nine patients (23.7%) discontinued the study. Mean (range) age was 34.6 years (19–65 years); 15 (44.1%) were male. At baseline, 94.1% had moderately active disease (Mayo score 6–10) and 5.9% ($N = 2$) had severe disease; 27 (79.4%) were treated with immunosuppressants and 16 (47.1%) were taking glucocorticoids. At W6, 16/34 (47.1%) patients were in clinical response and 5/34 (14.7%) in clinical remission; 18/29 (62.1%) and 11/29 (37.9%) at W16, respectively. At W6, GLM TL quartile values were significantly correlated with clinical response ($p = 0.0035$), with 1/8 (12%) and 9/11 (82%) responders in the lowest (<1.0 ug/mL) and highest GLM TL quartile (≥3.2 ug/mL), respectively. Median W6 GLM TL in clinical responders ($n = 16$) *vs.* nonresponders ($n = 18$) was 3.7 *vs.* 1.3 ug/mL ($p = 0.0013$); and 3.1 *vs.* 1.7 ug/mL in endoscopically inactive disease ($n = 14$) *vs.* active disease ($n = 20$) ($p = 0.021$). W6 GLM TL was negatively correlated with the total Mayo score ($p = 0.0008$); the endoscopic Mayo score ($p = 0.0262$), the histological activity score ($p = 0.0057$), and FC level ($p = 0.0044$).
Conclusion: Low GLM TLs are associated with poor clinical, endoscopic, histological, and fecal calprotectin outcomes at W6 in UC patients treated with GLM. Our data add further evidence for an early exposure-response relationship in UC patients treated with golimumab.
Disclosure: Patrícia Machado is an employee of MSD Portugal. Freddy Cornillie is an employee of Merck Sharp and Dohme, Kriens, Switzerland. Isabel Redondo was an employee of MSD Portugal at the time the study was conducted.

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P1000 RATE OF ADVERSE EVENTS ASSOCIATED WITH THE TREATMENT OF INFLAMMATORY BOWEL DISEASE IN GERMANY

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Introduction: Treating patients with inflammatory bowel disease (IBD) is challenging, as available therapies might be associated with substantial rates of adverse events (AEs). Our aim was to evaluate the rate of drug-related severe AEs and the associated health care costs among patients with IBD, who are receiving aminosalicylate (ASA), oral corticosteroid (OCS), immunosuppressant (IS), anti-tumor necrosis factor (aTNF) or anti-integrin (aI) agents in Germany.

Aims and Methods: We conducted a retrospective cohort study of patients diagnosed with ulcerative colitis (UC) or Crohn's disease (CD) who were newly initiating treatment with IS, aTNF or aI from 01/01/2013-31/12/2015; chronic ASA and OCS use was also observed. Patients were identified from a German sickness fund (AOK PLUS), had continuous insurance coverage, and had no evidence of IS, aTNF or aI use for 12 months before the index date (date of newly initiating therapy during the study period). The period after the index date was defined as follow-up. Rate of AEs, based on 28 different codes associated with inpatient encounters, and direct health care cost were reported separately for patients who experienced/did not experience AEs. Only treatment periods lasting ≥60 days were considered; patients could be assigned to >1 treatment during follow-up.

Results: A total of 1,126 (UC: 450; CD: 676) met the inclusion criteria. Mean age of UC and CD patients was 42.5 and 36.5 years; 47.6% and 60.5% were female. Among UC patients, 51.2% of observed follow-up time was covered by IS monotherapy index treatment, followed by aTNF mono (17.7%), ASA mono (15.0%), and OCS + IS (5.2%). Among CD patients, IS mono was the most common (45.3%) index treatment, followed by aTNF mono (27.3%), OCS + IS (9.0%), and OCS mono (5.3%).

A total of 157 patients (UC: 74; CD: 83) had at least 1 coded AE during follow-up, overall AE rate was 1,546 events per 10,000 patient years (TTPY). Most common AEs among patients with UC or CD were (rates per TTPY) severe infection (UC: 320; CD: 90), diabetes mellitus (UC: 460; CD: 73), perianal disease (UC: 153; CD: 169) and bone-related conditions (UC: 292; CD: 51). Among the 157 patients, 126 patients (80.3%) experienced at least 1 switch from 1 treatment to another during the whole follow-up period, respective number in the whole sample was 66.5%.

In a multivariate analysis adjusting for key confounders available in the database, a higher comorbidity was associated with a higher AE rate in UC patients. In CD patients, presence of a previous extraintestinal manifestation was associated with a higher AE rate. However, none of the treatments were significantly associated with a higher AE rate. Cost for patients with an AE were generally higher than for those without an AE (UC: 11,279 € vs 7,965 €; CD: 20,723 € vs 8,538 €).

Conclusion: Burden of severe AEs is substantial in IBD patients, with an event rate of 1,546/TTPY in this dataset. AE rates did not differ between IBD treatments in our study, which may also be due to low sample size. We observed that AEs are associated with higher health care cost. Our results show that there is urgent need for development of IBD treatments that are associated with lower rates of severe AEs.

Disclosure: This study was financially suported by Genentech Inc.. Thomas Wilke has received honoraria from several pharmaceutical/consultancy companies e.g. Novo Nordisk, Abbvie; Merck; GSK, BMS, LEO Pharma, Astra Zeneca, Bayer, Boehringer Ingelheim, Pharmerit. Study number: MA39587

P1001 ANTI-TNF USE IS ASSOCIATED WITH WORK PRODUCTIVITY LOSS IN IBD PATIENTS

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Introduction: Inflammatory bowel disease (IBD) has a negative impact on work productivity, which is associated with indirect health care costs and lower quality of life.

Aims and Methods: The aim of this ongoing study is to determine treatment-related risk factors for IBD-related work productivity loss in a Dutch IBD cohort. A web-based follow-up study was initiated in two tertiary and two secondary referral hospitals in the Amsterdam region. IBD patients between 16 and 63 years old were invited to participate if they were (self-) employed. Patients received a baseline questionnaire, which included sociodemographic, work-related and disease-related questions. Patient-reported simple clinical colitis activity index (p-SCCAI) for ulcerative colitis (UC) and patient-reported Harvey Bradshaw Index (p-HBI) for Crohn's disease (CD) were used to determine clinical disease activity. IBD-related work productivity loss was measured using the WPAI questionnaire. Moderate to severe absenteeism was defined as > 20% work time missed, presenteeism as >20% reduced productivity while working, and overall work productivity loss as >20% overall work impairment due to IBD (including absenteeism and presenteeism). Risk factors were identified using logistic regression. Factors with a p-value < 0.1 in univariate analysis were entered into multivariate analysis with stepwise selection.

Results: In total, 1590 patients were invited of which 516 (32%) responded to the invitation so far: 368 agreed to participate and 148 patients were not eligible or refused to participate. Up to now, 321 patients completed the baseline questionnaire (61% female, 65% CD and 35% UC) with a mean age of 43 ± 12 years and median disease duration of 13 [IQR 7–23] years. Immunomodulators were used in 28% of patients, 29% received anti-TNF treatment (infliximab, adalimumab or golimumab), 5% received vedolizumab, 3% received ustekinumab, 8% had an ostomy and 4% had an ileal pouch-anal anastomosis. Moderate to severe absenteeism was reported in 49 (15%) and presenteeism in 138 (43%) patients. Moderate to severe overall work productivity loss was reported in 152 (47%) patients (107 (51%) CD and 45 (41%) UC). In multivariate analysis, the risk of moderate to severe overall work productivity loss was significantly greater in patients with prior anti-TNF use (OR 2.40 [95% CI 1.34–4.29]), in patients using anti-TNF agents at the time of this study (OR 1.89 [95% CI 1.04–3.46]), and in patients with clinical disease activity (OR 7.63 [95% CI 3.84–15.14]). Neither significant associations were found between work productivity loss and type of IBD (CD versus UC), immunomodulators (i.e. azathioprine, mercaptopurine and methotrexate) or other biologics such as vedolizumab or ustekinumab, nor between patients with an ostomy or ileal pouch-anal anastomosis and work productivity loss.

Conclusion: Prior and active anti-TNF use, as well as clinical disease activity are risk factors for work productivity loss in IBD patients. Anti-TNF use may be a marker for more severe IBD, however for vedolizumab and ustekinumab an association with work productivity loss was not (yet) found. These findings will be analyzed in more detail in a prospective follow-up study using this cohort.

Disclosure: This study was financially supported by Dr. Falk Pharma Benelux B.V.

P1002 REAL-WORLD EFFECTIVENESS OF VEDOLIZUMAB AND ANTI-TUMOUR NECROSIS FACTOR-ALPHA OVER 6 MONTHS IN ULCERATIVE COLITIS PATIENTS: A GERMAN RETROSPECTIVE CHART REVIEW

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Introduction: Vedolizumab (VDZ), an $\alpha_4\beta_7$ integrin antagonist, was approved in Germany in 2014 for the treatment (Tx) of moderately to severely active ulcerative colitis (UC). This study descriptively assessed the real-world effectiveness and safety of VDZ and anti-tumour necrosis factor-alpha (anti-TNFα) after VDZ was introduced in Germany.

Aims and Methods: A retrospective chart review (15 sites) investigated patients (pts) with UC who were biologic- (bio-) Tx naïve or had received one prior anti-TNFα at initiation of index Tx with VDZ or anti-TNFα between 15 July 2014 and 20 October 2015. Time to first chart-documented clinical remission (total Mayo or partial Mayo score ≤2 and no subscore >1), rectal bleeding (RB) resolution (score of 0) and stool frequency (SF) resolution (score of 0 or 1) were assessed using time-to-event Kaplan-Meier analyses over 26 weeks.

Abstract No: P1002

Follow-up Week	Outcome	Bio-naïve: Anti-TNFα	Bio-naïve: VDZ	Prior anti-TNFα: Anti-TNFα	Prior anti-TNFα: VDZ	Total: Anti-TNFα	Total: VDZ
Week 6	**Clinical remission**	10.6 (5.8)	29.4 (11.1)	0 (0)	17.2 (6.4)	7.4 (4.1)	21.2 (5.7
Week 6	**RB resolution**	17.0 (6.9)	46.4 (12.9)	7.7 (7.4)	22.5 (7.5)	14.2 (5.4)	30.4 (6.8)
Week 6	**SF resolution**	29.2 (8.2)	33.0 (12.1)	22.6 (11.5)	30.0 (8.4)	27.2 (6.7)	30.8 (6.9)
Week 14	**Clinical remission**	22.2 (8.1)	50.1 (12.8)	9.1 (8.7)	39.9 (8.7)	18.6 (6.4)	43.3 (7.2)
Week 14	**RB resolution**	27.4 (8.3)	68.8 (12.5)	7.7 (7.4)	48.5 (9.5)	21.5 (6.4)	55.2 (7.7)
Week 14	**SF resolution**	39.3 (8.9)	68.8 (12.5)	30.4 (12.7)	41.5 (9.3)	36.8 (7.3)	50.9 (7.8)
Week 26	**Clinical remission**	31.5 (9.4)	50.1 (12.8)	30.7 (15.0)	55.5 (9.4)	31.7 (8.1)	53.7 (7.6)
Week 26	**RB resolution**	57.0 (10.1)	68.8 (12.5)	52.0 (15.0)	65.7 (9.5)	55.8 (8.4)	66.8 (7.6)
Week 26	**SF resolution**	51.0 (9.4)	68.8 (12.5)	49.2 (14.8)	54.8 (9.9)	50.7 (8.0)	59.8 (7.9)

[Kaplan-Meier Estimates of Responders Over 26 Weeks, % (standard error)]

Results: The study investigated 76 VDZ (29% bio-naïve; 47% female) and 57 anti-TNFα (12 adalimumab, 14 golimumab, 31 infliximab; 70% bio-naïve; 58% female) pts. At baseline, pts' median age was 40 years (y; VDZ) vs 34 y (anti-TNFα); median disease duration was 6 y (VDZ) vs 5 y (anti-TNFα); and 43% (VDZ) vs 47% (anti-TNFα) received a corticosteroid. The outcomes of interest were available in the medical chart for a subset of pts: total or partial Mayo in 60 VDZ (18 bio-naïve) and 47 anti-TNFα (33 bio-naïve) pts; RB in 50 VDZ (16 bio-naïve) and 44 anti-TNFα (31 bio-naïve) pts; and SF in 50 VDZ (16 bio-naïve) and 46 anti-TNFα (32 bio-naïve) pts. A higher proportion of VDZ vs anti-TNFα pts achieved each outcome by Week 6 (clinical remission [21% vs 7%], RB [30% vs 14%], and SF [31% vs 27%]), Week 14 (clinical remission [43% vs 19%], RB [55% vs 22%], and SF [51% vs 37%]), and Week 26 (clinical remission [54% vs 32%], RB [67% vs 56%], and SF [60% vs 51%]; **Table**) although differences were not significant (log-rank test: clinical remission = 0.081; RB = 0.066; SF = 0.411). These trends in VDZ vs anti-TNFα outcomes were also seen in bio-naïve (Week 26: clinical remission [50% vs 32%], RB [69% vs 57%], and SF [69% vs 51%]) and one prior anti-TNFα (Week 26: clinical remission [56% vs 31%], RB [66% vs 52%], and SF [55% vs 49%]) pts (**Table**). Independent of index Tx, more bio-naïve vs one prior anti-TNFα pts achieved clinical remission and symptom resolution at Week 6 and Week 14 (**Table**). Differences between cohorts by prior Tx history were not significant (log-rank test: clinical remission = 0.374; RB = 0.193; SF = 0.489). Adverse events occurred in 39% of VDZ vs 44% of anti-TNFα pts.

Conclusion: In this descriptive analysis of Tx outcomes in bio-naïve and one prior anti-TNFα experienced German UC pts, VDZ and anti-TNFα achieved similar clinical remission and symptom resolution, assessed at Weeks 6, 14, and 26. Bio-naïve pts were consistently more likely to have responded than pts who had received one prior anti-TNFα. These data suggest VDZ is an effective biologic Tx option in UC for both bio-naïve pts and pts who have received a prior anti-TNFα.

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TUESDAY, OCTOBER 23, 2018 09:00–17:00

Paediatric: Lower GI – Hall X1

P1003 THE RELATIONSHIP BETWEEN INTESTINAL DYSBIOSIS AND INFLAMMATORY BOWEL DISEASE IN CHILDREN

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Introduction: Small intestinal bacterial overgrowth (SIBO) is characterized by an abnormal bacterial proliferation in the small bowel. Crohn's disease (CD) and ulcerative colitis (UC) share many common features with SIBO-diarrhea, bloating, weight loss, abdominal pain. SIBO has not been studied in children with inflammatory bowel disease (IBD).

Aims and Methods: The aim of this study was to assess the prevalence of SIBO among children with IBD and the relationship between SIBO and disease phenotype, localization and activity. Methods: 43 children with IBD (29 CD and 14 UC) and 40 healthy controls were enrolled. 23 patients had active disease, whereas in 20 subjects the disease was in remission. SIBO was assessed using glucose hydrogen breath test (GHBT). Concentration of hydrogen was measured by LactoFAN analyser.

Results: 15 children with IBD (12 CD, 3 UC; 34.8%) and two control subjects (5%) were positive for GHBT. SIBO prevalence was significantly higher in IBD children as compared to controls ($p < 0.001$). The occurrence of SIBO in CD (41.3%) was higher compared to UC group (21.4%) ($p < 0.05$). Dysbiosis had a higher frequency among children with active disease (52.1%) compared to those in remission (15%) ($p < 0.05$). There was no correlation of SIBO with the Pediatric Crohn's Disease Activity Index in CD group. SIBO was significantly more frequent in CD children with stricturing pattern and ileum involvement.

Conclusion: SIBO is a frequent but underestimated condition in IBD, that might mimic acute flares. Stricturing phenotype in CD and active disease were associated with dysbiosis. SIBO diagnostic work-up followed by directed treatment is recommended in IBD children who present stricturing disease, especially in those with concurrent intestinal inflammation.

Disclosure: Nothing to disclose

P1004 REMISSION INDUCTION IN CORTICOSTEROID NAïVE CHILDREN AND ADOLESCENTS WITH ULCERATIVE COLITIS BY ADSORPTIVE LEUCOCYTAPHERESIS AFTER FAILURE OF FIRST-LINE MEDICATIONS

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Introduction: During active ulcerative colitis (UC), myeloid lineage leucocytes are elevated with activation behaviour including the CD14+CD16+ monocytes, which are a major source of inflammatory cytokines including tumour necrosis factor-α (*J Immunol* 2002; 168: 3536–42). Therefore, selective depletion of elevated/activated myeloid leucocytes is expected to induce remission, or enhance drug efficacy.

Aims and Methods: We were interested to see if selective depletion of myeloid leucocytes by adsorptive granulocyte/monocyte apheresis (GMA) with an Adacolumn induces remission in children and adolescents who had active disease despite receiving first-line medications. In clinical practice setting, 31 consecutive patients with active UC, age 11–19 years, bodyweight 33–55.5kg were given mesalazine (n = 24) or sulphasalazine (n = 7) as the first-line medication. Twenty patients relapsed while receiving first-line medication or did not respond and received GMA, at 2 sessions in the first week, then weekly, up to 11 sessions. Patients who achieved ≥5 decrease in the clinical activity index (CAI) continued with GMA, while non-responders received GMA plus a low-dose prednisolone (0.5–1.0mg/kg). At entry and week 12, patients were clinically and endoscopically evaluated with each patient serving as her or his own control.

Results: Eleven patients achieved stable remission with the salicylates and did not receive GMA. Six patients did not respond well to the first 5 GMA sessions and received prednisolone together with GMA, 12 patients achieved stable remission with GMA and 2 withdrew to receive high dose prednisolone. Prednisolone was tapered to 0mg within 3 months in those who received to induce remission. Therefore, at week 12, all 31 patients were in remission.

Conclusion: GMA in young corticosteroid naïve patients with active UC refractory to the first-line salicylates induced remission and mucosal healing, while in non-responders to GMA monotherapy, addition of a low dose prednisolone enhanced the efficacy of GMA and tapering of the prednisolone dose was not associated with relapse. Additionally, GMA has a good safety profile, which is a very favourable feature in growing patients.

Disclosure: Nothing to disclose

P1005 FAECAL CALPROTECTIN IN HEALTHY CHILDREN (0 TO 18 YEARS OLD) AND THE INFLUENCE OF AGE, GENDER AND ANTHROPOMETRY

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Introduction: Previous studies report that faecal calprotectin (FC) can be altered by factors like weight, Body Mass Index (BMI) and age (see references 1–9), but many of them have methodologic limitations.

Aims and Methods: Our primary aims were to (i) establish normal levels of FC in healthy children living in a Spanish urban environment; and (ii) analyse correlation of FC with age, gender and anthropometry.

A multicentre, cross-sectional and observational study from January 2015 to December 2016 enrolled healthy donors under 18 who attended the participating primary health centers for routine pediatric controls. The exclusion criteria were: (i) immunodeficiency; (ii) autoimmune disease; (iii) gastrointestinal disease; (iv) intake of drugs; (v) gastrointestinal symptoms; or (vi) any positive finding in the associated microbiological study. We determined the FC levels (Quantum Blue® test), and perfomed stool cultures, parasites, rotavirus and adenovirus detection. The statistical analysis (SPSS® software) considered a P value < 0.05 statistically significant.

Results: We included 395 subjects from 3 days to 16.9 years old (mean 4.2 years, standard deviation (SD) 4.7 years); 51.6% boys and 48.4% girls. Table 1 displays the results. FC values showed a non-normal distribution using the Kolmogorov-Smirnov test. The correlation between age (days) and FC (μg/g) was analyzed via Spearman correlation coefficient, with a bilateral significance of 0.00.

Weight was recorded in 389 subjects, mean 17.9 Kg (95% CI 16.4–19.6), and median 11.8 Kg (range 2.2–73 Kg). Height was measured in 383 children, mean 94.2 cm (95% CI 90.4–98 cm), and median 85.0 cm (range 46–185 cm). Using these data, we calculated the BMI of 382 subjects, mean 16.4 Kg/m2 (IC 95% of 16.1 a 16.6), and median 11.3 Kg/m2 (range 10.2- 25.4 Kg/m2).

Boys had a FC mean of 196.8 μg/g, and median 86.0 μg/g. Girls had a FC mean of 186.0 μg/g, and median 71.0 μg/g. The Mann-Whitney U test showed no significant differences ($p > 0.05$).

The association of weight, height (both absolute values and SD) and BMI with FC was analysed via Spearman, with a bilateral significance of 0.00 ($p < 0.05$), suggesting a negative correlation. However, no correlation of weight SD and BMI SD with FC was found (Spearman correlation coefficient $p > 0.05$).

Conclusion: FC values in healthy children were higher than those considered as pathological in adults. A negative correlation with age was observed, with no correlation with gender. Our results suggest that weight and BMI do not influence FC values, since the negative correlations of their absolute values and FC

were not confirmed when analysing their SDs. This may reflect the role of age as a confounding factor. We found a negative correlation between height (both absolute values and SD) and FC, that had not been previously described. Based on this, it seems necessary to reconsider the levels of FC deemed pathological in pediatric patients by age group and further investigate the role of anthropometric data.

Age group	No. of Subjects	Mean FC (μg/g)	10 th (μg/g)	50 thP (μg/g) (median)	90thP (μg/g)
<1 month	43	344.3	156	303	620
1–6 months	64	424	76	325.5	993
6–12 months	46	167.7	30	63	488
12–24 months	42	217.7	30	97	533
2–4 years	45	116.1	30	71	271
4–8 years	64	89.1	30	46	163
8–12 years	46	85.4	30	34.5	143
12–18 years	45	45.2	30	30	75
Total (0- 18 years)	395	191.6	30	77	508.4

[Table 1: FC levels in each age group. 10thP: 10th percentile. 50thP: 50th percentile. 90thP: 90th percentile.]

Disclosure: Nothing to disclose

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P1006 OUTCOME OF INFLAMMATORY BOWEL DISEASE IN CHILDREN WITH PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Inflammatory bowel disease (IBD) seems to have a unique phenotype in patients with primary sclerosing cholangitis (PSC). However, in children with PSC there are few data on the clinical course of IBD [1,2].

Aims and Methods: The aim of this retrospective case-control population-based study was to investigate the outcome of IBD in a cohort of subjects with a paediatric-onset of IBD-PSC and in a matched group of patients with IBD only. Twenty-seven IBD-PSC cases diagnosed with a paediatric-onset of disease (male 18, mean age at IBD diagnosis 13 years, range: 6–18 years and mean age at PSC diagnosis: 14 years, range: 5–18) were identified. Diagnosis of IBD-PSC was done between 1993–2011. For each case three IBD controls matched for age and year of diagnosis were selected from IBD Register at Helsinki University Hospital (HUH). However, three of the controls developed PSC during the follow-up and were excluded. Thus, overall 78 IBD-controls were included (males 50; age at IBD diagnosis 12 years, range: 4–18). All data regarding patients' baseline characteristics and intestinal/liver diseases were collected at diagnosis and at the end of follow-up (median follow-up 13 years, range: 4–26). Mean age in IBD-PSC group was 26 years (range: 14–39) and in IBD control group 25 years (range 15–41) at the end of follow-up. Data are presented as number with percentage when categorical and as mean/median and range when continuous. Differences were tested by using Fisher's Exact Test for categorical variables and Mann-Whitney Test for continuous variable. The study was approved by the Ethics Committee of HUH (number 64/13/03/03/2012).

Results: At diagnosis, 20 IBD-PSC children (74%) had pure PSC and 7 (26%) PSC-AIH-overlap syndrome. Of these, 22/27 (82%), 3/27 (11%) and 2/27 (7%) had ulcerative colitis (UC), unclassified colitis (IBDU) and Crohn's disease (CD), respectively. Correspondingly, in the IBD-control group 32/78 (41%), 6/78 (8%) and 40/78 (51%) had UC, IBDU and CD, respectively. The difference in IBD subtype between IBD-PSC cases and IBD-controls was not statistically significant ($p = 0.2$).

At diagnosis no difference in disease extent/localisation and severity between IBD-PSC cases and IBD-controls was found. Colitis was histologically detected in 22/27% (81%) of IBD-PSC patients and in 67/78 (86%) of IBD-controls ($p =$ not significant). At last follow-up, IBD-PSC cases tended to be more frequently in remission (40% vs 21% of IBD-controls, $p =$ not significant) and they showed less active colitis (37% vs 63% of IBD-controls, $p = 0.002$). IBD-controls had used more frequently TNF-alfa-inhibitors (49% vs 7% of IBD-PSC cases, $p = 0.0001$). The number and type of surgery was similar between IBD-PSC cases and IBD-controls, but patients with IBD-PSC turned out to need more often proctocolectomy, with J-pouch (26% vs 18% of IBD-cases, $p =$ not significant). However, they tended to have less pouchitis (57% vs 86% of IBD-controls, $p =$ not significant). Low-grade dysplasia was detected in the colon in 1 IBD-PSC patient (age 24 years, 10 years from IBD diagnosis) and colon cancer in 1 IBD control (age 31, 17 years from IBD diagnosis). All patients in both group were alive at the end of follow-up.

Conclusion: The course of paediatric onset IBD in patients with IBD-PSC seems to be more benign than in those with pure IBD, in line with reports in adult population. Colon dysplasia/cancer may though occur in both.

Disclosure: Nothing to disclose

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P1007 PLANNED TRANSITION OF ADOLESCENT INFLAMMATORY BOWEL DISEASE PATIENTS FROM PEDIATRIC TO ADULT CARE RESULTS IN HIGHER REMISSION RATES

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Introduction: As a result of increasing incidence of pediatric-onset inflammatory bowel disease (IBD) growing number of adolescents need handover to adult care. Whereas transfer is essentially only an event, transition is a well-planned, coordinated process. Recent data support that structured transition programs in IBD may improve patient compliance and disease control.

Aims and Methods: We aimed to evaluate the effect of our current structured transition process on clinical outcomes in adolescent inflammatory bowel diseases (IBD) patients.

Two groups of IBD patients diagnosed in pediatric care were compared: Group A patients did not attend the transition process, whilst Group B patients entered the planned transition service. Outcomes at 1- year after transfer to adult care were evaluated.

Results: Forty-five IBD patients (18 males and 27 females) diagnosed under the age of 18 years were identified of whom 35 had Crohn's disease and 10 had ulcerative colitis. 24 patients were in Group A (without transition), and 21 patients in Group B (with at least one planned transition visit). Mean age at diagnosis was 15.1 ± 2.2 and 13.7 ± 3.0 years ($p = 0.086$), respectively. There were no significant differences in disease duration before transfer, Montreal classification at diagnosis, body mass index, anti-TNF therapy usage, and disease status at transfer between the two groups. Significantly higher number of Group B patients were in remission at 12-month after transfer when compared to patients in Group A (11 vs. 18, respectively, $p = 0.037$). There was a significant difference between groups regarding the number of elective admissions within the examined period (9 vs. 16, $p = 0.011$, respectively).

Conclusion: Planned transition visits resulted in higher disease remission rate at 1-year follow-up after transfer from pediatric to adult health care system in adolescent IBD patients. Well-established transition programs in IBD are needed.

Disclosure: Nothing to disclose

P1008 EFFICACY AND SAFETY OF GRANULOMONOCYTAPHERESIS AS REMISSION INDUCTION THERAPY IN ULCERATIVE COLITIS PATIENTS INCLUDING ADOLESCENTS AND ELDERLY

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Introduction: At our gastroenterology clinic, we receive patients with ulcerative colitis (UC) who wish to avoid hospitalization, require treatment in an outpatient setting. Additionally, with the availability of granulomonocytapheresis (GMA, Adacolumn) therapy, most of our patients favour this non-pharmacologic option as the first-line therapy to avoid pharmacologicals. In fact, most elderly UC patient have multiple other complications as co-morbidities, which may include diabetes, hypertension, cardio-cerebral disease, and therefore, are likely to be on

other medications. Likewise, in younger UC patients, we like to avoid corticosteroids, which may adversely affect their overall growth and development.
Aims and Methods: Therefore, we have been applying GMA as a first-line therapy before any drug based medication hoping to spare our young and elderly patients from pharmacologicals. In a retrospective setting, we reviewed the treatment outcomes measures in patients with UC who had received granulomonocytapheresis (GMA) with the Adacolumn as remission induction therapy at our gastroenterology clinic over the past 11 years. The patients were divided into three groups, under 18 years of age (Group 1, n = 8), 18 to 64 years of age (Group 2, n = 130), and beyond 64 years of age (Group 3, n = 13). In each group, patients' age, gender, UC profile, location, duration, and past medications were factored for analysis to determine the clinical response GMA therapy. Clinical activity index (CAI) ≤4 meant remission.
Results: Each patient had received up to a maximum of 11 GMA sessions at 1 to 5 sessions per week. The clinical response together with remission rates were 87.5% in Group 1, 77.7% in Group 2, and 84.6% in Group 3. Similarly, the clinical remission rates were 87.5% in Group 1 (all 8 patients), 63.8% in Group 2, and 53.8% in Group 3. Further, in Group 1, younger patients showed pancolitis, while in Group 3, elderly patients had a short disease duration, most of them had developed UC around 60 years of age, the so-called elderly onset UC. In all 3 groups, GMA therapy was well tolerated and was without any severe adverse event.
Conclusion: The efficacy outcomes in our patients are very much higher than previous studies reported for GMA in patients with severe UC, refractory to pharmacologicals. However, in our patients, GMA is a very much favoured treatment option for young and elderly patients because of its good safety profile, as well as for being a non-pharmacologic treatment option. Provided patients can afford to make frequent visits to the treatment centre and the medical personnel can achieve a straightforward blood access, GMA should be a first-line therapy before corticosteroids or other pharmacologicals.
Disclosure: Nothing to disclose

P1009 THE TRANSITIONAL PROCESS OF INFLAMMATORY BOWEL DISEASE FROM PEDIATRIC TO ADULT AGE

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Introduction: The transitional process of young patients affected by inflammatory bowel disease (IBD) from pediatric to adult care is a crucial step. It should ensure continuity of care and the maintaining of a well-being condition in a critical and delicate phase of life. It has been suggested that patients who take part in a transitional program show greater compliance and fewer adverse events.
Aims and Methods: The aim of our study was to investigate the 1-year success outcome of the transitional process of IBD patients in terms of maintenance of the nutritional status, patients' compliance to the care in the adult setting and disease activity control, after the implementation of a specific transition programme in our center. From January 2013 to January 2018 we evaluated the transitional process of patients with childhood onset of Crohn's disease (CD) or ulcerative colitis (UC), from the Pediatric to the Adult IBD center, at School of Medicine "Federico II" of Naples, Italy. For each patient we compared the following parameters 12 months before and 12 months after the transition from pediatric to adult care: Body Mass Index (BMI), albumin and hemoglobin level, smoker status. We also compared the number of outpatient visits and the pharmacological therapy in the 12 months prior to the transition with the one in course one year after the transfer to the adult center, as well as the number of disease exacerbations, hospitalizations and surgical interventions.
Results: We enrolled a total of 106 patients with IBD (43 with CD and 63 with UC). We did not find a statistically significant difference between the patients' BMI before and after the transition, while there was a lower percentage of smokers seen in the post-transition period (11% vs. 13.2%; p = ns). Furthermore, there was a statistically significant reduction in the number of exacerbations and hospitalizations in the 12 months following the transition (pre-transition exacerbations: 0.74 ± 0.79, post-transition exacerbations: 0.35 ± 0.57, $p < 0.001$; pre-transition hospitalizations: 0.28 ± 0.44, post-transition hospitalizations: 0.1 ± 0.3, $p < 0.001$). In contrast, there was no statistically significant difference in the number of outpatient visits (3.40 ± 1.4 vs. 3.25 ± 1.2; p = ns) and in the percentage of patients undergoing surgery (0.9% vs. 1.8%, p = ns). We also evaluated pharmacological strategies and we showed a significant difference ($p < 0.01$) in the use of nutritional therapy between the pre-transition phase (18.8%) and the post-transition phase: in fact, no patient in post-transition phase used this therapeutic approach. Moreover, in post-transition period there was a reduction in immunosuppressant use (methotrexate: 9% vs. 2%, p = 0.0031; azathioprine: 36% vs. 23%, $p < 0.01$).
Conclusion: The parameters used as success indicators of the transition program confirm the achievement of a continuity of care from Pediatrics to adult Gastroenterology, such as the maintenance of a state of well-being, in a generally critical phase of the natural history of IBD patients.
Disclosure: Nothing to disclose

P1010 EFFICACY AND DIAGNOSTIC ACCURACY OF FAECAL CALPROTECTIN IN CHILDREN IN PRIMARY CARE, A PROSPECTIVE PRIMARY CARE COHORT STUDY

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Introduction: Faecal calprotectin (FC) is recommended (NICE, DG11, 2013) as an option to support clinicians with the differential diagnosis of IBD and non-IBD (including IBS) in children who have been referred for specialist GI assessment, but data relating to its clinical utility in primary care as part of a referral pathway are limited. We hypothesised that FC would have clinically useful positive and negative predictive values in this setting and would perform better than existing clinical and blood biomarkers to guide appropriate referral.
Aims and Methods: GPs from all 49 local practices in the catchment area for the Royal Devon and Exeter Hospital were recommended to submit an FC test for children aged 4–18 yrs presenting with new GI symptoms where they suspected but were uncertain of an IBD diagnosis. We considered FC levels of ≥100μg/g as positive and recommended referral of positive tests and GP management for negative tests. Clinical symptoms and blood results were captured prospectively at the time of GP referral. Secondary care records after 12 months' follow-up were reviewed to ascertain diagnosis, with unreferred patients after this time assumed to have a non-IBD diagnosis. Mann-Whitney U, Students T-test and Chi-squared tests were used as appropriate. ROC curves and a stepwise backwards multivariable logistic regression were used to explore thresholds and fit models, respectively.
Results: 132 patients were included in the final analysis: 66 (54%) were female and median age was 15.1yrs [IQR 12.4–14.4].10 (8%) patients were diagnosed with IBD (7 CD, 1 UC, 2 IBD-U). The most frequent non-IBD (n = 122) diagnoses were: IBS/functional gut disorder 82%; anal fissure/haemorrhoids 3%; infective gastroenteritis 3% and coeliac disease 2%. FC ≥100μg/g had a sensitivity = 100% (95% CI 69–100%), specificity = 89% (82–94%), PPV = 43% (23–66%), NPV = 100% (97–100%). The AUROC for FC and CRP were 0.98 [0.96–1.00] and 0.94 (0.89–1.00) respectively (p = 0.22). The optimal threshold for distinguishing IBD from non-IBD was FC = 112μg/g and for CRp = 1.5mg/L. Patients with IBD had a higher FC ($p < 0.001$), CRP ($p < 0.001$), white cell count ($p < 0.001$), ferritin (p = 0.05) and platelet count (p = 0.023); lower albumin (p = 0.004) and haemoglobin (p = 0.004) and reported a shorter duration of symptoms (p = 0.037), looser motions (p = 0.007) and a change in stool appearance (p = 0.030) than non-IBD cases. In the multivariable model for every 10-fold increase in FC and CRP the odds of IBD increased by 4.90-fold (95% CI 1.9–2.6, p = 0.01) and 3.6-fold (95% CI 1.6–2.3, p = 0.02), respectively.
Conclusion: Calprotectin testing of paediatric patients in the primary care setting accurately distinguishes IBD from non-IBD conditions in situations of diagnostic uncertainty with clinically useful positive and negative predictive values. It is superior to other clinical and blood parameters except CRP. These data might inform patient care pathways and guide primary care clinicians.
Disclosure: Nothing to disclose

P1011 CARBOHYDRATES INTOLERANCE AND INTESTINAL DYSBIOSIS AMONG CHILDREN WITH RECURRENT ABDOMINAL PAIN

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Introduction: Functional gastrointestinal disorders (FGID), as defined by the Rome IV criteria, may appear in children of all ages and include a wide range of digestive related symptoms. Dietary intolerances to lactose, fructose, or intestinal dysbiosis might be related to FGID, but these conditions are often underdiagnosed and poorly managed.
Aims and Methods: The aim of this study was to assess the prevalence of lactose, fructose intolerance and small intestinal bacterial overgrowth (SIBO) by using hydrogen breath test (HBT) in children with recurrent abdominal pain. Methods:The authors enrolled 226 consecutive children admitted to our hospital with chronic abdominal pain between January 2017 and March 2018. After organic causes were ruled out, the remaining patients underwent lactose, fructose and glucose HBT. A standard dose of 1 g/kg of lactose, 1 g/kg fructose and 1 g/kg glucose were orally administered dissolved in 200 ml of water, with a maximum of 25 g for lactose and fructose, respectively 50 g for glucose. Exhaled hydrogen was measured at 20 minutes intervals for 3 hours. An increase with at least 15 parts per million (ppm) above baseline was considered suggestive for lactose and fructose malabsorption or indicative for SIBO after glucose intake. HBT were conducted in different days for each patient.
Results: Of 226 children analyzed, organic disorders were found in 82 children. The rest of 144 children with FGID (16 functional dyspepsia, 89 irritable bowel syndrome and 39 centrally mediated abdominal pain according to Rome IV criteria) underwent HBT. Lactose HBT was positive in 35 of 144 (24.3%), fructose HBT was positive in 14 of 144 (9.7%), while 29 (20.1%) had positive glucose HBT, indicating SIBO. 31 of 35 children (88.5%) improved on lactose-free diet, 12 of 14 children

(85.7%) improved after fructose exclusion and symptoms disappeared in 28 of 29 children with SIBO (96.5%) after oral rifaximin and probiotics.
Conclusion: Lactose and fructose malabsorption along with intestinal dysbiosis can contribute to recurrent functional abdominal pain in children. Symptoms improved after dietary changes and oral nonabsorbed antibiotic and probiotics.
Disclosure: Nothing to disclose

P1012 WHOLE GUT TRANSIT MEASUREMENT USING NOVEL MAGNETIC RESONANCE IMAGING MINI-CAPSULES

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Introduction: Current tests to measure gastrointestinal transit have limitations or use ionising radiation, making them undesirable, particularly for younger patients. We have previously developed and validated prototypes of magnetic resonance imaging (MRI) transit marker capsules (1), which detect differences in whole gut transit between constipation and health (2). Those prototypes are however quite large (20 mm x 7 mm) and large indigestible objects may not travel normally through the gut (3).
Aims and Methods: We aimed to develop an improved MRI alternative to the old x-ray radiopaque markers (ROM) methods to measure whole gut transit. Mini-capsules were manufactured by JEB Technologies (Suffolk, UK). They are small (8 mm × 4 mm), made of inert plastic material and filled with an oil-in-water emulsion that can be imaged uniquely by exploiting common water and fat selective MRI (4). Five healthy volunteers swallowed 24 mini-capsules for 3 consecutive days, for a total of 72 mini-capsules (a common X-ray ROM protocol). They were scanned on the 4th day using a 3.0 T MRI scanner.
Results: The new mini-capsules were easy to swallow and the protocol was accepted well by the volunteers. The mini-capsules were imaged successfully in the colon.
Conclusion: We have developed new MRI mini-capsule markers that can overcome limitations of previous whole gut transit tests. They are particularly well suited for younger patients and their production can be scaled up industrially.
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Disclosure: Nothing to disclose

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P1013 RECURRENT ABDOMINAL PAIN AND PAIN-PREDOMINANT FUNCTIONAL GASTROINTESTINAL DISORDERS FROM BIRTH TO ADOLESCENCE – A PROSPECTIVE SWEDISH BIRTH COHORT STUDY

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Introduction: Recurrent abdominal pain (RAP) is a common complaint during childhood, but the natural history of childhood RAP and pain-predominant functional gastrointestinal disorders (pFGID) in the general population remains poorly understood.
Aims and Methods: The aim of the current study was to describe the prevalence and turnover of childhood RAP during the first 16 years of life and explore the association between childhood RAP and Rome III defined pFGID in adolescence.
In this prospective Swedish population-based birth cohort study of 4089 children, parents and children answered questionnaires on gastrointestinal symptoms at 1, 2, 12, and 16 years and doctor's diagnosis of inflammatory bowel disease (IBD) and celiac disease (CD) at 12 and 16 years. RAP at 1 and 2 years was defined as repeated attacks of colic for the past 6 and 12 months respectively, and was pooled and called early childhood RAP. RAP at 12 and 16 years was defined as self-reported weekly abdominal pain with no parent-reported diagnosis of IBD and/or CD. pFGID at 16 years were defined according to the Rome III criteria and included irritable bowel syndrome (IBS), functional dyspepsia (FD) and functional abdominal pain (FAP). Sex-adjusted associations were examined using binominal generalized linear model and presented as relative risk (RR) with 95% confidence interval (CI).
Results: Any history of RAP between early childhood and 16 years was reported in 33.0% (890/2698) of children. The prevalence of RAP peaked at 16 years in both boys and girls. Prevalence rates were significantly higher for girls compared to boys at 12 ($p < 0.01$) and 16 years ($p < 0.01$), but not in early childhood. In the subgroup of children with RAP who had completed the detailed Rome III questionnaire at 16 years (498/609), 69.9% fulfilled the criteria for any pFGID. IBS was the most common phenotype in both boys and girls. The prevalence of pFGID was higher in girls than in boys ($p < 0.01$). See Table below.Early childhood: Total n = 3797; Boys n = 1925; Girls n = 1872. 12 years: Total n = 2764; Boys n = 1382; Girls n = 1382. 16 years RAP: Total n = 3039; Boys n = 1494; Girls n = 1545. 16 years pFGID: Total n = 2926; Boys n = 1451; Girls n = 1475. FAp = Functional abdominal pain; FD = Functional dyspepsia; IBS = Irritable bowel syndrome; pFGID = Pain-predominant functional gastrointestinal disorders; RAp = Recurrent abdominal pain.
Complaints of RAP over two assessment points was reported in 2.8% (70/2459) of the children (77.1% girls), and complaints over three assessment points was reported in four children (all girls). Children with RAP in early childhood and at 12 years reported persisting symptoms at the following assessment point in 6.8% (11/161) and 43.4% (43/99) of cases respectively. It was more common for girls than for boys to report persisting symptoms between early childhood and 12 years (10/81 vs 1/80, $p < 0.01$), but not between 12 years and 16 years (34/75 vs 9/24, $p = 0.50$).
Children with RAP at 12 years had an increased risk for RAP at 16 years (RR 2.4, 95% CI 1.9–3.0) for any pFGID at 16 years (RR 2.5, 1.8–3.4), and for IBS at 16 years (RR 3.2, 2.0–5.0). No association was found between early childhood RAP and RAP at 12 years or RAP, any pFGID, and IBS at 16 years.
Clinical follow-up of a subsample of children (87/175) fulfilling the Rome III criteria for IBS at the 16-year questionnaire, confirmed the diagnosis of IBS in 78.2% of cases.
Conclusion: RAP is common in childhood, but most children with RAP do not have persisting symptoms throughout childhood. However, reporting RAP at 12 years is an independent risk factor for RAP, any pFGID, and IBS at 16 years.
Disclosure: Nothing to disclose

P1014 EFFECT OF DIETARY PATTERNS AND LIFESTYLE ON THE DEVELOPMENT OF CHILDHOOD CONSTIPATION: THE TOYAMA BIRTH COHORT STUDY

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Introduction: Constipation is common and a nagging symptom around the world. Associated factors of childhood constipation have been reported, however, few research exist about the development. Our aim was to clarify the effect of dietary pattern and lifestyle on the development of childhood constipation.
Aims and Methods: Participants were aged 12–13 years and from the Toyama Birth Cohort Study in Japan, a prospective longitudinal study examining lifestyle and child's health. Children who completed questionnaires both in 1999 and 2002 were included. Children's dietary pattern, lifestyle factors such as sleep duration,

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			16 years					
				pFGID				
	Early childhood RAP	12 years RAP	RAP	Any	IBS	FD	FAP	IBS+FD
	N (%)	*N (%)*	*N (%)*	*N (%)*	*N (%)*	*N (%)*	*N (%)*	*N (%)*
Total	256 (6.7)	119 (4.3)	609 (20.0)	348 (11.9)	175 (6.0)	79 (2.7)	99 (3.4)	5 (0.2)
Boys	135 (7.0)	33 (2.4)	210 (14.1)	113 (7.8)	64 (4.4)	16 (1.1)	35 (2.4)	2 (0.1)
Girls	121 (6.5)	86 (6.2)	399 (25.8)	235 (15.9)	111 (7.5)	63 (4.3)	64 (4.3)	3 (0.2)

[Prevalence of RAP and Rome III pFGID in children and adolescents in a population-based birth cohort]

physical activity, and psychological status at baseline were inquired. Children with bowel movements of less frequently than once every 2 days was defined as being constipated. Children who had already constipated at baseline were excluded.
Results: Out of 10438, 6662 children (63.8%) were included in our longitudinal study. In total, 317 (4.8%) developed constipation during the three years. Logistic regression analysis showed that the development of constipation was significantly associated with being girl (odds ratio [OR] = 2.33), infrequent intake of fruit (OR = 1.60). Physical activity, TV viewing, sleep duration, and psychological status at baseline was not associated.
Conclusion: Only dietary pattern of taking fruits infrequently predicted a constipation in school children. Lifestyles and psychological status at baseline might change and not effect on development of constipation during the period. A longitudinal study with shorter follow up interval will be needed to clarify the risk factors of childhood constipation.
Disclosure: Nothing to disclose

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P1015 IDENTIFYING PREDICTIVE FACTORS FOR THE RECURRENCE OF PAEDIATRIC INTUSSUSCEPTION

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Introduction: Intussusception is one of the most emergent gastrointestinal disease in paediatric patients, which somtimes lead to the perforation, necrosis, and even death if the initial diagnosis is delayed.
Aims and Methods: The aim of this study was to identify the related factors of the recurrent intussusception in the paediatric patients. The medical record of the intussusception patients who were diagnosed and treated at Dongsan Medical Center from March 2015 to June 2017 was retrospectively reviewed. Baseline demographic findings, the time interval from the symptom onset to the treatment of reduction or operation, the reduction methods (barium enema vs. water enema), the presenting symptoms such as vomiting, bloody stool, abdominal pain or irritability, and lethargy, the history of previous or concurrent infection, the radiologic findings and laboratory findings were analyzed. The pathologic leading points and operation methods were investigated too.
Results: Among the total of 137 patients, the male to female ratio was 1.4 (male = 80, 56.7%, female = 57, 40.4%). The mean age was 2.17 ± 1.36 years with a range of 0.18 to 10.1 years. The mean interval time from the symptom onset to the reduction time was 24.39 ± 25.64 hours with a range of 2 to 168 hours. The mean age for recurrence group was 5.35 ± 2.72 years and the interval time from the initial reduction to recurrence was 50.96 ± 25.52 hours. The reduction methods were the water reduction (n = 69, 48.9%), the barium reduction (n = 64, 45.4%), operation (n = 1, 0.7%) and spontaneous reduction (n = 3, 2.1%). The type of intussusception was mostly ileocolic (n = 136, 96.5%) with one small bowel case (n = 1, 0.7%). The diagnosis age and the intussusception head size on ultrasonography were significantly related with the recurrence of intussusception ($p = 0.006$, $p = 0.028$, respectively). In laboratory analysis, CRP was significantly higher in the recurrence group (1.03 ± 1.49 vs.1.49 ± 2.68, $p = 0.024$). Bloody stool and history of infection were significantly more frequent in the non-recurrence group ($p = 0.001$, $p = 0.000$, respectively), and vomiting, abdominal pain or irritability, and lethargy did not show any significant difference between the two groups. No pathologic leading point except for enlarged lymph nodes was found.
Conclusion: The diagnosis age, CRP and the mass size in radiologic finding was significantly related with the recurrence of intussusception.
Disclosure: Nothing to disclose

P1016 PSYCHO-GASTROENTEROLOGICAL PROFILE IN PAEDIATRIC OUTPATIENTS AFFECTED BY DISORDERS OF GUT-BRAIN INTERACTION

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Introduction: Disorders of Gut-Brain Interaction (DGBI), previously known as Functional Gastrointestinal disorders (FGIDs), are common among children. Nevertheless, their pathophysiology is still uncertain, an efficacious therapy is lacking, and valid tools to evaluate these disorders during childhood are not available. We have developed a multi-parametric questionnaire that evaluates the psycho-gastroenterological profile (PGP) and socio-demographic characteristics of the paediatric population and have tested its validity in children with and without DGBI.
Aims and Methods: We studied a population of 119 Caucasians, aged 11–18, consisting of 28 individuals diagnosed with DGBI using the Rome IV criteria at our Outpatient Clinic and 91 controls enrolled in secondary schools. All subjects were asked to fill our Psycho-Gastroenterological Questionnaire (PGQ), which takes into account the following parameters: number of medical examinations due to gastrointestinal symptoms, sensation of pain evaluated with the Faces Pain Scale Revised (FPS-R), form of the feces established with the Bristol Stool Chart (BSC), gastrointestinal symptoms assessed with the Gastrointestinal Symptoms Rating Scale (GSRS), anxiety with the State-trait anxiety inventory (STAI Y-1 and STAI Y-2), alexithymia with the Toronto Alexithymia Scale 20 (TAS 20), perceived Self-efficacy in the management of negative emotions and expression of positive emotions with APEN-G and APEP-G, Quality of life with the Irritable bowel syndrome-Quality of Life (IBS-QoL) Questionnaire, school performances, tobacco use, history of familial trauma, digitalization. Differences between the two groups were evaluated by Student's t-test and considered significant for $p < 0.05$.
Results: Compared to controls, patients with DGBI had significantly higher school performances ($p < 0.05$) and were significantly less frequently tobacco users (0% vs 16%, $p < 0.05$). A history of familial trauma was significantly more common in DGBI subjects than controls (28% vs 1%, $p < 0.05$). No differences between the two groups were found in terms of level of digitalization and BSC. Subjects with DGBI reported more frequent medical examinations due to gastrointestinal symptoms than controls. They also reported a significantly higher percentage of pain classified as 4 at the FPS-R (14% vs 7%, $p < 0.05$). Scores of GSRS and APEN-G were significantly higher in patients than controls (12.2 ± 8.1 vs 6.9 ± 4.0, $p < 0.05$ and 24.3 ± 6.8 vs 22.1 ± 5.0, $p < 0.05$, respectively). On the other hand, scores of STAI Y-1 (33.5 ± 12.1 vs 48.6 ± 10.9, $p < 0.05$), STAI Y-2 (39.3 ± 10.7 vs 47.4 ± 10.6, $p < 0.05$), TAS 20 (48.2 ± 8.0 vs 51.8 ± 11.4, $p < 0.05$), and IBS-QoL ($p < 0.05$ for dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, relationships, overall) were significantly lower among DGBI patients than controls.
Conclusion: Our PCQ detected, among subjects with ≤ 18 years of age affected by DGBI compared to controls, higher prevalence of history of familial trauma, lower QoL, more medical examinations, lower anxiety levels (both STAI Y1 and STAI Y2), and higher perceived self-efficacy in the management of negative emotions. It also detected lower levels of alexithymia and tobacco use. The PGQ is a novel, easy-to-use, questionnaire deserving further investigation for its potential utility in the assessment of the psycho-gastroenterological profile of children and adolescents affected by DGBI.
Disclosure: Nothing to disclose

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TUESDAY, OCTOBER 23, 2018 09:00–17:00

Other Lower GI Disorders II – Hall X1

P1017 A LINK BETWEEN STOOL FREQUENCY AND GUT MICROBIOTA

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Introduction: Recently, a number of studies have reported that gut microbiota could contribute to human condition including obesity, inflammation, cancer development and behavior. We hypothesized that the composition and distribution of gut microbiota are different according to the stool frequency. And we tried to identify the association between gut microbiota and stool frequency.
Aims and Methods: We collected faecal samples from healthy people who divided into three groups according to the stool frequency. Group 1, a small number of defecation (≤ 2 times/week); Group 2, normal defecation (1 time/day or 1 time/2 days); Group 3, a large number of defecation (≥ 2–3 times/day). The defecation patterns (number of defecation and associated Bristol stool scale (BSS) scores from 1-week diaries) were recorded. And we evaluated the composition and distribution of gut microbiota in each group by 16S rRNA-based taxonomic profiling of faecal samples.
Results: Faecal samples were collected from a total of sixty individuals (31 males and 29 females, aged 34.1 ± 5.88), and each group was 20 individuals. We identified microbial richness of Group 1 was significantly higher than that of Group 3, and tendency to decrease with increasing a number of defecation. The biological community composition was fairly different based on the number of defecation, and the ratio of Bacteroidetes/Firmicutes was higher in Group 1 than in other groups. And we found specific strains at family and genus level which exist in Group 1 and Group 3, respectively.
Conclusion: Stool frequency might be associated with richness and community composition of gut microbiota and these findings could be supported by the assessment in further metagenome-wide association studies of gut microbiota.
Disclosure: Nothing to disclose

P1018 THE ROLE OF THE METABOLIC ACTIVITY OF THE INTESTINAL MICROFLORA IN CHILDREN WITH IMMUNE THROMBOCYTOPENIC PURPURA RESISTANT TO CORTICOSTEROID THERAPY

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Introduction: Immune thrombocytopenic purpura (ITP) is a disease characterized by isolated thrombocytopenia of less than $150x10^9$/l with a normal or increased amount of megakaryocytes in the bone marrow and the presence of autoantibodies on the surface of platelets causing their increased destruction. Gastrointestinal disorders in ITP directly related to the underlying diseases cause the development of intestinal microbiota disorders in children.

Aims and Methods: To evaluate the metabolic activity of the intestinal microflora based on the assessment of the spectrum of stool short chain fatty acids in children with ITP resistant to corticosteroid therapy.

The study included 41 patients (19 girls and 22 boys) aged from 2 to 17 years (mean age – 10.27 years, median age – 10 years) with ITP resistant to corticosteroid therapy. All patients were observed in the department of the hematology and oncology of the Russian Children's Clinical Hospital (Moscow).

All patients underwent conventional clinical-instrumental and an assessment of the metabolic activity of the intestinal microflora based on the stool short chain fatty acids levels assessment by gas-liquid chromatography.

Results: In children with ITP resistant to corticosteroid therapy a wide range of gastroenterological symptomps were identified, including abdominal pain (14/41, 34.15%) belching (8/41, 19.5%), heartburn (7/41, 17.1%), stool disorders (8/41, 19.5%), indirect signs of intestinal digestion (4/41, 9.76%) and absorption abnormalities (41/41, 100%). The revealed disturbances in the metabolic activity of the intestinal microflora were characterized by an increased production of the acetic, propionic, butyric, valeric acids and also isovanoic acid. A significant increase in the isocyanates production and a slightly increased ratio of EiC/EC (10/16, 62.5%), indicating a predominance of iso-acids over non-isoforms, a significant predominance of isovaleric acid (an increase in the ratio of iC5/C5 in 68.75% of patients with ITP) were observed. Additionally, the anaerobic index was increased.

Conclusion: In children with ITP resistant to corticosteroid therapy, a wide range of gastroenterological complaints were identified, as well as changes in intestinal microbiota expressed in disturbance of short chain fatty acids production, indicating an increase in the activity of the saccharolytic flora, accompanied by an increase in the activity of proteolytic microorganisms uncharacteristic for normal microbiota with an increase in the fraction anaerobes.

Disclosure: Nothing to disclose

P1019 INHIBITORY EFFECT OF URSODEOXYCHOLIC ACID ON *CLOSTRIDIUM DIFFICILE* GERMINATION IS INSUFFICIENT TO PREVENT *C. DIFFICILE* COLITIS: A STUDY IN HAMSTERS AND HUMANS

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Introduction: *Clostridium difficile* infection (CDI) is a public threat due to its recurrences and severity. Faecal transplantation is more effective than antibiotics in reducing recurrences, but with some unknown risks. Bile acids (BA) are known to influence germination and growth of *C.difficile*: taurocholate acid (TCA), a primary BA, promotes germination and growth of *C. difficile* (1). Secondary BA inhibit germination and growth (2). Ursodeoxycholic acid (UDCA), a tertiary BA minor in human, inhibits germination and growth of *C. difficile in vitro* (2,3), but was never tested *in vivo* with an infectious challenge. We hypothesized that we could use UDCA for prevention of CDI. We evaluated the effects of UDCA on *C.difficile in vitro* on germination and growth and *in vivo* in an animal model, with pharmacokinetics study and prevention of CDI. We then studied the infection incidence in UDCA-treated patients.

Aims and Methods: *In vitro* trials evaluated germination and growth of several strains of *C.difficile* by optical density measurements and colony count, with 0.01%, 0.05% and 0.1% UDCA, in competition with 0.1% TCA. We analysed faecal BA of hamsters receiving antibiotics and UDCA (50mg/kg/day), antibiotics alone, or UDCA alone. Then, we challenged with spores of *C.difficile* at D6 hamsters treated with UDCA (50 mg/kg/day) from D1 to D13, versus control. Their survival, colonization and BA were evaluated. In human, we analysed the database of a cohort that studied CDI in acute flares of inflammatory bowel disease (IBD) from September 2012 to May 2014 (4). As PSC-IBD patients were under UDCA treatment, we compared PSC-IBD patients to IBD patients without PSC.

Results: *In vitro*, UDCA strongly inhibited germination and growth of *C.difficile* at 0.05% and 0.1%, competing with 0.1% TCA (0.05% $\pm$0.05% colony forming unit versus 100% $\pm$0%, $p<0.0001$). UDCA reached high proportions of faecal BA pool only in hamsters that received UDCA with antibiotics, with a 43.5% UDCA peak at D5. Without antibiotics, we didn't observe any similar UDCA peak in faeces of hamsters (max. 4.28% UDCA), probably because of UDCA transformation into lithocholate by gut microbiota. During infectious challenge, mortality was high (62.5%, n = 5/8) and similar in animals treated or not with UDCA ($p=0.78$). UDCA percentage in group A was high, similar and with the same kinetics in dead and surviving hamsters (the day of infection: 46.03% UDCA versus 40.82%, respectively, $p=0.14$). However, dead hamsters had a higher ratio of primary over secondary BA compared to surviving hamsters: first hamsters to die had the highest ratios of primary over secondary BA. 9% (n = 41/445) of patients with IBD without PSC (not treated with UDCA) had a CDI at the time of admission for an IBD flare, versus 25% (n = 4/16) of patients with PSC-IBD treated with UDCA.

Conclusion: We confirmed the strong inhibitory effect of UDCA on growth and germination of *C.difficile in vitro*, with 0.05% or 0.1% UDCA competing with 0.1% TCA. However, in our hamster model, UDCA was inefficient to prevent CDI, despite high levels of UDCA in faeces (41–46%). Patients with PSC-IBD treated with UDCA did not have less CDI than IBD patients.

Disclosure: Mayoli Spindler (financial support for hamsters and ursodeoxycholic acid) ; H. Duboc: Biocodex, IPSEN ; S. Hoys and C. Janoir: Biocodex, MSD

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P1020 SIGNIFICANT DIFFERENCES IN THE GUT MICROBIOME OF PATIENTS WITH ACTIVE PSORIASIS

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Introduction: Alterations in the gut microbiome have been implicated in the pathogenesis of several immune-mediated inflammatory diseases such as in patients with psoriatic arthritis. Psoriasis is a chronic, inflammatory, multi-organ disease characterized by papulosquamous lesions with varying morphology, distribution, severity and course.

Aims and Methods: To characterize the gut microbial signature of patients with active psoriasis as compared to matched non psoriatic control participants and to determine whether these changes translate to differences in expression of significant metabolic pathways.

This observational prospective multicenter study was conducted at the Tel Aviv Medical Center (TLVMC) and Maccabi healthcare services (MHS). Patients' clinical details were recorded and stool was collected and stored at −80 °C. In parallel matched controls were recruited. Fecal samples were processed and 16S rRNA was sequenced using the Illumina platform. This data as well as clinical data of the patients and healthy cohorts were compared. A false discovery rate (FDR)≤0.1 was considered statistically significant. A multivariate analysis was performed to correct for confounding variables. PICRUSt was used to determine whether there were differences in genes encoding various metabolic pathways between the cohorts.

Results: Forty-six participants were recruited to the study of whom 52% (n = 24) suffered from psoriasis. Psoriatic patients were older (52.7 ± 11.6 vs. 43.9 ± 12.7, $p=0.02$) and had a lower body mass index (BMI) (25 ± 2.9 vs. 27 ± 3.4 kg/m^2, $p=0.05$) compared to control patients, respectively. There was a significant difference in beta-diversity between the two patient groups. Psoriatic patients had a significant increase in the Firmicutes and Actinobacteria phyla, while Bacteroidetes and Proteobacteria were decreased compared to the control cohort. At the genus level, significant differences were detected between the 2 patient groups, using the LEfSe analysis (Table 1). At the species level, there were significant increases (FDR < 0.05) in *Ruminoccocus gnavus, Dorea formicigenerans*, and *Collinsella aerofaciens,* in the psoriasis group, while *Prevotella copri,* and *Parabacteroides distasonis* were significantly increased in the control group. A metabolic gene analysis (PICRUSt) revealed increases in metabolic pathways related to lipopolysaccharide function in the psoriatic cohort. These differences are summarized in Table 1.

Genus	Psoriatic cohort	Healthy cohort	P-value	FDR
Blautia	0.131	0.025	0	0.00002
Faecalibacterium	0.069	0.033	0.006	0.028

(continued)

Continued

Genus	Psoriatic cohort	Healthy cohort	P-value	FDR
Ruminococcus	0.057	0.016	0.001	0.005
Prevotella	0.055	0.37	0.0003	0.003
Coprococcus	0.039	0.01	0.0002	0.002
Bifidobacterium	0.035	0.01	0.0003	0.003
Dorea	0.02	0.003	0	0.00001
Lachnospira	0.007	0.015	0.009	0.04
Collinsella	0.004	0.0007	0.006	0.03
Sutterella	0.001	0.005	0.00001	0.0003
Actinomyces	0.0002	0.00006	0.0006	0.004
Christensenella	0.0001	0.00001	0.012	0.05

[Table 1: Taxonomic differences between the healthy cohort and psoriatic patients at the genus level].

Conclusion: The data demonstrate a unique fecal microbial and metabolic signatures for psoriatic patients. These may directly impact regulation of the immune responses and influence the pathogenesis of psoriasis.

Disclosure: Nothing to disclose

P1021 DIFFERENCE OF COLORECTAL CANCER MICROBIAL COMMUNITY A BY METAGENOMICS AND CULTURE-BASED METHODS

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Introduction: Dysbiosis of intestinal microbiota is promoting the development of colorectal cancer (CRC). We confirmed the intestinal microbiota composition from fecal sample of Korean CRC patients. Metagenomic analysis was performed and we isolated single microbes through culture-based method.

Aims and Methods: CRC fecal samples were collected from 12 individuals. Metagenome Sequencing was based on the 16S rRNA gene amplicon on the Illumina MiSeq platform. The bacteria strains were subcultivated on the agar plate medium in aerobic and anaerobic and further identified by using the 16s rRNA gene sequencing.

Results: Bacteria diversity by metagenome analysis was decreased in CRC group compared to control group. In CRC group, relative abundance of Firmicutes and Bacteroidetes were increased while the prevalence of Proteobacteria was decreased. The difference of microbial composition between control and CRC group was found at the genus level. Bacteroides, Parabacteroides of Bacteroidetes have increased and Acinetobacter, Pseudomonas of Proteobacteria have significantly decreased in CRC compared to control group. Using culture method, we isolated diverse bacteria of species level including 5 strains of Bacteroides; *B. ovatus, B. uniformis, B. salyersiae, B. vulgatus and B. xylanisolvens* and 2 strains of Fusobacterium; *F. gonidiaformans* and *F. necrophorum* from CRC patients.

Conclusion: Metagenome analysis showed the genus Bacteroides, Parabacteroides of the phylum Bacteroidetes has increased and the genus Acinetobacter, Pseudomonas of Proteobacteria decreased in CRC group compared to control group. In addition to, we have isolated various strains associated with CRC by culture-based method.

Disclosure: Nothing to disclose

P1022 A HEALTHY LIFESTYLE IS INVERSELY ASSOCIATED WITH BOTH PROXIMAL AND DISTAL COLORECTAL ADENOMAS

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Introduction: Diet and lifestyle characteristics were previously shown to be associated with colorectal neoplasia, mainly in the distal colon and less at the proximal colon. However, these associations need further confirmation and elaboration and were not tested with a global lifestyle score.

Aims and Methods: We aimed to explore the association between nutritional and lifestyle components, and a global lifestyle score, with the presence and laterality of colorectal polyps. We conducted a case-control study among patients undergoing colonoscopies during 2010–2015 at our department. Cases were defined by detection of an adenomatous or serrated polyps. Polyp location was defined as proximal (cecum to splenic flexure), or distal (descending to anus). Controls were defined as those without past/current colonic polyps. Data collection included: anthropometrics, medical history and dietary intake evaluated by a structured questionnaire. We adopted a lifestyle score composed of four healthy lifestyle factors from the strategic goals of the American Heart Association: refraining from current/past smoking, absence of obesity, regular performance of physical activity, and a healthy diet (adherence to ≥5 of 11 dietary recommendations).

Results: A total of 328 cases of adenomas (proximal n = 164 and distal n = 164), and 376 controls were included in the study. The proportion of participants adhering to an unfavorable lifestyle pattern (≤2 lifestyle factors) was lower among controls relative to cases of colorectal adenomas (28.3% vs. 44.2% $p < 0.001$). This difference was detected both in cases with proximal adenoma (39.6%, $p = 0.009$ compared with controls) and distal adenomas (48.8%, $p < 0.001$ compared with controls). Similar results were obtained for all polyps types (adenomas and serrated polyps).

In multivariate analysis, each addition of one of the four healthy lifestyle factors was negatively associated with colorectal adenomas (OR = 0.76, 95% CI 0.65–0.90). Associations were significant for both distal and proximal adenomas (OR = 0.78, 0.63–0.96 and OR = 0.73, 0.60–0.90, respectively). Refraining from smoking and maintaining a healthy diet were the factors most strongly associated with lower odds of colorectal adenomas (OR = 0.69, 0.50–0.97 and OR = 0.63, 0.45–0.89, respectively), after adjustment for age, gender, low socio-economic status, use of aspirin, NSAIDs, statin and antidiabetic medication, daily caloric intake, colonoscopy indication and for one another. These associations were significant for both distal adenomas (OR = 0.63, 0.42–0.95 and OR = 0.63, 0.42–0.96, respectively) and proximal adenomas (OR = 0.70, 0.46–1.65 and OR = 0.59, 0.38–0.90, respectively). The number of healthy lifestyle factors was negatively associated with odds of colorectal adenoma, both distal and proximal (Table 1). Also in these analyses similar results were obtained for all polyps types, and for serrated polyps compared with controls.

Conclusion: Adherence to a healthy lifestyle is inversely associated with both distal and proximal colorectal adenomas. The protective association seems to start from adherence for a minimum of 2 healthy lifestyle characteristics. An independent protective association was detected between refraining from smoking and maintaining a healthy diet.

Number of healthy lifestyle factors	All adenomas (n = 403)	Cases of proximal adenomas (n = 198)	Cases of distal adenomas (n = 205)
0–1	Reference	Reference	Reference
2	0.51 (0.34–0.76)	0.62 (0.38–1.01)	0.41 (0.25–0.66)
3–4	0.50 (0.32–0.77)	0.55 (0.32–0.96)	0.43 (0.25–0.73)

[Adjusted association between the number of healthy lifestyle factors and colorectal adenomas.]

Disclosure: Nothing to disclose

P1023 COMPARISON OF FIT-BASED COLORECTAL CANCER SCREENING PROGRAMMES

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Introduction: Many countries or regions have implemented colorectal cancer (CRC) screening by faecal occult blood testing (FOBT), in particular by means of faecal immunochemical testing (FIT). (1) FOBT as screening method is also recommended by the European guidelines.(2) The effectiveness of population-based screening programmes is not only driven by the sensitivity of the screening method, but also depends on the availability of resources, healthcare infrastructure and population preferences in each country. Population preferences will especially be reflected in participation rate.

Aims and Methods: This study compared design and performance of four faecal immunochemical testing (FIT)-based screening programmes for colorectal cancer (CRC) in Flanders (Belgium), France, Basque country (Spain) and the Netherlands with the aim of future optimization of the different programmes. Background information and data on main performance indicators were collected and compared for the four screening programmes.

Results: Invitation approach differed most strikingly between the four programmes: In France only an invitation letter is send by mail, while the sample kit needs to be collected at general practitioner (GP). In the other programmes, an invitation letter including the sample kit is send by mail. In addition, Basque country and the Netherlands also send a pre-invitation letter prior to the invitation. Interestingly, participation rates vary substantially with method of invitation with the highest participation rates in the Netherlands (73.0%) and Basque country (72.4%), followed by Flanders (54.5%) and France (33.5%). FIT positivity rate ranged from 4.6–6.6% in the programmes. Basque country (91.5%) and France (88.9%) had the highest participation rate with colonoscopy following a positive FIT test.

Conclusion: Large differences in screening participation were observed between programs in line with invitation method used. This finding suggests that changes to the design of the programme, such as a pre-invitation latter and including the sample kit with the invitation, might increase participation. The high participation to colonoscopy in Basque country and France might indicate that in programmes with active involvement of GPs individuals are more likely to undergo a colonoscopy.

	France	Flanders	Netherlands	Basque country
Year	2015–2016	2016	2016	2016
Age (year)	50–74	56–74	55–75	50–69
Participation rate FIT	28.6%	54.5%	73.0%	72.4%
Cut-off level (Hb/g feces)	30 µg	15 µg	47 µg	20 µg
Positivity rate	4.6%	6.6%	5.5%	5.2%
Participation rate colonoscopy	88.9%	85.8%	82.8%	91.5%
Detection rate Advanced neoplasia	1.3%	1.1%	2.3%	1.9%
Diagnostic yield program Advanced neoplasia	0.5%	0.5%	1.6%	1.4%

[Table 1: Performance indicators for France, Flanders, the Netherlands and Basque country]

Disclosure: Nothing to disclose

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P1024 IMPACT OF COLORECTAL CANCER SCREENING PROGRAMS ON SURGICAL PROCEDURES IN THE VENETO REGION (NORTHEAST ITALY)

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Introduction: Colorectal cancer (CRC) is a leading cause of cancer mortality in the Veneto Region (North-east Italy). Population screening of adults between 50 and 74 for CRC was begun in 2002, and it became standard practice in all 21 local health units (LHU) of the region in 2008.
This study was carried out to evaluate the impact on surgery rates of CRC screening programs.

Aims and Methods: This is a retrospective cohort study carried out from a population-based archives represented by hospital discharge records (HDR) that includes all hospitalizations with up to six diagnoses recorded according to the ICD9-CM.
All discharges from 1 January 2000 to 31 December 2017 of Veneto population in screening age with principal diagnosis of CRC treated with surgery were included in the study
The number of patients studied by screening rose approximately of 20% reaching 1,597,826 for the last year (2017) and Veneto region can be subdivided into 3 areas stratifying by screening programs introduction period: A – early (2002–2004), B – intermediate (2005–2007), and C – late (2008) areas.
The Standardized Hospitalization Ratio (SHR) per five-year age group (ref. pop. Veneto 2009) was calculated and espressed per 100,000 population.

Results: During the study period, 29,704 surgical procedures for colorectal cancer were performed (colon 63%, rectum 36%, secondary malignant neoplasm 1%) with a SHR of 116.1, higher in males (OR: 1.65; 95% CI: 1.61–1.72; $p < 0.05$).
An analysis of the annual SHR distribution uncovered two distinct phases: during the first phase there was a rising tendency that reached a maximum value in 2007 (143.1; $\chi 2$ trend: 43.731; $p < 0.001$) and during the second there was a falling tendency that reached its minimum value in 2017 (85.3; $\chi 2$ trend: 438.784; $p < 0.001$), with a total reduction of 29.7%.
The cancer stratification by site shows that the rate of surgical procedures of the proximal colon during the last year was the same as the 2000 value (33.2), instead there was a significant decrease (−41.8%; $\chi 2$ trend: 531.356; $p < 0.001$) in the rate of procedures on the distal colon and rectum which fell from 86.5 to 50.3.
The stratification for screening programs intrductions shows how the peak of surgical procedures was reached about in three years from the introduction and then started to drop.

Conclusion: Study findings confirmed that CRC screening was effective in reducing the number of oncological surgical oncology procedures particularly with regard to the distal colon and rectum.
Data analysis showed that in Veneto Region the screening seemed to accelerate reaching the peak rate in surgical procedures that took place in 2007 and then started to fall off.

Disclosure: Nothing to disclose

P1025 ADDING FAMILY HISTORY OF COLORECTAL CANCER TO THE FIT-BASED SCREENING PROGRAM IN A DUTCH COLORECTAL CANCER SCREENING POPULATION SAMPLE

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Introduction: Screening for colorectal cancer (CRC) with the fecal immunochemical test (FIT) has suboptimal sensitivity for detecting advanced neoplasia (cancer and advanced adenomas). To increase the sensitivity and yield of a FIT-based screening program, FIT could be combined with other risk factors for advanced neoplasia, such as family history of CRC. We evaluated the incremental yield of adding questionnaire on family history of CRC and Lynch syndrome associated tumors to a FIT-based screening program.

Aims and Methods: In this prospective population-based CRC screening trial, we randomly selected 6,000 screening-naive men and women in North-Holland, aged 59 to 75 years. All of them received an invitation to complete a FIT (FOB-Gold) and a validated, online family history questionnaire. Participants with a positive FIT (cut-off value 275ng/ml) and/or a positive family history, confirmed after genetic counseling, were referred for colonoscopy. The yield of detecting advanced neoplasia in the FIT-only strategy was compared to the combined strategy.

Results: Of the 5,979 invitees, 1,952 (33%) participants completed FIT only, 2,379 (40%) completed both FIT and the family history questionnaire and 95 (2%) completed only the family history questionnaire. Of the 125 participants eligible for referral to a clinical geneticist based on their questionnaire responses, only 50 (40%) underwent genetic counseling; 46 (37%) declined referral and 29 (23%) had previously received genetic counseling or colonoscopy surveillance. After genetic counseling, fourteen additional colonoscopies were performed in individuals with a FIT negative result, with no additional advanced neoplasia detected. The positive predictive value for advanced neoplasia of the combined strategy was 54% (95% CI: 47–61%) compared to 58% (95% CI: 51–65%) using the FIT only strategy (p-value = 0.43).

Conclusion: In this study in the Dutch FIT-based screening program we observed no added value of using a validated, online family history questionnaire in detecting advanced neoplasia. However, patients at increased risk of developing CRC, who should undergo colonoscopy screening instead of participating in the CRC screening program, were identified.

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P1026 THE EPIDEMIOLOGY OF THE SERRATED POLYPOSIS SYNDROME IN AN AUSTRALIAN SETTING – MORE COMMON THAN PREVIOUSLY APPRECIATED

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Introduction: The Serrated Polyposis Syndrome (SPS) is defined by the World Health Organisation (WHO) revised clinical criteria and is characterised by the presence of multiple Sessile Serrated Lesions (SSLs) within the colon. It confers an increased risk of colorectal malignancy. The exact prevalence of the condition is unknown and is there is significant geographic variability. There is a lack of data on the epidemiology of the SPS in an Australian setting.

Aims and Methods: To evaluate the epidemiology of the SPS in an Australian setting. All patients undergoing colonoscopy at an Australian regional gastroenterology practice between January 2015 and March 2018 were screened for this study. Patients found to have the SPS, as defined by the WHO revised criteria, were included. Polyp histology was independently reviewed by a histopathologist to confirm the diagnosis. Clinical records of patients were reviewed to extract demographic and clinical data.

Results: In the study period, 3725 separate patients underwent colonoscopy and the SPS was identified in 110 of these (2.95%). This group was predominately female (68/110; 62%) and had an average age of 66.3 years (SD = 13.1; range 24–88 years). Baseline characteristics for this group are presented in table 1. The majority of patients (107/110, 97%) were diagnosed with the SPS based on WHO criterion two (five or more polyps proximal to the splenic flexure with at least two greater than 10mm). 3 (3%) patients had a 1st degree relative with SPS and at least one SSL. The median number of SSLs detected during colonoscopy was 8

(range: 5–30) and then mean size of the largest SSL was 18mm (SD = 5.4mm). Dysplasia was detected within a serrated polyp in 30% of patients. In the majority of patients other polyp types were also detected during colonoscopy (83%) with conventional tubular adenomas (33%) and hyperplastic polyps (7%) being the most common (42% had multiple other polyp types).

Characteristic	N = 110
Gender	Female (62%)
Mean age	66.3 years (range 24–88 years)
Smoking history	Current smokers – 5% Former smokers – 16%
Diabetes	9%
Alcohol (≥2SD/day)	20%
Family history of bowel cancer	1st degree relative – 32% 2nd degree relative – 15%
FOBT positive	15%

[Table 1- Baseline characteristics for SPS patients]

Conclusion: The SPS is more common that previously recognised, being detected in 2.95% of Australian patients undergoing colonoscopy in a regional centre. This data set confirms a slight female predominance to the condition. Patients with the SPS are also at increased risk of conventional adenomas.

Disclosure: Nothing to disclose

P1027 CLINICOPATHOLOGICAL AND COMPREHENSIVE ANALYSIS BY NEXT GENERATION SEQUENCING (NGS) IN APPENDICEAL MUCINOUS TUMOR

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Introduction: Appendiceal mucinous tumors (AMTs) are reported to be rare, therefore their tumorigenesis and progression pattern are still unclear. AMTs are classified histologically into low-grade mucinous appendiceal neoplasms (LAMNs) or mucinous adenocarcinomas (MACs). These tumors have been considered to be genetically distinct tumors: MACs harbor frequently *TP53* but not *GNAS* mutations, while LAMNs contain frequent *GNAS* but not *TP53* mutations. However, a recent report demonstrated a possibility that LANM could show progression into MAC, because MAC contained a focal area of LAMN component within tumor and could have sometimes the same genetic mutations such as *KRAS* and *GNAS* reported to be frequently occur in LAMNs.

Aims and Methods: The aims of this study are to evaluate the tumorigenesis and the progression mechanism of the AMTs and to deeply examine the clinicopathological and the molecular characteristics of AMTs. We examined 44 cases of AMTs (LAMN: 33, MAC: 11) surgically resected at the Juntendo University Hospital, Tokyo, JAPAN and its affiliated hospital (Shizuoka hospital, Nerima hospital, Urayasu hospital, and Tokyo Koto geriatric medical center) between 2001 to 2018. Among 11 MACs, 7 cases accompanied with LAMNs within the same tumors. DNA was extracted from formalin-fixed paraffin-embedded (FFPE) samples. We performed NGS for 17 cases (LAMN: 11, MAC: 6) using Ion PGM[™] system and cancer hot spot panel v2 targeting 50 genes, 2,790 sites (Thermofisher Scientific). We also performed *KRAS, GNAS* and*TP53* mutation analysis by the Sanger method for the specimens for the remaining cases. Furthermore, mutations of *RNF43*, which was not listed on the hot spot panel and had been shown to be frequently mutated in mucinous tumors of other organs, were examined for all cases.

Results: The mean age of patients with MAC is 64.2 years (from 43 to 81 years) and LAMNs is 58.2 years (from 36 to 81 years). Both MACs and LAMNs occurred preferentially in female patients. Eight out of 33 patients with LAMNs had pseudomyxoma peritonei at operation, and 4 out of them experienced disease relapse. In contrast, 3 out of 11 patients with MAC had pseudomyxoma peritonei at operation, and 3 patients with MAC experienced relapse, whereas 2 of them did not have pseudomyxoma peritonei at operation. NGS revealed the *KRAS* and *GNAS* as the most frequently mutated genes in AMTs. By combination with Sanger sequencing data, both LAMNs and MACs showed almost the same mutation rate for the oncogenic driver, including *KRAS* (54.5%, 18/33 vs 54.5%, 6/11), *GNAS* (21.2%, 7/33 vs 36.4%, 4/11), *RNF43* (33.3%, 11/33 vs 36.4%, 4/11). In addition, six LAMNs (18.2%) and three MACs (27.3%) had both mutations in *KRAS* and *GNAS*. *TP53* mutations were frequently occurred in MAC (36.4%; 4/11) than LAMN (6%; 2/33), being this difference statistically significant. Notably, LAMN component within MAC showed more complicated mutation patterns than pure LAMN by NGS. Furthermore, both components in MAC with LAMN shared common alterations, however, it also seemed that each component obtained their own additional genetic alterations after development of MAC, respectively.

Conclusion: Pure LAMNs had simple mutation patterns compared to LAMN components within MAC.

The shared mutation profiles between both components within MAC with LAMN support the hypothesis that LAMNs at least in part progress into MACs. In addition, relapse in MAC was not associated with the presence of pseudomyxoma peritonei at operation.

Disclosure: Nothing to disclose

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P1028 EPITHELIAL TO MESENCHYMAL TRANSITION IN RESPONSE TO *E. COLI*-INDUCED SENESCENCE-ASSOCIATED SECRETORY PHENOTYPE INDUCED CHEMOTHERAPEUTIC DRUG RESISTANCE

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Introduction: Colorectal cancer (CRC) tumors are highly colonized by *Escherichia coli*. Interestingly these *E. coli* frequently possess the *pks* genomic island (*E. coli pks*) responsible for the synthesis of a not yet purified genotoxic compound named colibactin. Colibactin-producing *E. coli* increase the number of tumors and promote invasive carcinoma in CRC mouse models. It has been shown that *pks E. coli*-infected cells secrete growth factors responsible for proliferation of uninfected cells. Epithelial to mesenchymal transition (EMT), as first described in embryonic development, results in the transition of epithelial (E) cells to cells with a mesenchymal (M) phenotype. EMT plays important roles in cancer progression from primary tumor growth, invasion, dissemination and metastasis as well as in resistance to therapy.

Aims and Methods: We investigated whether *pks E. coli*-infected cells induce, through their secretions, EMT in uninfected cancer cells. Human intestinal epithelial cells HT29 were infected using a *pks E. coli* strain isolated from a human CCR biopsy or its isogenic mutant unable to produce colibactin (Δ*pks E. coli*). 5-days post-infection, conditioned media (CM) were collected and used to stimulate uninfected cells. EMT markers were analyzed by Western blot and qRT-PCR. Cell motility was assessed by scratch tests and drug sensitivity assays were performed *in vitro* and in a xenograft mouse model.

Results: We found that CM derived from *pks E. coli*-infected cells induced EMT in recipient uninfected cells. This was characterized by an increase of Zeb1 and Snail transcription factors involved in EMT, an increase of the mesenchymal marker vimentin and a decrease of the epithelial marker E-cadherin. Furthermore, wound healing was greater in cells receiving CM derived from *pks E. coli*-infected cells. Importantly, EMT led to an increase of resistance of chemotherapeutic drugs 5-fluorouracil and irinotecan. Finally, when cells treated with CM derived from *pks E. coli*-infected cells were engrafted to *nude* mice, they exhibited a higher resistance to irinotecan compare to cells treated with CM derived from Δ*pks E. coli*-infected cells.

Conclusion: Our work demonstrates that colibactin-producing *E. coli* might increase the severity of CCR by inducing EMT which leads to chemotherapeutic drug resistance.

Disclosure: Nothing to disclose

P1029 FECAL INCONTINENCE IN CHRONICALLY CONSTIPATED WOMEN: CLINICAL FEATURE, MANOMETRIC MEASUREMENTS AND PELVIC FLOOR ANATOMICAL ANATOMICAL PATHOLOGIES

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Introduction: Fecal incontinence (FI) and chronic constipation (CC) are not only physically and psychologically disabling symptoms, but also a significant social and public health problem. The pathophysiological basis of combined constipation and fecal incontinence in active women is not fully understood.

Aims and Methods: The aim of the study was to compare clinical, manometric and pelvic floor anatomical pathologies between chronically constipated women with or without fecal incontinence.

In a cross-sectional study, we compared clinical information, anal manometric results and pelvic anatomical pathology as assessed by dynamic pelvic ultrasound in a group of 62 constipated women with FI to that of 207 women with CC without FI

Results: The CC group was older (55 vs 50 years, p = 0.07). The number of vaginal and instrumental assisted deliveries was similar in both groups (2.8 vs. 2.3, p = 0.3; 2.15 vs 1.8, p = 0.3, respectively). The number of pelvic surgeries was similar in both groups. Anal resting and squeeze pressures were significantly lower in the FI group (48 vs. 64, p = 0.001; 97 vs 141, p = 0.03, respectively). Rectal hypersensitivity was more common in the FI group (OR = 1.59, p = 0.05), and dyssynergic defecation was more common in the CC group (0R = 1.8,

p = 0.04); however, the rates of other pelvic floor anatomical pathologies were similar in both groups.
Conclusion: Specific clinical and physiologic parameters define women with coexisting FI and CC.
Disclosure: Nothing to disclose

P1030 INTEGRATIVE ANALYSIS OF GENE MUTATIONS AND DNA METHYLATION IN COLORECTAL SERRATED LESIONS

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Introduction: Recent studies have shown that colorectal serrated lesions, including sessile serrated adenomas (SSAs) and traditional serrated adenomas (TSAs), are precursors of colorectal cancers. However, these molecular mechanisms of carcinogenesis are still not well characterized.
Aims and Methods: To clarify the molecular and clinicopathological characteristics of serrated lesions, we assessed mutations and DNA methylation of cancer-associated genes in these lesions. Seventy-eight patients with colorectal serrated lesions were endoscopically diagnosed and treated in Nagoya City University Hospital, Fukui Prefectural Hospital, and Komatsu Municipal Hospital. Hematoxicilin and eosin-stained slides were examined to confirm the diagnosis by a pathologist who was blinded to the clinical and molecular information. The lesions included TSAs (n = 36), SSAs (n = 18), microvesicular hyperplastic polyps (MVHPs, n = 22), and serrated lesions (MVHP or TSA) with adenoma (n = 2). After extracting DNA from formarin-fixed, paraffin-embedded (FFPE) sections, we performed target exon sequence analyses of 39 genes including frequently mutated genes in colorectal cancers and/or serrated lesions, as well as genes known to be associated with WNT signaling pathway. We also assessed the methylation status of a number of tumor-associated genes including *SFRP1, SFRP2, IGFBP7, SOX5*, *MLH1,* and *SMOC1*, as well as marker genes of CpG island methylator phenotype (CIMP) (*MINT1, MINT2, MINT12, MINT31*, and *CDKN2A*) using bisulfite pyrosequencing. A cutoff value of 15% was used to define genes as methylation-positive. Tumors were defined as CIMP-positive when methylation was detected in three or more out of five methylation markers.
Results: *BRAF* mutations were observed in 64% of TSAs and 78% of SSAs, while *KRAS* mutations were observed in 31% of TSAs and 6% of SSAs, respectively. Mutations in WNT pathway-associated genes including *APC*, *CTNNB1*, *FBXW7*, and *RNF43* were significantly higher in TSAs than SSAs (58% and 28%, respectively, p = 0.046). Additionally, prevalence of CIMP-positive lesions in TSAs and SSAs was not significantly different (44% and 42%, respectively). Notably, frequency of methylation-positive cases of *SMOC1* was significantly higher in TSAs than in SSAs (53% and 0%, respectively, $p < 0.01$).
Conclusion: Significance of gene mutations in WNT signaling pathway components was emphasized in carcinogenesis of colorectal serrated lesions, especially in TSAs. It was confirmed that epigenetic silencing of *SMOC1* was significantly associated with development of TSAs, as a previous report indicated.
Disclosure: Nothing to disclose

P1031 PREDICTION OF ADVANCED METACHRONOUS LESIONS IN COLONOSCOPIC SURVEILLANCE ACCORDING TO GENETIC PROFILE OF ADENOMATOUS AND SERRATED POLYPS

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Introduction: Surveillance of colonic polyps is based on their size, number and pathological features. The role of their genetic profile to predict advanced metachronous lesions (AML) remains poorly investigated.
Aims and Methods: The aim is to study the relation between genetic profile of adenomatous and serrated polyps regarding as risk of AMLs as time to develop them along the surveillance. 308 patients with colonic polyps were consecutively enrolled between 2007 and 2009, and followed until 2014, for this retrospective cohort study. They were divided according to the presence of adenomatous (249 patients) or serrated polyps (59 patients) in the first colonoscopy. 995 polyps were analyzed for somatic mutations on BRAF and KRAS genes using allelic discrimination by real-time PCR and direct DNA sequenciation, respectively. High level of methylation on CpG islands (CIMP-H) was also tested using MS-MLPA. AML was defined by a size higher than 9mm, high-grade dysplasia or villous component for adenomas and size higher than 9mm with any grade of dysplasia or proximal location for serrated lesions. Risk of AML for genetic markers was studied using Chi-square test and logistic regression for univariate and multivariate analysis, respectively. Log-rank test for univariate and Cox-regression model for multivariate analysis were also performed. Logistic and Cox regressions were adjusted by sex, age, previous colorectal cancer, smoking and features of AML in first colonoscopy. P value of 0.05 was considered significant.
Results: Patients were followed up for a median of 36 months (range 5–75). Those ones with adenomatous polyps in the first colonoscopy presented mutations on BRAF and KRAS in 8% and 24% of cases, respectively. 17% contained polyps with CIMP-H pattern. Concerning patients with serrated polyps, mutations on BRAF and KRAS were found in 47% and 36% of cases, respectively, besides 20% of patients with CIMP-H polyps. Only the presence of BRAF-mutations differed between both groups (8% in patients with adenomatous polyps vs 47% in those with serrated polyps; $p < 0.001$). Regarding patients with adenomatous polyps, a higher risk of AML was seen examining KRAS (48% KRAS-mutated vs 29% non-mutated; p = 0.02) in the univariate analysis, with similar results regarding CIMP-H (55% CIMP-H vs 30% non-CIMP; p = 0.008). No association was found with BRAF-mutated ones. Logistic regression showed as KRAS (OR 5.2, 95% CI 1.4–19.8; p = 0.015) as CIMP-H (OR 11.6, 95% CI 2.3–58.4; p = 0.003) as genetic markers of risk for AML. There were found shorter intervals to develop AML in patients with CIMP-H polyps (median of 33 vs 45 months in CIMP-H vs non-CIMP; p = 0.005) in univariate analysis, and also in multivariate (HR 7.9, 95% CI 3.1–20.0; $p < 0.001$). No differences concerning BRAF and KRAS status were seen. Concerning patients with serrated polyps, they showed higher risk of AML (67% CIMP-H vs 22% non-CIMP; p = 0.01) and shorter intervals to develop them (median of 33 vs 51 months in CIMP-H vs non-CIMP; p = 0.045) related to CIMP-H pattern in univariate analysis, but not in the multivariate. No significant results were obtained examining BRAF and KRAS genes.
Conclusion: Presence of CIMP-H and mutations on KRAS in adenomatous polyps associates higher risk of subsequent AML, but only CIMP-H correlates with shorter intervals to their development. In serrated polyps, CIMP-H shows results only in univariate analysis. Genetic profile of polyps emerges as useful tool for colonoscopy surveillance.
Disclosure: There's no conflict of interest of any author

P1032 EMILIN2, A MATRICELLULAR MOLECULE, IMPACTS ON MDSC RECRUITMENT AND MACROPHAGE POLARIZATION IN A MODEL OF COLORECTAL CARCINOGENESIS AND CORRELATES WITH IMMUNOSCORE IN CRC PATIENTS

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Introduction: Inflammation could contribute to carcinogenesis through the activation of immune cells, the release of pro-inflammatory cytokines and the sustained stimulus for epithelial cells to proliferate. In this context, extracellular matrix proteins play a role by modulating cellular adhesion and migration, tumor angiogenesis, and growth factor activation. EMILIN2 is an extracellular matrix molecule playing multifaceted functions in the tumor microenvironment, overall functioning as a tumor suppressive molecule[1,2,3]. Interestingly, EMILIN2 expression is down-modulated by methylation in a number of tumors including colorectal cancer (CRC)[4].
Aims and Methods: Given EMILIN2 function as negative regulator of the Wnt axis[5], a crucial pathway in colon carcinogenesis, we took advantage of the EMILIN2 null mouse model (*Emilin2*$^{-/-}$) to assess its role in the development of CRC. Mice were treated with AOM/DSS to induce CRC. DSS was administered to induce acute inflammation and colitis. Colitis progression and tumor development were assessed by colonoscopy. Histopathological and IHC analyses were performed on colon samples at 1 week for acute inflammation, 12 weeks for colitis and 25 weeks for CRC. Wnt pathway activity was assessed by WB and qPCR. Cytokine analyses were performed through Luminex Screening and qPCR. The inflammatory infiltrate was analysed by flow cytometry and IHC.
Results: Upon AOM/DSS treatment, *Emilin2*$^{-/-}$ mice developed a significantly higher number of tumors compared to control mice. Moreover, tumors from

Emilin2$^{-/-}$ mice were more undifferentiated and at an advanced stage. Contrary to our expectations, the increased number of lesions was not associated with a misregulation of the Wnt signaling pathway. Interestingly, *Emilin2*$^{-/-}$ mice displayed an altered tumor associated inflammatory microenvironment characterized by an higher number of macrophages and granulocytes and an altered expression of many important molecules as IL-10 and Ccl5. Notably, the immune checkpoint proteins PD-1 and PD-L1 were increased in *Emilin2*$^{-/-}$ mice. Moreover, *Emilin2*$^{-/-}$ tumors were characterized by an increased percentage of M2 polarized macrophages displaying low MHCII. *In vitro* analysis confirmed that macrophages isolated from *Emilin2*$^{-/-}$ mice were more prone to acquire an M2 phenotype. Similar alterations in the *Emilin2*$^{-/-}$ model were found during the acute fase of inflammation: mice subjected to DSS treatment alone developed a more severe colitis than *wild type* mice. Interestingly, *Emilin2*$^{-/-}$ mice were characterized by an impaired expression of inflammatory cytokines such as IL-1beta, INF-gamma, TNF-α and IL-10, which was associated with an increased number of myeloid-derived suppressor cells (MDSC) in the colonic mucosa. Consistently, computational analyses of CRC patients datasets highlighted a correlation between EMILIN2 expression levels and the immune landscape characterizing the tumors[6].

Conclusion: The absence of EMILIN2 in the murine model led to the formation of a higher number of colorectal tumors associated with enhanced pro-tumorigenic inflammation. In particular, we found increased expression of the immune checkpoints proteins PD-1 and PD-L1 and a higher percentage of MHCII low macrophages. Moreover, in the very early steps of tumorigenesis, the lack of EMILIN2 expression promoted MDSC recruitment, which could account for the higher tumor number observed in *Emilin2*$^{-/-}$ mice. Preliminary observation highlighted a correlation between EMILIN2 and the traits of the immune microenvironment also in samples from CRC patients, suggesting that EMILIN2 could represent a prognostic marker.

Disclosure: Nothing to disclose

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P1033 MOLECULAR CHARACTERISTICS OF THE DEPRESSED EARLY COLORECTAL CANCERS (DEPRESSED CRC)

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Introduction: The adenoma-carcinoma sequence is generally recognized as a main route of colorectal cancers (CRC). We proposed the presence of depressed and flat colorectal lesions at early phase, and some of these lesions are regarded as "*de novo*" cancers. Depressed cancers have an inclination to invade massively nevertheless the small tumor size, and indicated the severe malignant potentials to metastasize.

Aims and Methods: The aim of this study is to clarify the molecular characteristics of depressed CRC with integrated genomic analysis using next-generation sequencer. We extracted DNA and RNA from 8 submucosal-invasive depressed CRC and 8 submucosal-invasive protruded CRC, and conducted whole exome sequence (WES) and RNA sequence (RNA-seq). We compared the mutation and copy number profile, and expression of RNA using Gene Set Enrichment Analysis (GSEA), which enable to analysis the comprehensive gene expression in multiple molecular pathways, between depressed CRC and protruded CRC.

Results: The results of WES showed that the rates of APC and TP53 mutations were higher in depressed CRC (100%, 75%, respectively) than in protruded CRC (62.5%, 62.5%, respectively). While, the rate of KRAS mutations was lower in depressed CRC (12.5%) than protruded CRC (62.5%) remarkably. The copy number analysis showed that the arm level amplification in 20q, 7p, 7q, and 8q were observed in both cases, however the amplification in 20p, 13p, and 13q arms were observed specifically in depressed CRC (87.5%, 37.5%, and 37.5%, respectively). GSEA clarified that the Epithelial-Mesenchymal Transition (EMT) related genes and angiogenesis pathway related genes were expressed overwhelmingly in depressed CRC than protruded CRC.

Conclusion: According to the genomic analysis, we validated the presence of the depressed early CRC, and unveiled the difference with protruded CRC. In comparison to the protruded CRC, the depressed CRC showed the APC and TP53 mutations and high copy number amplifications, which might activate EMT and angiogenesis-related genes and exacerbate the clinical outcome of cases with depressed CRC.

Disclosure: Nothing to disclose

P1034 ANALYSIS OF METHYLATION FIELD DEFECT IN SERRATED POLYPOSIS SYNDROME

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Introduction: Serrated polyposis syndrome (SPS) is characterized by the development of multiple serrated polyps throughout the colorectum and an increased CRC risk. Etiology of this disease remains largely unknown, with scarce evidence of familial aggregation. Aberrant promoter hypermethylation is associated with the serrated pathway of carcinogenesis, and the existence of a methylation field effect in the normal mucosa of SPS patients has been suggested. However, comprehensive analysis of methylation in this setting is lacking.

Aims and Methods: We aimed at investigating the methylation profile of normal colorectal mucosa of patients with SPS and healthy subjects to better understand the etiology of this disease. We analyzed the methylation status of the normal colonic mucosa in two segments of the colon (proximal and distal to splenic flexure) using Illumina Infinium 850k array in 30 cases with SPS (14 with CRC and 16 without CRC) and 10 healthy individuals (normal colonoscopy). We calculated differentially methylated CpGs (DMCs; Δ20%) for the comparison of normal mucosa from SPS vs. healthy individuals (FDR $<$ 0.05) using ChAMP software, adjusting for age, sex, location and tobacco use. Differential methylation within mucosa from patients with SPS was analyzed controlling for potential confounders (age; sex; CRC).

Results: Overall, we found that patients with SPS display a differential and heterogeneous methylation profile in their normal mucosa compared to healthy individuals, who showed an homogeneous methylation profile. When comparing SPS with and without CRC, we did not observe differences in their methylation profiles (n.s. FDR for Δ20% DMCs), and thus we analyzed them together for further analysis. In SPS patients we found that mucosas from the proximal colon display more DMC and more hypomethylation than distal mucosas (proximal colon: 3,017 DMC, 954 hypermethylated and 2,063 hypomethylated; distal mucosa: 149 DMC, 116 hypermethylated and 33 hypomethylated). Up to 18% of the DMC were located in promoter regions (15% of the hypomethylated DMCs; 18% of the hypermethylated), and a great proportion of the remaining DMC allocate at intronic and intergenic regions (77% of the hypomethylated DMC and 73% of the hypermethylated DMC).

Interestingly, when we studied the cellular pathways involving the nearest genes to DMCs we found a significant enrichment in cancer-related pathways and MAP-kinases pathways, including *PRDM8*, *PRDM6*, *MAD1L1* and *DIP2C*.

Conclusion: Patients with SPS display a methylation field defect in their normal mucosa, especially in the proximal colon and mainly based on hypomethylation. Methylation profiles do not differ in patients with and without CRC. Aberrant methylation occurs in genes involved in CRC-related pathways suggesting a role in the carcinogenesis. Analyses for validation, including methylation and expression experiments in an independent cohort of patients, are ongoing.

Disclosure: Nothing to disclose

P1035 COMPARISON OF IMMUNOPROFILING BETWEEN COLITIS-ASSOCIATED CANCER AND SPORADIC COLORECTAL CANCER

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Introduction: Immunoprofiling is useful for predicting prognosis and provides a target for immunotherapy in various malignancies. The immune system of colitis-associated cancer (CAC) can be different from that of sporadic colorectal cancer (CRC) because chronic inflammation contributes to the pathogenesis of CAC. A quantitative multispectral imaging system, which allows simultaneous detection

of several immune markers, is a novel method to comprehensively examine the tumor immune environment.
Aims and Methods: The aim of our study is to compare the expression of immune cells in CAC and in sporadic CRC by using this method and to assess the clinical implications of immunoprofiling in CAC. The tumor specimens from 24 CAC patients (8 Crohn's disease and 16 ulcerative colitis) and 48 sporadic colorectal cancer patients, matched by age, sex, and tumor location to CAC, were included in the analysis. The expressions of $CD3^+$, $CD8^+$, $Foxp3^+$ or programmed death-ligand 1 $(PD\text{-}L1)^+$ cells at the invasive margin of tumor tissue were evaluated by quantitative multispectral imaging, and the mean counts per mm^2 of immune cells between CAC and sporadic CRC were compared.
Results: CAC showed more advanced stage (stage IV, 33.3% *vs.* 8.4%; $p = 0.015$) and higher disease-related deaths (41.7% *vs.* 14.6%; $p = 0.018$) compared to sporadic CRC. The $CD3^+$, $CD8^+$, $Foxp3^+$, and $PD\text{-}L1^+$ cells of the CAC group were significantly less dense than those of the sporadic CRC group as measured by both the phenotyping method and the co-expression method. The co-expression densities of $CD3^+Foxp3^+$ and $CD8^+Foxp3^+$ cells were significantly lower in CAC than in sporadic CRC (all, $p < 0.001$). In the CAC group, the expressions of $CD3^+$, $CD8^+$, and $Foxp3^+$ cells were significantly lower in patients with stage IV than in those at stages I-III. In addition, the patients with high expression of $CD3^+$ and $CD8^+$ had better overall survival than the patients with low expression of those cells.
Conclusion: The immune profiling pattern of CAC is different from that of sporadic CRC, indicating distinct disease phenotypes. Immunoprofiling can be helpful for the evaluation of clinical prognosis in CAC and sporadic CRC.
Disclosure: Nothing to disclose

P1036 CLINICOPATHOLOGIC FEATURES, MICROSATELLITE INSTABILITY STATUS AND CHARACTERISTIC MOLECULAR ALTERATIONS OF COLORECTAL SIGNET RING CELL CARCINOMAS

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Introduction: Signet ring cell carcinoma (SRCC) is an uncommon subtype of colorectal carcinoma (CRC), accounting for only 0.1–2.4% of all CRCs. By definition of World Health Organization classification, SRCC consists of more than 50% of tumor cells with signet ring cell morphology. Colorectal SRCCs are often diagnosed at an advanced stage and in young aged patients showing a poor prognosis with reported 5-year overall survival rate of 40%. Although clinicopathologic features of colorectal SRCCs are relatively well known, molecular alterations and microsatellite instability (MSI) status of this variant has not well elucidated. We investigate further clinicopathologic findings, MSI status and overall somatic mutations of SRCCs revealed by next-generation sequencing (NGS).
Aims and Methods: We retrospectively reviewed cases of CRCs with signet ring cell component and selected 203 cases of SRCC for review and 80 SRCCs subject to molecular profiling using NGS on the Ion Torrent PGM and Iron Proton (Thermo Fisher Scientific). We examined substitutions and small indels in 50 cancer-related genes using Ion ampliseq Cancer Hotspot and Iron ampliSeq Comprehensive Cancer panels. Sequence alignment and analysis were performed using Torrent Suite software (Thermo Fisher Scientific) and lab-developmented software (OncoSeek). MSI analysis was performed by immunohistochemistry followed by multiplex polymerase chain reaction (PCR) with seven quasi-monomorphic mononucleotide repeat markers.
Results: Study patients comprised of 128 (63%) males and 75(37%) females aged 52.4yr. Twenty-two (11%) patients have a history of inflammatory bowel disease (7%) or Lynch's syndrome (4%). Histologically, colorectal SRCCs occurred frequently in ulcerated mass (88%) and consists of two subtypes; mucin-rich and mucin-depleted tumors (48% and 52%). Lymphovascular invasion (91%), extramural venous invasion (80%), tumor deposits (44%), positive margin status (14%), lymph node metastasis (88%) and distant metastasis (40%) at the time of diagnosis were more frequently identified in 203 colorectal SRCCs (all, $p < 0.05$) compared to those of the 200 conventional CRCs. Twenty-four (12%) SRCCs revealed high level of microsatellite instability by mismatched repair proteins subsequently confirmed by MSI PCR. Molecular alterations revealed by next-generation sequencing demonstrated low frequencies of common oncogenic driver mutations including *KRAS* ($p < 0.001$), *APC* ($p < 0.001$), *TP53* ($p = 0.0018$) and *PIK3CA* ($p < 0.001$) compared to those of 200 conventional CRCs.
Conclusion: In our study, patients with colorectal SRCCs have shown to be significantly related with underlying inflammatory bowel disease or Lynch's syndrome, a male predominance, young age onset, predisposition to ulcerated mass and consist of mucin-rich or depleted tumors. Colorectal SRCCs revealed worse histologic factors related with a poor prognosis such as high frequencies of lymphovascular invasion, extramural venous invasion, presence of tumor deposits, positive resection margin and lymph node and distant metastasis compared to those of conventional CRCs. Overall, colorectal SRCC has shown 12% of MSI-high tumors and low frequencies of main oncogenic mutations; *KRAS*, *APC*, *TP53* and *PIK3CA*. This distinct activating or inactivating mutations of these genes suggest different therapeutic approaches and promising consideration of targeted therapy by inhibiting related pathways in patients with advanced colorectal SRCC.
Disclosure: Nothing to disclose

P1037 CLINICOPATHOLOGICAL DIFFERENCES BETWEEN RIGHT AND LEFT-SIDED T1 COLORECTAL CANCER: A SINGLE CENTER RETROSPECTIVE STUDY

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Introduction: It has been reported that the clinicopathological features and prognosis of right- and left-sided advanced colorectal cancers (CRCs) are different. However, there are few reports on these differences in T1 CRCs. In this study, we aimed to compare the clinicopathological features of right- and left-sided T1 CRCs.
Aims and Methods: Subjects were 738 cases with T1 CRCs undergoing surgical resection with lymph node dissection between April 2001 and April 2017 at Showa University Northern Yokohama Hospital. Of these, 214 cases were right-sided (cecum to transverse colon), and 524 cases were left-sided (descending colon to rectum). Analyzed clinicopathological features included patient age, sex, initial treatment, tumor size, morphology, invasion depth, histological grade, lymphatic invasion, vascular invasion, tumor budding, and lymph node metastasis.
Results: Right-sided T1 CRCs showed significantly lower rates of lymph node metastasis (right-sided 4.7% vs. left-sided 11.5%, $p < 0.05$) and were accompanied by lower rates of lymphatic invasion (right-sided 34.1% vs. left-sided 41.4%, $p < 0.05$) and initial surgical cases (right-sided 36.4% vs. left-sided 50.2%, $p < 0.05$). In contrast, right-sided T1 CRCs showed significantly higher rate of depressed-type morphology (right-sided 35.0% vs. left-sided 27.7%, $p < 0.05$) and poorly differentiated carcinomas/mucinous carcinomas (right-sided 10.7% vs. left-sided 3.4%, $p < 0.05$). Patients with right-sided T1 CRCs were older (right-sided 67.0 ± 11.7 years vs. left-sided 64.6 years ± 11.0 years, $p < 0.05$). No significant difference was found between the other factors.
Conclusion: Right-sided T1 CRCs exhibited significantly lower rates of lymph node metastasis than left-sided T1 CRCs, followed by lower rate of lymphatic invasion. This may influence the prognosis or management of these lesions.
Disclosure: Nothing to disclose

P1038 RISK FOR LYMPH NODE METASTASIS AND RECURRENT CANCER IN NON-PEDUNCULATED T1 COLORECTAL CARCINOMA STRATIFIED FOR CONSENSUS MOLECULAR SUBTYPES AND THE IMMUNOSCORE

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Introduction: Based on current histologic risk stratification, most T1 colorectal carcinomas (CRC) are classified as high-risk T1 CRCs. However, the majority of these patients are not found to have lymph node metastasis (LNM) when referred for surgery, and could – in hindsight – also have been treated with endoscopic resection. In advanced CRC, the mesenchymal consensus molecular subtype (CMS-4) and a low Immunoscore have been associated with poor prognosis.[1,2] In this study, we aimed to evaluate whether molecular- and immune-based tumor

subtypes could be of value for risk stratification in patients with non-pedunculated T1 CRC.

Aims and Methods: A multicenter case-cohort study was performed. Data from 653 patients with non-pedunculated T1 CRC (median follow-up time: 46 months; IQR 19–76) treated with surgery, diagnosed from January 2000 through December 2014, were collected from 13 Dutch hospitals. Primary endpoint was adverse outcome, defined as LNM or recurrent cancer. The case-cohort included a random sample of 50% of the cohort and all patients with the outcome outside the random sample. H&E stained slides were reviewed by a blinded expert pathologist on conventional histological risk factors (i.e. poor differentiation, deep submucosal invasion, (lympho-) vascular invasion, and tumor budding). Tissue microarray samples were immunostained to determine the Immunoscore (I-low or I-high) and the CMS (CMS-1, CMS-2-3 or CMS-4). Uni- and multivariable Cox proportional hazard models for case-cohort data were performed to evaluate the association between the CMS-classification and Immunoscore and adverse outcome.

Results: The distribution of the CMS-classification was: CMS-1: 7%, CMS-2-3: 91%, and CMS-4: 2%. I-low was observed in 36% of patients. Although no significant association was observed between the CMS-classification and the Immunoscore ($p = 0.40$), a trend was observed towards higher Immunoscores for CMS-1 vs the other molecular subtypes (p-trend = 0.07). The case-cohort included 60 patients with an adverse outcome (46 patients with LNM and 22 with recurrence among which 5 patients with both LNM and recurrence). Risk for an adverse outcome was 6%, 14% and 33% for CMS-1, CMS-2-3 and CMS-4, respectively, and 11% and 18% for I-high and I-low, respectively. CMS-4 was associated with an increased risk for adverse outcomes (HR 3.9, 95% CI 1.1–13.7, $p = 0.04$; reference CMS-2-3), which remained after adjusting for conventional risk factors (adjusted HR 4.6; 95% CI 1.3–16.4, $p = 0.02$; reference CMS-2-3). In univariable analysis, I-low showed a trend towards increased risk for adverse outcomes (HR 1.6, 95% CI 1.0–2.8, $p = 0.08$). However, no significant association was observed for I-low when adjusting for conventional risk factors (adjusted HR 1.3; 95% CI 0.7–2.3, $p = 0.44$).

Conclusion: Non-pedunculated T1 CRCs with CMS-4 have an increased risk for LNM and recurrent cancer, in line with the poor prognosis of this subtype in advanced CRC. In contrast to advanced CRC, the aggressive mesenchymal subtype (CMS-4) has a very low prevalence in early CRCs which might limit its use for risk stratification in these patients. Our results suggest limited additional value of the Immunoscore for risk stratification in T1 CRC.

Disclosure: Nothing to disclose

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P1039 LIQUID BIOPSY IN COLORECTAL CANCER: DECIPHERING NOVEL NON-INVASIVE METHYLATION BIOMARKERS FOR COLORECTAL CANCER SCREENING IN SERUM CIRCULATING CELL-FREE DNA

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Introduction: Colorectal cancer (CRC) diagnosis at early stages associates with good prognosis and reduced mortality rates, while detection and removal of premalignant advanced adenomas (AA) result in the reduction of CRC incidence [1]. Invasive approaches for CRC screening, such as colonoscopy, have low participation rates and high cost. On the other hand, non-invasive procedures like faecal immunological test have the advantage of increased acceptance, though sensitivity for proximal colorectal tumours and AA is moderate to low [2]. Thus, there is a clear demand for novel non-invasive tests for the early detection of CRC and AA, to be used in population-wide screening programs.

DNA methylation detected in liquid biopsies, such as serum circulating cell-free DNA (cfDNA), is a promising source of non-invasive biomarkers, because it has been demonstrated that cfDNA reflects the aberrant methylation events occurring in neoplastic and tumour cells [3].

Aims and Methods: In a previous work we reported that, when using cfDNA, a sample pooling strategy offers a new affordable approach for methylation biomarker discovery [4]. In this study, applying the sample pooling strategy, we aim to identify novel non-invasive methylation biomarkers for the early detection and screening of colorectal advanced neoplasia (AN: CRC or AA).

We extracted cfDNA from serum samples from 130 individuals with no colorectal neoplasia (including individuals with no colorectal findings, benign pathologies and non-advanced adenomas) and from 150 advanced neoplasia cases (comprising patients with proximal AA, distal AA, and CRC stage I-IV). Pooled samples were prepared for each pathological group using equal amounts of cfDNA from 10 individuals, sex-, age- and recruitment hospital-matched. DNA methylation levels of 866,836 CpG positions across the genome were measured with the MethylationEPIC array. Bioinformatics preprocessing and statistical analyses were conducted with methylation specific R/Bioconductor packages.

Results: The epigenome-wide analysis of serum cfDNA revealed 376 differentially methylated positions (DMPs) at 10% false discovery rate, between no neoplasia and advanced neoplasia cases, mostly of which (86.7%) were hypermethylated in AN. Some of the differentially methylated CpG sites were found within 49 differentially methylated regions. Unsupervised clustering analyses showed that differential methylation patterns could distinguish advance neoplasia samples from no neoplasia controls.

We applied the Statistically Equivalent Signature algorithm [5] for feature selection and we identified 3,256 combinations of 118 DMPs with statistically equivalent predictive value for "no neoplasia vs advanced neoplasia" classification. We used cross-validation to select a subset of 30 CpG sites as the most robust and predictive candidate set for biomarker validation.

Conclusion: We found a differentially methylated signature between no neoplasia and advanced neoplasia groups using pooled serum cfDNA, obtaining promising biomarker candidates for colorectal cancer screening. The diagnostic performance of our novel non-invasive methylation candidates should be further evaluated in an independent cohort.

Disclosure: Nothing to disclose

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P1040 COLORECTAL CANCER AND EXPERIENCE IN TESTING FOR LYNCH SYNDROME IN A WEST LONDON HOSPITAL

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Introduction: Colorectal cancer (CRC) causes over 16000 deaths every year and it is the second most common cause of cancer death. NICE guideline DG27 recommends universal testing for Lynch Syndrome (LS) at diagnosis of colorectal cancer, by testing the CRC for mismatch repair (MMR) status, a hallmark of the disease.

Aims and Methods: We collected data prospectively from Nov 2016 to December 2017 of consecutive newly diagnosed CRC patients at West Middlesex University Hospital (WMUH) in London. CRCs were universally screened for tumour features suggestive of LS (Defective MMR, or dMMR) with immunohistochemistry. We also collected clinicopathological data including age at diagnosis, stage, tumour site, histological findings and MMR tumour-status. Statistical analysis was performed using chi-square test and 2 tailed T test for binary and continuous variables respectively.

Results: A cohort of 123 consecutive CRC patients were universally tested for dMMR. Twelve patients (9.8%) were MMR-deficient of which only 6 (50%) were predicated by the Bethesda Criteria. 11/12 dMMR CRCs were early stage tumours (Dukes' A or B, $p = 0.002$), and in 20 Dukes' B CRCs in patient under 70 years of age, the result was directly relevant to personalised treatment with 5-FU based chemotherapy. The median age in patients with normal or abnormal MMR IHC was 64.6 years and 68.3 years respectively (p 0.41). With regard to histological features: mucinous tumours were more frequently manifested dMMR (p 0.0052), with the presence of this, signet ring cells or a lymphocytic response predictive of dMMR CRC (p 0.023). In all 12 patients with dMMR the cancer was located in the right colon (p 0.00001). MMR germline mutations were

found in a total of 4 patients of which 2 (50%) had mutation of *MLH1*, in 1 case (25%) of *MSH2* and in 1 case (25%) of *MSH6*.
Conclusion: Our results demonstrate that universal testing is feasible and effective in the UK. There were significant differences with regard to dMMR CRC site, stage and histological features compared to proficient MMR CRCs. Our data also indicates the importance of genetic testing and personalised oncological care as we were able to identify patients that may have not be selected for MMR testing by the Bethesda criteria.
Disclosure: Nothing to disclose

P1041 SOX21 GENE PROMOTER METHYLATION ANALYSIS IN PERIPHERAL BLOOD MONONUCLEAR CELLS IS SENSITIVE PREDICTOR OF COLORECTAL CANCER

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Introduction: Early detection of colorectal cancer (CRC) has considerable value in treatment and prognosis. The aim of this study was evaluating predictive value of methylation SOX21 gene's promoter testing for diagnosis of CRC.
Aims and Methods: This cross-sectional study was done on 64 eligible patients with colorectal cancer (case group) and 64 healthy volunteers. Then 5cc of blood sample was taken and DNA was extracted. DNA was extracted using GeNet Bio DNA extraction kit. The quality and quantity of extracted DNA assessed by spectrophotometry method in 260 and 280 nm wavelength and electrophoresis in agarose gel %1After primer designation methylation-quantification was assessed using Real-time PCR, and expressed in two groups. The Chi-square test performed on both groups using SPSS V.20 software.
Results: There were 32 (50%) and 28 males (43.8%) in case and control group respectively (p-value = 0.62). The mean age of case and control group were 55.9 ± 16.6 and 56.7 ± 10.7 years respectively (p-value = 0.8). The value of methylation of SOX21 gene's promoter in case and control group were 71.6% ± 20.1% and 31.9% ± 11.3% respectively ($p < 0.001$) with sensitivity and specificity of %81.3 and %71.9 respectively. Positive predictive value and negative predictive value were %74.3 and %79.3 respectively.
Conclusion: The quantity of SOX21 gene promoter methylation in the genomic DNA of peripheral blood samples can be used as a good screening test for early diagnosis of CRC.
Disclosure: Nothing to disclose

P1042 CORRELATION BETWEEN LONG-TERM FUNCTIONAL OUTCOME AND MR IMAGING PATTERNS OF RESPONSE IN CLINICAL COMPLETE RESPONDERS UNDERGOING WAIT-AND-SEE AFTER CHEMORADIOTHERAPY FOR RECTAL CANCER

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Introduction: Patients who are managed non-operatively with a 'wait-and-see' policy after chemoradiotherapy are typically monitored using a combination of imaging (MRI) and endoscopy. On MRI, morphologic patterns indicating a complete response can vary from a completely normalised rectal wall to various degrees of fibrotic scar tissue.
Aims and Methods: Aim of this study was to study whether morphologic imaging patterns of response are related to long-term functional outcome, assessed in terms of the Vaizey-score, a 0–24 point score on bowel function/faecal incontinence.
N = 68 patients were retrospectively analysed. All patients were included in a wait-and-see programme and had a sustained clinical complete response (median FU 34 months; range 16–62). Patients underwent follow up with MRI 3–6 monthly as part of the wait-and-see programme. Morphology of the rectal wall was assessed by two radiologists in consensus on the various MRIs and classified according to 4 patterns: [1] no fibrosis (= normalised rectal wall), [2] minimal fibrosis, [3] thick but regular fibrosis or [4] irregular/spiculated fibrosis. Long-term functional outcome was assessed using the Vaizey-score, which was acquired using questionnaires after 1–2 years of FU. Mean Vaizey-scores were compared between the 4 morphological patterns.
Results: 5 patients showed no fibrosis, 45 minimal, 15 thick and 3 irregular/spiculated fibrosis. Mean Vaizey-score was 1.6 for the patients with no fibrosis versus 4.5/3.9/4.0 for the patients with minimal/thick/irregular fibrosis, respectively (p = 0.56 when comparing the 4 individual patterns; p = 0.24 when comparing the 3 patterns with fibrosis combined to the no fibrosis group). No significant differences in Vaizey scores were observed amongst the different fibrosis patterns, although there was a slight trend towards lower scores for patients with only minimal fibrosis, particularly in patients who originally presented with distal rectal tumours (≤3 cm from the anorectal junction) where the mean Vaizey-score was 4.7 for the minimal fibrosis patients versus 6.5 for the other fibrosis patterns (p = 0.198).
Conclusion: Rectal cancer patients with a clinical complete response after CRT who show a normalised rectal wall without any signs of fibrosis on MRI appear to have a more favourable functional outcome in terms of incontinence and bowel function compared to patients with visible fibrosis, although results did not reach statistical significance in this small patient cohort.
Disclosure: Nothing to disclose

P1043 THE VALIDITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION WITH SMALL-CALIBER ENDOSCOPE FOR THE LESIONS SPREADING TO APPENDIX ORIFICE

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Introduction: The difficulty of colorectal endoscopic submucosal dissection (ESD) sometimes depends on the location. The lesion spreading to the appendix orifice is one of the most difficult location, because the working space during ESD is very narrow and it is hard to confirm a distal border of the lesion invading the vermiform appendix. From the view point of the tip diameter size, we consider small-caliber endoscopes (GIF-Q260J, tip diameter 9.9mm or PCF-PQ260L, tip diameter 9.2mm), which can go into the vermiform appendix easier, are more efficient than conventional therapeutic colonoscopy (PCF-Q260JI, tip diameter 10.5mm). In this study, we evaluated the efficacy and the safety of small-caliber endoscope for ESD of lesions spreading to appendix orifice.
Aims and Methods: We retrospectively reviewed 341 lesions in cecum performed ESD at Omori Red Cross Hospital and NTT Medical Center Tokyo from May 2011 to December 2017. Among them, 36 lesions were spreading to appendix orifice. We classified according to the scope and compared the treatment outcomes.
Results: 17 cases treated by conventional scope (PCF-Q260JI) (C group), and 19 cases treated by small-caliber scope (GIF-Q260J or PCF-PQ260L) (S group) were enrolled. There was no significant differences between C group and S group in morphological type (Is/ IIa/ LST-G/ LST-NG = 1/8/8/0 vs. 0/13/5/1), histology of tumor (adenoma/ cancer/ SSA/p = 5/4/8 vs. 9/4/6), fibrosis (8 vs. 7), tumor diameter (29.6 ± 12.5mm vs. 29.4 ± 12.3mm), en bloc resection rate (100% vs. 100%), and resection rate of the margin negative (88.2% vs. 100%). With respect to complications, there were 2 cases of perforation in C group (0 case in S group). Mean procedure time was significantly shorter in S group (66.5 ± 42.8min vs. 46.1 ± 18.3, $p < 0.05$). There was 1 case that we ceased ESD for the flat elevated lesion spreading to appendix orifice because the border of lesion could not be confirmed with PCF-Q260JI and succeeded the procedure with PCF-PQ260L later. There was no recurrence and delayed appendicitis in mean follow-up period 26.3 months.
Conclusion: ESD with small-caliber endoscope for the lesions spreading to appendix orifice, especially for the lesions of that we could not confirm the border, can be effective and safe.
Disclosure: Nothing to disclose

P1044 THE PREDICTORS OF SEVERE SUBMUCOSAL FIBROSIS IN PATIENTS UNDERGOING COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Although colorectal endoscopic submucosal dissection (CESD) has been spread as an effective therapy for epithelial neoplasms, its application to lesions with severe fibrosis is difficult because of technical difficulties and risks of complications.
Aims and Methods: This study aimed to investigate the predictors of severe submucosal fibrosis in CESD. From April 2012 to February 2018, consecutive 457 lesions were performed CESD at Omori Red Cross Hospital. Submucosal tumors and non-neoplastic tumors were excluded and 399 lesions were evaluated retrospectively. The degree of submucosal fibrosis was determined during ESD procedures and classified as F0 (no fibrosis), F1 (mild fibrosis), or F2 (severe fibrosis) and we divided the lesions into two groups, group F (F2) and group N (F0/1). We investigated the clinical backgrounds, features of tumors, and

preoperative procedures (biopsy, local injection, tattooing), and analyzed the predictors of severe submucosal fibrosis. We also evaluated the safety of performing CESD to lesions with severe fibrosis by reviewing the postoperative courses and outcomes of the patients. We defined that lesions step over folds were called ''over the fold lesions'' and Ip or Isp lesions exceeding 30mm were called ''large protruded lesion''. In addition, recently we proposed Double Tunnel Method (DTM) which could resect lesions with severe fibrosis or with muscle retracting sign (Chiba H et al. *Endoscopy*, 2018 in press) and we evaluate the feasibility of the new method.
Results: 19 lesions (4.8%) were assigned to group F (66.9 ± 12.1 years old), and 380 lesions (95.2%) were assigned to group N (69.5 ± 11.2 years old). Characteristics of the patients (age, sex, BMI and comorbidities) were similar. With respect to the features of the lesions, over the fold lesions were 12 (63.2%) in group F and 107 (28.2%) in group N ($p = 0.003$). Lesions with tattooing before ESD were 3 (15.8%) / 2 (0.5%), large protruded lesions were 7 (36.8%) / 7 (1.8%), lesions over 50mm in size were 5 (26.3%) / 22 (5.8%), and cancers with submucosal invasion were 9 (47.4%) / 30 (7.9%) in group F and N respectively ($p < 0.01$). On the other hand, the rate of lesions performed biopsy or local injection, and local recurrence were similar. The lesion size was 36.2 ± 15.9 mm in group F, and 28.2 ± 14.0 mm in group N. Multivariate analysis (Variables were included in the multivariate model if the p value was < 0.10 on univariate analysis) showed the predictors were lesions over the fold, lesions with preoperative tattooing, and large protruded lesions. Postoperative courses were similar between two groups. ESD procedure time was 134.2 ± 69.0 min in group F, and 42.1 ± 32.1 min in group N ($p < 0.01$). En bloc resection rate and curative resection rate (%) were 94.7 / 57.9 in group F, and 100 / 96.6 in group N ($p < 0.05$), but there were no differences in complication rate between two groups. DTM was done for two cases safely.
Conclusion: Lesions over the fold, lesions with preoperative tattooing, and large protruded lesions might be the predictors of severe submucosal fibrosis. DTM could be an effective treatment for them.
Disclosure: Nothing to disclose

P1045 USEFULNESS OF HYBRID ENDOSCOPIC SUBMUCOSAL DISSECTION USING MULTIFUNCTIONAL NEW DEVICE

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Introduction: Hybrid endoscopic submucosal dissection (ESD) was developed as relatively easier procedure compare of colorectal ESD that still remains technically difficult. Hybrid ESD has advantage both ESD and EMR because the snaring is performed after mucosal incision and submucosal dissection. However, cost is one of the problem since it needs ESD device and snare. In this study, we evaluated the efficacy of hybrid ESD using the new device, SOUTEN, that has 1.5mm needle-knife at the top of loop.
Aims and Methods: We retrospectively reviewed lesions treated at Omori Red Cross Hospital and NTT Medical Center Tokyo from April 2012 to February 2017. We compared 33 lesions performed hybrid ESD (Hybrid group) and 33 lesions performed ESD (ESD group), those were matched by location, tumor diameter, and macroscopic type. Indication of hybrid ESD is mucosal tumor 20–30mm diameter that could be snared en bloc. We excluded obvious submucosal invasive cancer, recurrent tumor, and lesion with severe scar.
Results: The tumor locations were as follows: 7 were in cecum, 11 were in ascending colon, 6 were in transverse colon, 3 were in descending colon, 2 were in sigmoid colon, 4 were in rectum. Morphological type was that LST-G-H was 2, LST-G-M was 2, LST-NG-FE was 26, and LST-NG-PD was 3 in each group. The mean diameter of Hybrid group and ESD group was 22.8 ± 4.4mm and 23.0 ± 7.2mm, respectively. Mean procedure time was significantly shorter in Hybrid group (13.2 ± 6.6min vs. 34.4 ± 21.8min, $p < 0.01$). There was no significant difference in fibrosis (3 vs. 4) and pathological diagnosis (adenoma/ mucosal cancer = 10/23 vs. 11/22). En bloc resection was 100% in both groups. The mean hospitalization was significantly shorter in Hybrid group (4.9 ± 1.7 days vs. 6.5 ± 1.1 days, $p = 0.020$). The complications were not significantly different between the two groups: 1 vs. 0 episodes of bleeding, and there was no perforation.
Conclusion: It was considered that hybrid ESD using the new device, SOUTEN, has efficacy for reducing the procedure time and hospitalization.
Disclosure: Nothing to disclose

P1046 RECURRENT AND SECOND PRIMARY CANCERS AT THE ONE YEAR SURVEILLANCE COLONOSCOPY FOLLOWING CURATIVE COLORECTAL CANCER RESECTION

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Introduction: After curative resection of colorectal cancer (CRC), postoperative surveillance is aimed at reducing disease specific morbidity and mortality by early detection of recurrent or second primary cancers. Even though endoscopic surveillance has become a routine part of clinical practice, controversy exists on the timing of the first postoperative colonoscopy. Several studies have reported the highest incidence of CRC within two to three years after surgery, reason why most guidelines now recommend a one year surveillance interval after resection.
Aims and Methods: To assess the yield of CRC at the one year surveillance colonoscopy after CRC resection.
Retrospectively, files of patients having undergone a curative surgical resection of a first CRC between June 2013 and April 2016 were checked for eligibility in four hospitals. Patients were included in the database when a complete clearing colonoscopy was performed prior to surgery and when the interval between the pre- and postoperative colonoscopy was 6–20 months. Patients with hereditary CRC or inflammatory bowel disease were excluded. Data were collected on patient demographics, quality of colonoscopy, baseline CRC characteristics, and adenomas and serrated polyps detected during the preoperative colonoscopy and one year surveillance colonoscopy. A sample size of 571 individuals was needed to assess whether the CRC yield exceeded the 0.5% yield of CRC of primary colonoscopy screening. A multivariable logistic regression was performed to identify risk-factors associated with finding advanced neoplasia (*i.e.* CRC, advanced adenomas or advanced serrated lesions) at follow-up.
Results: Five-hundred seventy-two patients (54.9% male, mean age 66.2 (±9.9) years) met the inclusion criteria and were enrolled in the study. After a mean surveillance interval of 13.7 (±2.8) months, 10/572 (1.7%, 95% CI: 0.7–2.8%) were diagnosed with CRC. Of these, five were second primary cancers and five were recurrences at the anastomosis. The second primary CRCs encompassed mostly T3 and T4 tumours (4/5; 80%), of which two qualified for palliative treatment only. In two of these five patients a polyp had been resected at the preoperative colonoscopy in the same segment as the second primary cancer (*i.e.* 25mm tubulovillous adenoma with low-grade dysplasia (clear resection margin) and 8 mm hyperplastic polyp). Of the recurrent CRCs, 4/5 (80%) were either T3 or T4, and one of these qualified for palliative treatment only. Resection margins of the baseline CRC were clear in all five patients with recurrent CRC. In 11.4% (95% CI: 8.9–13.8%) of all patients included in the study advanced neoplasia was detected at the one-year surveillance colonoscopy. Synchronous baseline advanced neoplasia was a risk-factor for finding advanced neoplasia at follow-up.
Conclusion: The yield of CRC at the one year surveillance colonoscopy after CRC resection was 1.7% (95% CI: 0.7–2.8%). This concerned recurrences as well as second primary tumours, which were often of advanced stage. The high yield justifies the increased colonoscopy demand of one-year surveillance interval.
Disclosure: G.A. Meijer: Exact Sciences and Sysmex: provision of materials, equipment or (sample) analyses. E. Dekker: FujiFilm: equipment on loan, research grant, personal consultation-fee; Olympus: equipment on loan, research-grant. Other authors: nothing to disclose.

P1047 ENDOSCOPIC RESECTION OF T1 COLORECTAL CANCER – INFLUENCE OF THE RISK FACTORS ON DECISION-MAKING AND PROGNOSIS

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Introduction: Colon lesions diagnosed as T1 colorectal cancer (CRC) might be treated only with an endoscopic approach. Additional surgery or surveillance depends on the presence of high-risk factors for lymph node metastasis (LNM). The follow-up strategy for these patients remains controversial.
Aims and Methods: We intend to know the influence of histopathological risk factors on therapeutic offering and the overall prognosis of patients with resected T1 CRC at our unit.
Prospective cohort study of T1 CRC lesions endoscopically removed between January/2013 and January/2018 and in follow-up at our unit. ''High-risk lesion'' if at least 1 of the criteria: histological high grade, lymphovascular invasion,

budding, Kikuchi-sm2/3 or Haggitt-4, deep submucosal invasion > 1000μm, distance to margin < 1mm.
Results: Resected 92 lesions in 92 patients (67% male, age 65 ± 10.5 years). Mostly pedunculated (65.2%), mean size 19 ± 1 mm; Left colon in 89%, particularly in sigmoid colon (n = 53); Histological high grade – 11%; lymphovascular invasion – 16%; Haggitt-4 in 4 lesions; Kikuchi-sm2/3 in 15 lesions; Median distance to margin – 1.5 mm.
Median follow-up time of 36 months. 56.5% (n = 52) categorized as ''High-risk lesion'', with 30 patients undergoing surgery and 22 surveillance due to patient choice or relevant comorbidities. In the patients intervened surgically residual tumor in 13% (n = 4). Disease progression confirmed in 6 cases (6.5%), all ''High-risk lesion'' (11.5% vs. 0%; p = 0.03); From those, 4 had surgery and 2 were on endoscopic surveillance (13% vs. 9%; p = 0.08). Two deaths reported, 1 ''high-risk'' and 1 ''low-risk'' patient (2% vs. 2.4%; p = 1). On multivariable analysis lymphovascular invasion presented as the only statistically significant criteria for disease progression (OR 6.2, IC 95% 1.1–34.2).
Conclusion: Endoscopic resection appears to be effective on treating low-risk lesions and we confirm the risk of disease progression on high-risk lesions. In our sample, lymphovascular invasion has a major influence in the prognosis. More studies are needed to optimize decision-making and follow-up strategy to offer based on patients risk profile.
Disclosure: Nothing to disclose

P1048 BETTER RESULTS OF STOMA RATE AND ADVERSE EVENTS WHEN USING STENTS AS BRIDGE TO SURGERY FOR LEFT-SIDED MALIGNANT COLONIC OBSTRUCTION COMPARED WITH EMERGENCY SURGERY: A RETROSPECTIVE BICENTRIC STUDY

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Introduction: Symptomatic left-sided malignant colonic obstruction is a medical and surgical emergency and it is present in about 10% of the patients[1]. This condition requires an emergency intervention, which has been classically emergency surgery (ES), wich still represents a high morbidity (30–60%) and mortality (10–30%) compared with elective surgery (mortality rate less than 5%)[2].
The aim of stenting bridge to surgery (SBTS) is to restore intestinal transit and transform emergency surgery into elective surgery. Since the first report of this technique, it has been the subject of many reviews which highlight its efficacy, particulary in reducing ostomy rates[3].
Aims and Methods: The aim of our study is to determine wether the SBTS strategy confers clinically relevant short-term advantages in terms of stoma rate, short-term morbidity and short-term mortality over ES in the treatment of symptomatic left-sided malignant colonic obstruction.
We retrospectively selected patients with clinically and radiologically left-sided malignant colonic obstruction between January 2006 to May 2012 in two Specialty Hospitals of Spain. Exclusion criteria were age under 18, tumour located in right or transverse colon, or in medium/inferior rectum; metastasic disease (stage IV of the American Journal Committee on Cancer (AJCC)) and perforation at the moment of the diagnosis.
Firstly, we analyzed demographic data, perioperative data, short-term mortality and global mortality rates between both hospitals, achieving an homogeneous sample for the analysis without statistical differences.
Results: After applying exclusion criteria, there were 137 patients suitable for the study, 71 in the SBTS group and 66 in the ES group. There was no difference between groups in sex, ASA score or tumor location.
We found a significant higher anastomosis rate (p < 0.005) in the SBTS group (83.1%) compared to the ES group (45.5%). In addition, stoma rate including temporary ostomies was lower in the SBTS group (16.9% vs. 54.5%)(p < 0.005).
There was not any difference between both groups regarding the median time from admission to the emergency procedure, 1(0–26) days in the SBTS and 0(0–24) in the ES group (p = 0.310).
There were 11 perforations after stenting that required surgery.
There was a trend to lower rate of postoperative complications in the SBTS group (11 vs 19, p = 0.060) without differences in the type of complication. We observed a higher number of reinterventions in the ES group (p = 0.018).
Median time from stent insertion to programmed surgery was 13 days (1–184).

	SBTS (n = 71)	ES(n = 66)	p
Age	69(61;77)	73.5(62.5;81)	0.077
Primary anastomosis	59(83.1)	30(45.5)	<0.005
Stoma at discharge	12(16.9)	36(54.5)	<0.005
Postoperative complications	11(15.5)	19(28.8)	0.060
Reintervention rate	2(2.8)	9(13.8)	0.018
In-hospital 30-days mortality	5(7.0)	5(7.6)	0.905
Global mortality rate	29(40.8)	37(56.1)	0.075

[Results of the analysis between groups. Values are presented as median (p25-p75) or n (%)]
Conclusion: Our study shows statistically significant better results for SBTS compared to ES in terms of ostomy rate, primary anastomosis rate and reintervention rate, and a trend towards fewer postoperative complications. We did not find differences in terms of short and long-term mortality.
Disclosure: Nothing to disclose

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P1049 STENT PLACEMENT AS BRIDGE TO SURGERY VERSUS EMERGENT SURGERY FOR MALIGNANT LEFT-SIDED COLONIC OBSTRUCTION

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Introduction: Self-expanding metal stents (SEMS) as bridge to surgery (BTS) are an alternative to emergent surgery (ES) in acute malignant colonic obstruction (AMCO). However, there are controversies regarding their use due to the association between adverse events (AEs), oncological outcomes and impact on survival.
Aims and Methods: The aim of this study was to compare the efficacy, morbidity, short and long-term oncological outcomes between SEMS and ES in the management of AMCO.
Single-center retrospective study that evaluated patients who underwent SEMS placement or ES due to left-sided AMCO between January 2010 and December 2017. Clinical success was defined as resolution of occlusive symptoms after SEMS placement or ES, without need for further intervention or surgical reintervention. Morbidity was defined as the occurrence of any AE directly or indirectly related to SEMS placement and/or ES. Surgery AEs were classified according to the Clavien-Dindo classification.
Results: A total of 94 patients were included; 48 were submitted SEMS placement and 46 underwent ES. The median age was 69 years (IQR 58–80) and 53% were male. The majority (58%) of the tumors were located in the sigmoid colon. Tumor stage was significantly higher in the SEMS as BTS group compared with ES (stage III/IV: 71% vs. 37%, p = 0.002), with no differences regarding age (p = 0.175), gender (p = 0.839), ECOG status (p = 0.113), ASA-score (p = 0.708), tumor location (p = 0.326) and tumor size (p = 0.556). Overall clinical success was 87%, with no significant differences in the two groups (88% SEMS vs. 87% CE, p = 0.937). In the SEMS group, all patients underwent surgery after a median of 10 days (7–17). The rate of immediate AEs was 6%, with no difference between the two groups (6% SEMS vs. 7% ES, p = 0.957). The overall morbidity was 25% in the SEMS group (13% post-procedure stent-related AEs and 15% surgery-related AEs) and 41% in the ES group; however, no statistically significance was found (p = 0.125). SEMS placement was also associated with a lower rate of surgery-related AEs (15% vs. 41%, p = 0.005); no differences were observed regarding surgery-related AEs Clavien-Dindo classification (III-V: 43% SEMS vs. 41% ES, p = 0.838). In the ES group 41% underwent stoma reversal with anastomosis construction, with a rate of surgical AEs of 23% (Clavien-Dindo III-V: 33%). The permanent stoma rate was significantly lower in SEMS group (17% vs. 43%, p = 0.006). There were no differences between SEMS and ES regarding recurrence-free survival (median: 52 months vs. 69 months, p = 0.119) and overall survival (median: 37 months vs. 55 months, p = 0.654). Overall morbidity (BTS and ES) was associated with a lower survival (median: 25 months vs. 74 months; p = 0.008) – SEMS group: 5 months vs. 52 months, p = 0.039; ES group: 28 months vs. 74 months, p = 0.05. In the multivariate analysis, only SEMS-related AEs were independently associated with survival estimate (HR 4.3, 95% CI 1.1–16.5; p = 0.037).
Conclusion: SEMS placement as BTS when compared to ES is associated with a lower rate of surgical AEs and definitive stoma rate, with no significant differences in oncological outcomes and long-term survival. However, the occurrence of SEMS-related AEs has a significant impact on survival. These results highlight the need for reference centers with enough expertise in order to achieve a high technical success with low SEMS-related AEs, maximizing the potential benefits of this approach.
Disclosure: Nothing to disclose

P1050 APOPTOSIS INDUCTION IN COLON CANCER CELL BY NEWLY DEVELOPED ENDOSCOPIC IRREVERSIBLE ELECTROPORATION ABLATION DEVICE

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Introduction: Irreversible electroporation (IRE) effectively removes unwanted cells without thermal damage of surroundings. We used multiphoton microscopy (MPM) to evaluate IRE ablation response to cancer cell. By using MP (multiphoton) probes, we focused on two vital intracellular organelles, nucleus and mitochondria, and could get real-time image of IRE-induced apoptosis.
Aims and Methods: Colon cancer cell lines (normal & neoplasm tissues) obtained from 10 patients were stained with MP probes, ABI-Nu for nucleus and PMT for mitochondria respectively. To observe IRE response using MPM, we first compared the states of colon cancer cell lines before and after the IRE with electrical pulses administered in a Harvard apparatus. Then, compared those of normal colon and colon cancer tissue in the same manner. 3-D images, co-labelled with ABI-Nu and PMT were reconstructed. To assess apoptosis, colon cancer cells were stained with the fluorescent dye Annexin V or propidium iodide (PI). To determine whether IRE induces apoptosis, membrane blebbing was examined after applying.
Results: MPM images of cancer cells stained with MP probes revealed that ABI-Nu stained quicker after IRE ablation. Nuclear staining was present earlier and more prominent after IRE application. IRE had a relatively stronger effect on cancer. We obtained MPM images of each tissue slice, including 4 images for every 150 section at a depth of 90–150 μm along the z-direction. Staining was positive for Annexin V and PI, providing the evidence of apoptosis. Blebs, which are distinctive of apoptosis were developed after IRE in the colon cancer cell.
Conclusion: Using MPM, we observed that nuclear staining due to increased cell membrane permeability and bleb was formed after electric pulse exposure. Those real time images may help us to understand the process of IRE more. MPM can replace other apoptosis assessment methods, including Annexin V-FITC and PI staining by providing in vivo images.
Disclosure: Nothing to disclose

P1051 EFFECT OF ORAL ANTICOAGULANTS AND NSAIDS ON THE ACCURACY OF FECAL IMMUNOCHEMICAL TESTS (FIT) WITHIN A COLORECTAL CANCER SCREENING PROGRAMME – A SYSTEMATIC REVIEW AND META-ANALYSIS -

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Introduction: Most colorectal cancer (CRC) screening programmes globally are now based on fecal immunochemical testing (FIT). The positive predictive value for advanced neoplasia (PPV_{AN}) of FIT has been reported to range between 35 and 55%. The PPV_{AN} is known to depend on gender, FIT cut-off, and screening round. A significant proportion of subjects in the screening age range use oral anticoagulants (OACs) or non-steroidal anti-inflammatory drugs (NSAIDs). These may in theory increase the tendency of neoplastic lesions to bleed, and thus increase PPV_{AN}. In contrast, these drugs could increase the tendency of non-neoplastic lesions to bleed too, and cause a decrease in PPV_{AN}. Previous studies into the effect of OAC and NSAID use on FIT performance were inconclusive. Screening guidelines thus lack recommendations on FIT screening in NSAID / OAC users. The aim of this meta-analysis was to study the effect of OAC and NSAID use on FIT performance.
Aims and Methods: A systematic search was conducted until June 2017 to retrieve studies from Pubmed, Embase, Medline, Web of science, Cochrane central and Google Scholar. Studies were included when reporting on FIT results in users versus non-users of OAC and/or NSAID in average risk FIT-based CRC screening populations. Primary outcome was PPV_{AN} of FIT in relation to NSAID / OAC use. Values were obtained by conducting analysis for pooled OAC use and also separately for NSAIDs (including aspirin) by random-effect forest plots.
Results: Our literature search identified 2022 records, of which 8 studies were included in total. Four studies provided data on OAC use and six studies on NSAID use. A total of 3563 FIT positive screening participants were included for OAC analysis and a total of 2901 for NSAID analysis. Pooled PPV_{AN} of FIT in OAC users vs. non-users was 37.6% (95% CI 33.9–41.4) vs. 40.3% (95% CI 38.5–42.1) ($p = 0.75$). Pooled PPV_{AN} in NSAID users vs. non-users was 38.2% (95% CI 33.8–42.9) vs. 39.4% (95% CI 37.5–41.3) ($p = 0.59$). Subgroup analysis of one included study showed that the detection rate of advanced neoplasia significantly decreased with long-term aspirin use (>5 years) compared to short-term use (<5 years); 38.5% vs. 61.2%, respectively ($p = 0.03$).
Conclusion: Accuracy of FIT is not affected by OAC and NSAID use at time of sampling. Based on the current literature, withdrawal of OACs or NSAIDs before FIT screening is not recommended. Future studies should focus on duration of use and drug specifics in association with accuracy of FIT to conduct specific guideline recommendations.
Disclosure: Nothing to disclose

P1052 COMPARISON OF INCIDENCE AND SURVIVAL OUTCOMES IN MUCINOUS AND SIGNET-RING CELL COLORECTAL CANCERS WITH CLASSICAL ADENOCARCINOMA: A SEER ANALYSIS

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Introduction: Besides classical adenocarcinoma (AC), mucinous adenocarcinoma (MAC) and signet-ring cell carcinoma (SRCC) are less frequent subtypes of colorectal cancer, and their recent epidemiologic data are lacking. The current study was designed to explore the evolving epidemiology and prognosis of patients with colorectal MAC and SRCC, compared with AC.
Aims and Methods: The Surveillance, Epidemiology and End Results (SEER) registry database was adopted for patients with pathologically confirmed colorectal neoplasms as their first malignancy. Incidence and survival trends were estimated by age and histologic subtype. 5-year cancer specific survival (CSS) were evaluated for entire cohort, and compared in subgroups by age, grade and stage. Multivariate analysis of CSS was conducted for entire cohort.
Results: MAC incidence (per 100,000) declined slightly from 6.1 in 1975 to 5.6 in 2001, and fell to 2.5 in 2012 with an APC of −7.8% (95% CI = −8.8%–6.8%, $p < 0.001$), then reached a plateau. SRCC incidence gradually climbed from 0.1 in 1975 to 0.6 in 1999 with an APC of 8.3% (95% CI = 7.2%–9.4%, $p < 0.001$) and went down to 0.4 in 2014 with an APC of −3.0% (95% CI = −5.0%–1.0%, $p < 0.001$). Among patients younger than age 50 years, MAC incidence decreased at an APC of −2.6% (95% CI: −3.6%–1.6%, $p < 0.001$), and SRCC remained stable, whereas AC incidence increased greatly at an APC of 1.9% (95% CI: 1.6%–2.2%, $p < 0.001$). Survival of both MAC and AC increased over time, while the survival of SRCC fluctuated without evident improvement. The 5-year CSS of SRCC was 31.3%, significantly lower than AC (66.6%) and MAC (60.4%). For AC and MAC Survival rate of patients aged below 50 years was superior to those aged 50 years or over through time, while in SRCC, after follow-up of approximately 20 months, the survival rate of younger patients dropped and became lower than older patients. Histologic subtype was an independent factor for CSS of CRC.
Conclusion: The incidence and survival of colorectal MAC and SRCC differs from traditional AC. Despite the low incidence of SRCC, the survival is significantly worse than AC and MAC, especially for patients aged younger than 50 years. Further studies of the etiologies and treatment for rare subtypes of CRC are needed.
Disclosure: Nothing to disclose

P1053 A SEER ANALYSIS OF INCREASING DISPARITIES IN AGE-RELATED CAUSE SPECIFIC SURVIVAL (CSS) AMONG PATIENTS WITH COLORECTAL CANCER

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Introduction: Survival for patients with colorectal cancer (CRC) has improved over the past decades. However, it is unclear whether older patients have benefited to the same extent as younger patients.

Aims and Methods: The Surveillance, Epidemiology, and End Results (SEER) 9 registries database was queried for patients diagnosed with colorectal cancer from 1975 to 2009. Patients were categorized by age as being ≤54, 55–64, 65–74, 75–84, and ≥85 years. We presented yearly data for survival with overlying loess smoothing lines across all age groups. Another cohort was created using the SEER 18 registries database for patients diagnosed with CRC from 1973 to 2014. Survival analyses for the periods of 1973–1979, 1980–1989, 1990–1999, and 2000–2012 were conducted. Yearly data for surgery-performed rate and stage proportion were performed with overlying loess smoothing lines across all age groups.

Results: In the analysis of the SEER 9 registries database, 5-year CSS of patients aged ≤54, 55–64 and 65–74 years showed robust increase since 1975; however, survival of patients aged 75–84 years remained low despite modest improvement, and patients aged 85 or older even showed no survival gains since 1990. Same trend exists after stratifying the disease as localized, regional and distant. In the analysis of the SEER 18 registries database, there has been a steady increase in the survival of patients aged ≤54, 55–64, 65–74 and 75–84 years as time period advanced; however, of CRC patients aged 85 years and older, the survival curves of period 1990–1999 and 2000–2012 couldn't be distinguished from each other and presented with a negligibly small gap from the survival curve of 1980–1989.

Conclusion: The strong interaction between age and year of diagnosis implies that older patients have benefited less over time than younger patients, especially for patients aged ≥85 years. Further studies are needed to determine the cause for these trends and identify potential strategies.

Disclosure: Nothing to disclose

P1054 IMPACT OF OBESITY AND VISCERAL FAT DISTRIBUTION ON SURVIVAL AND PERITONEAL SEEDING METASTASIS OF STAGE III COLORECTAL CANCER

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Introduction: There has been studies about the relationship between increased body mass index (BMI), and risk of colorectal neoplasia. Visceral obesity may affect outcome of colorectal neoplasia.

Aims and Methods: This study aimed to investigate the associations between visceral fat and oncologic outcomes in stage III colorectal cancer (CRC). 472 patients were identified with stage III CRC (2007.01.01–2009.12.31). BMI, subcutaneous fat and visceral fat were measured volumetrically via CT scan for each patient at three levels, lumber spine 3 to 4 (L3-4), 4 to 5 and lumbar spine 5 to sacrum. Adjusting age, sex, medication and underlying condition, the effect of visceral fat volume on mortality and recurrence were evaluated using Cox proportional hazard regression.

Results: Total 111 deaths and 114 cases of recurrence were noted and among recurrent cases, 25 cases were peritoneal seeding recurrence. Higher visceral fat volume was not associated with overall survival or progression-free survival. However, higher visceral fat to total fat volume ratio (HR 1.069, 95% CI 1.01–1.131, $p = 0.02$) and higher visceral fat to subcutaneous fat volume ratio (HR 1.024, 95% CI 1.003–1.045, $p = 0.023$) were both related to higher risk of peritoneal seeding recurrence. Moreover, among each level, higher visceral to total adipose tissue ratio of L3-4 showed higher risk of peritoneal seeding recurrence (HR 4.969, 95% CI 1.303–18.949, $p = 0.019$). In the additional survival analysis, patients with BMI under 18.5 were associated with higher risk of cancer-specific mortality (HR 3.236, 95% CI 0.122–0.855, $p = 0.024$).

Conclusion: Visceral obesity is closely related with increased risk of peritoneal seeding recurrence in patients with stage III colorectal cancer. Furthermore, underweighted patients are associated with higher risk of cancer-specific mortality.

Disclosure: Nothing to disclose

P1055 RISK OF RECURRENCE AND LYMPH NODE METASTASIS AFTER ENDOSCOPIC AND SURGICAL REMOVAL OF MALIGNANT COLORECTAL POLYPS: A COMPARATIVE STUDY

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Introduction: Guidelines consider both endoscopic and surgical removal as first-line treatment options, but the optimal therapeutic approach to malignant colorectal polyps is still debatable.

Aims and Methods: The aim of this single center retrospective observational study was to assess medium-term outcomes of endoscopic removal of early malignant colorectal polyps at the University of Szeged between 2012 and 2016, and to compare them with that of surgical resection. For endoscopic removal (group I), inclusion criteria consisted of histopathological diagnosis of pT1 adenocarcinoma after endoscopically completed (based on the endoscopist's opinion) polyp removal without additional surgery. For surgical removal (group II), inclusion criteria included surgical resection of pT1 adenocarcinoma with superficial submucosal invasion with or without previous endoscopic removal attempt. Recurrence (primary outcome; including local recurrence and distant metastases) was compared between the two groups. Secondary outcome was nodal involvement in those underwent surgical resection (with vs. without prior endoscopic polypectomy). Mean follow-up was 24 ± 2 months [7–67 months], follow-up endoscopy was available in 69% of the cases.

Results: Complete endoscopic removal was achieved in 69 patients (en bloc resection was carried out in 76%), of which 15 underwent additional surgical resection, and follow-up was chosen in the other 54 patients. Primary surgical resection was performed in 31 cases; thus, surgery was performed in a total of 46 cases. Mean patient age was 68.1 ± 1 years, 43% were female, and median polyp size was 20 mm (range: 6–80 mm). There was no difference between the rate of flat/sessile polyps in the groups (35% for endoscopic and 50% for surgical removal, $p = 0.139$), while pedunculated polyps were predominantly removed endoscopically (52% vs. 24%, $p = 0.004$). Endoscopically removed lesions located mainly in the left colon (54%), followed by the rectum (39%), and the right colon (7%), while surgically resected lesions tended to be in the rectum (48%), followed by the left (28%) and the right colon (24%). No difference was found between patient and lesion characteristics of those underwent surgery with and without previous endoscopic removal.

Recurrence rate was 1.9% for group I, and 4.3% for group II, $p = 0.485$. All recurrences were distant metastases, no local recurrence was observed in either group during the follow-up period. In case of pedunculated lesions, recurrence was only observed after endoscopic removal (3.6%), and for flat/sessile lesions, only after surgical removal (8.7%). Lymph node involvement was detected in a total of 11% of all surgically resected specimens. All lymph node positive cases ($N = 5$) were primarily operated without previous endoscopic removal attempt.

Conclusion: No significant difference was found between recurrence rate of malignant colorectal polyps removed endoscopically and surgically. Previous endoscopic removal does not increase the risk of lymph node involvement in case of surgical removal of malignant polyps. Thus, endoscopic polypectomy can be recommended in case complete removal is expected to be achieved, with additional surgery if necessary.

Disclosure: Nothing to disclose

P1056 QUANTITATIVE FLUORESCENCE ENDOSCOPY: A NEW AND PROMISING TOOL TO PREDICT AND EVALUATE RESPONSE TO NEOADJUVANT CHEMORADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER PATIENTS

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Introduction: Patients with locally advanced rectal cancer (LARC) are treated with neoadjuvant chemoradiotherapy (nCRT) followed by surgery. To date, there is a growing interest in the non-operative 'watchful waiting' management of patients with a clinically complete response to nCRT, as this is associated with good survival rates and reduced long-term morbidity. However, current restaging techniques are suboptimal to identify patients that might benefit from watchful waiting. Therefore, we investigated if quantitative molecular fluorescence endoscopy (Q-MFE) can improve clinical response assessment after nCRT in LARC patients.

Aims and Methods: We evaluated Q-MFE with 4.5mg of the near-infrared (NIR) fluorescent tracer bevacizumab-800CW targeting vascular endothelial growth factor A in 30 patients with LARC. Q-MFE procedures were scheduled at two different time points during neoadjuvant treatment: 1) at baseline, prior to the start of nCRT; 2) following completion of nCRT. At both time points, fluorescence was visualized using a NIR molecular fluorescence endoscopy platform. Additionally, fluorescence signals were quantified *in vivo* and *ex vivo* using multi-diameter single fiber reflectance and single fiber fluorescence (MDFSR/SFF) spectroscopy. Results were correlated with current clinical standards:

radiological restaging, white-light endoscopy and the pathological outcome of the surgical specimen.
Results: Firstly, Q-MFE procedures performed at baseline showed clear fluorescence in tumor tissue ($Q\mu^{f}_{a,x} = 3.7510^{-4}$) compared to normal rectal tissue ($Q\mu^{f}_{a,x} = 1.2010^{-4}$). Higher fluorescence signals were seen in tumor tissue of good responding patients compared to patients with an intermediate and poor response to nCRT ($4.6210^{-4} \pm 0.2910^{-4}$, $3.7410^{-4} \pm 0.4410^{-4}$ and $2.4810^{-4} \pm 0.5610^{-4}$ respectively). Secondly, Q-MFE procedures performed after nCRT showed significantly higher fluorescence in tumor tissue compared to normal rectal tissue and fibrosis, with an area under the curve of 0.925. Q-MFE results showed a promising correlation to pathological staging of the surgical specimen with for Q-MFE and white-light endoscopy respectively a positive predictive value after nCRT of 92% vs. 90% and negative predictive value of 100% vs. 20%. Overall, Q-MFE correctly changed restaging diagnosis in 4 (16%) of the LARC patients.
Conclusion: VEGFA-targeted Q-MFE showed to be a promising new tool for individualized treatment of LARC patients by prediction of tumor response to nCRT already at baseline and recognizing a clinical complete response after nCRT. These results might lead to a paradigm shift in the management of patients with locally advanced rectal cancer.
Disclosure: GMvD and WBN received unrestricted research grants from SurgVision BV.

P1057 WHICH IS THE REASON FOR WE NEED TO REPEAT COLONOSCOPIES IN COLORECTAL CANCER (CCR) SCREENING PROGRAM? ANALYSIS OF THE IMPACT OF ADDITIONAL COLONOSCOPIES IN THREE CONSECUTIVE ROUNDS

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Introduction: The implementation of CRC screening program has conditioned assistance and economic burden to our Health care System. The findings on baseline colonoscopy has generated the need for other subsequent colonoscopies, which cannot be considered following up. The incidence and the presence of prior factors associated with additional explorations are unknown. Moreover, the accumulation of consecutive rounds may have modified the indication of them.
Aims and Methods: We assess the incidence; analysis the modification of the additional colonoscopies and identify factors associated with a population CCR screening program in three consecutive rounds.
Data were collected from all colonoscopies included first (1R), second (2R) and three (3R) round screening program for colorectal cancer of Barcelona, Spain. Definition- *additional colonoscopy*: colonoscopy performed before one year from baseline colonoscopy and not indicated for follow-up once the resection of all basal polyps has been assured.
Results: We review 3981 colonoscopies in three consecutive rounds. A total of 330 colonoscopies (8.6%) had to repeat en a second time. The number of additional colonoscopies has decreased in the consecutive rounds; 133 (13.0%), 62 (5.1%) and 80 (6.0%) in 1R, 2R and 3R, respectively ($p < 0.001$).
The main indications for repeat colonoscopy were different depends of the round: control of complete resection of a polyp mostly by fragmented resections (58% in 1R, 8.1% in 2R and 10% in 3R), additional polypectomy (13% in 1R, 11.3% in 2R, 1.2% in 3R) and poor preparation (16.3% in 1R, 62.2% in 2R, and 80% in 3R). The values associated with the additional colonoscopy were: the participation in 1R (OR 2.34; IC 95%: 1.78–3.07), male but only in the 1R (OR 1.49; *IC 95%: 1.08–2.06*), the presence of high risk adenomas (OR 5.15; *IC 95%: 3.48–7.62*) and the fecal hemoglobin concentration assessed by immunochemical test (OR 1,4; *IC 95%: 1.46–1.80*). The previous factors to baseline colonoscopy independently associated with the need to repeat the test were the participation in 1R (OR 2.48; *IC 95%: 1.97–3.12*) and fecal hemoglobin concentration (OR 1,38*; IC 95%: 1,10–1,74*).
Conclusion: The need to repeat colonoscopies determines an additional burden on CRC screening program. Additionally, having a positive immunochemical test is a cause the repetition and therefore the message of adequate intestinal preparation must be reinforced, especially as it participates in consecutive rounds.
Disclosure: Nothing to disclose

P1058 ARTIFICIAL INTELLIGENCE CAN DETERMINE THE NEED FOR ADDITIONAL SURGERY AFTER ENDOSCOPIC RESECTION OF T1 COLORECTAL CANCER: ANALYSIS BASED ON BIG DATA FOR MACHINE LEARNING

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Introduction: Most T1 colorectal cancers (CRCs) undergo surgical colectomy in accordance with established clinical guidelines despite the low incidence (approximately 10%) of lymph node metastasis (LNM). Decisions concerning additional surgery after endoscopic resection of T1 CRC are difficult because preoperative prediction of LNM is problematic. In this study, we investigated whether artificial intelligence (AI) can predict LNM presence of T1 CRCs, thus optimizing the treatment strategy for additional surgery of these lesions.
Aims and Methods: A total of 700 consecutive patients with T1 CRCs that were surgically resected in 2001–2016 were retrospectively analyzed. We divided patients into two groups according to date: data from 590 patients were used for machine learning for the AI model, and the remaining 110 patients were included for model validation. The AI model analyzed 45 clinicopathological factors (patient age, sex, tumor size, location, lymphatic invasion, depth of invasion, blood test result and so on) and then predicted positivity or negativity for LNM based on support vector machine which is a representative machine learning method. Operative specimens were used as the gold standard for the presence of LNM. The AI model was validated by calculating the sensitivity, specificity, and accuracy for predicting LNM, and comparing these data with those of the American, European, and Japanese guidelines.(1–5)
Results: Sensitivity was 100% (95% CI, 59%-100%) in all models. Specificity and accuracy of the AI model, American, European and Japanese guidelines were 66% (56%-75%) vs. 44% (34%-54%) vs. 0% (0%-5%) vs. 0% (0%-5%), and 69% (60%-78%) vs. 49% (39%-59%) vs. 9% (4%-16%) vs. 9% (4%-16%), respectively. The rate of unnecessary surgeries of the AI model was calculated as 31% in comparison with American 51% ($P < 0.01$), European 91% ($P < 0.01$), and Japanese 91% ($P < 0.01$).
Conclusion: Compared with the current guidelines, AI significantly reduced unnecessary additional surgery after endoscopic resection of T1 CRC without missing LNM positivity. AI will help in making decisions as to whether additional surgery is indicated after endoscopic resection of T1 CRCs.
Disclosure: Nothing to disclose

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P1059 LOCAL INJECTION OF A WATER JET AND MAGNIFIED ENDOSCOPIC OBSERVATION USING SPECIAL LIGHT ARE USEFUL FOR PREVENTING RESIDUAL LESIONS IN COLD POLYPECTOMY

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Introduction: Cold polypectomy, which does not require an electric current, is of 2 types: cold snare polypectomy (CSP) and cold forceps polypectomy (CFP). Compared to hot polypectomy, which uses an electric current, cold polypectomy has advantages such as easier preparation and procedures, less muscle layer damage, and lower risk of postoperative hemorrhage. Therefore, both cold techniques have been widely accepted for excising small polyps of the large intestine. However, in contrast to hot polypectomy, which can be performed with a clear field of vision, with cold polypectomy, it is difficult to judge whether polyps have been completely removed. Thus, there is a possibility that residual lesions remain. Therefore, we examined whether the local injection of a water jet and magnified endoscopic observation using a special light are useful for preventing residual lesions.
Aims and Methods: We conducted a prospective study, from October 2016 to April 2017 at our hospital, of 200 consecutive patients who underwent cold polypectomy for endoscopic excision of large intestinal polyps. Patients were randomly assigned to either Group A (100 patients) in whom local injection of a water jet after excision and magnified endoscopic observation using special light were performed or Group B (100 patients) in whom those procedures after excision were not performed. We excluded all patients diagnosed with cancer via magnifying endoscopy with narrow-band imaging (M-NBI) or with blue laser imaging (M-BLI). The size, shape, and degree of dysplasia of lesions and the rate of complete resection were histopathologically investigated in both groups. In Group A, additional excision was performed instantly if residual lesions were observed. For local injection of the water jet, we used the Olympus Flushing Pump (Olympus, Ltd., Japan) as a water supply machine, and an endoscope (Olympus, Ltd., Japan or Fujifilm Ltd., Japan) that was used with the machine.
Results: There were no differences in lesion size, shape, or degree of dysplasia between both groups. The rate of complete resection was 96% in Group A and 84% in Group B, showing that Group A had a significantly higher rate.
Discussion: In Group A, the margin of the resection surface was observed with local injection of the water jet after polyp excision. By using a combination of image-enhanced endoscopy and magnified endoscopic observation (M-NBI or

M-BLI), we could observe the presence or absence of residual lesions instantly without a pathological diagnosis.
This allowed us to resect the residual part of polyp as required. Therefore, our ability to completely resect the lesion improved.
Conclusion: To prevent residual lesions in cold polypectomy, local injection of a water jet and magnified endoscopic observation using a special light are useful. This should therefore be performed as a routine procedure.
Disclosure: Nothing to disclose

P1060 SYSTEMATIC REVIEW AND META-ANALYSIS: CONDITIONED PAIN MODULATION IN IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is common and is characterised by recurrent abdominal pain, which is a major contributor to healthcare seeking. The neurobiological basis of this pain is incompletely understood. Conditioned pain modulation (CPM), a way the brain controls the afferent barrage by descending pathways, has been implicated in the pathophysiology of IBS, although to date only in studies with relatively small sample sizes. We aimed to clarify this relationship by undertaking a systemic review and meta-analysis.
Aims and Methods: A systematic review off MEDLINE and Web of Science databases were searched (up to April 2017). Studies examining CPM in adults with IBS and healthy subjects were included. Data were pooled for meta-analysis to calculate the odds ratio of abnormal CPM in IBS, with 95% confidence intervals (CI).
Results: The search strategy identified 645 studies, of which 24 were relevant and 12 met the inclusion criteria. CPM was reduced in IBS patients versus healthy subjects, odds ratio 4.84 (95% CI 2.19–10.71, $p < 0.0001$). There was significant heterogeneity in effect sizes (Q-test $\chi^2 = 52$, $p < 0.001$, $I^2 = 78.8\%$) in the absence of publication bias. Numerically, the Rome III criteria was associated with more deficient CPM than Rome II odds ratio 5.65 (95% CI 1.87–17.04) vs 3.44 (95% CI 1.76–6.70), respectively.
Conclusion: CPM is significantly reduced in patients with IBS when compared to healthy subjects. These data provide evidence that abnormal descending pathways are an important pathophysiological facet in IBS, which could represent a novel investigation target to allow personalization of neuromodulatory therapy.
Disclosure: Nothing to disclose

P1061 ASSOCIATIONS BETWEEN SYMPTOMS AND GAS PRODUCTION DURING FODMAP BREATH TESTS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Functional gastrointestinal disorders (FGID) are characterized by a broad range of gastrointestinal (GI) and extra-GI symptoms, and an absence of recognizable disease. Mechanisms underlying these phenotypes are unclear, but may be linked to host or microbiome metabolism.
Aims and Methods: We investigated underlying mechanisms by studying associations between gas production and symptom genesis during fructose and lactose breath tests in 2042 successive patients with FGID. Breath hydrogen and methane gas concentrations and evoked GI and extra-GI symptoms were assessed for 5 hours following sugar ingestion. Symptom and gas time profiles were compared, Treelet Transforms were used to derive data-driven symptom clusters, and the symptom severities of the clusters were analyzed for their association with breath gas characteristics.
Results: The time profiles of eleven symptoms, as well as of hydrogen and methane gas concentrations, showed significant changes over time following fructose and lactose ingestion ($p < 0.0001$). Treelet Transform analysis identified two distinct sugar-evoked GI and CNS symptom clusters. The intensities of the GI and CNS symptom clusters were closely correlated following both fructose and lactose (all $p < 0.0001$). The GI symptoms were significantly associated with the production of hydrogen and methane gases (all $p < 0.0001$), while this was not the case for the CNS symptoms.
Conclusion: Clearly defined clusters of GI and CNS symptoms were evoked by fructose and lactose ingestion in patients with FGID. The GI and CNS cluster time profiles correlated significantly, but only the GI symptoms were related to breath gas concentrations. This implies distinct underlying mechanisms likely relating to microbiome metabolism, such as mechanical and chemical sensitization.
Disclosure: Nothing to disclose

P1062 FAECAL METABOLIC PHENOTYPING IN IRRITABLE BOWEL SYNDROME

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Introduction: The complex pathophysiology of Irritable Bowel Syndrome (IBS) is based on incompletely understood disturbances in the microbiota-gut-brain interaction. Faecal microbiota profiles have been associated with IBS and severity of symptoms in IBS patients. However, while the composition of the intestinal microbiota may be altered, the available data on the metabolic activity in the intestinal lumen of IBS patients, which is modulated by diet, microbiota composition and microbial activity, use of medication and host metabolism, is limited.
Aims and Methods: The aims of the present study were to identify profiles of faecal metabolites associated to IBS, IBS subtypes and gastrointestinal (GI) symptom severity in IBS.
In a cross-sectional analysis we included 163 extensively phenotyped and clinically diagnosed IBS patients (all according to ROME III criteria) and 121 age and gender matched healthy controls (HC); a subset of the Maastricht IBS cohort. All subjects completed questionnaires on demographics, use of medication, GI symptom severity, anxiety and depression, quality of life, and dietary intake. Faecal water was extracted from stool samples and faecal metabolites were measured using proton nuclear magnetic resonance (^{1}H NMR) spectroscopy.
Outliers from the data were excluded based on auto-scaled Principal Component Analysis and the 95% CI of Hotelling's T^2 statistic. The remaining samples were modelled using Monte Carlo Cross-Validated Partial Least Squares Discriminant Analysis (MCCV-PLS-DA) with 250 iterations of the MC in which 1/5th of the data was left out completely to be used for validation. The left-out samples were predicted using the parameters from the training set. Variable importance was assessed using bootstrap resampling to estimate the variance of the regression coefficients used to calculate a t-score and *p*-value for each variable. The p-values were corrected for multiple testing using the false discovery rate (q-value).
Results: A total of 146 IBS patients and 121 HC were included in the data analysis. Most outliers contained high amounts of polyethyleneglycol, which was used as laxative by the patients. All 250 models consistent of two components with a goodness of fit (R^2_Y) of 0.58 across the MCCV. The goodness of prediction (Q^2_Y) was 0.22. The distributions of predicted IBS and HC samples show some overlap, but a Wilcoxon rank sum test indicates they are significantly different at $p = 2.18 \times 10^{-18}$. After multiple testing correction and pairwise comparisons, there were no differences witnessed in predicted values of the IBS subtypes compared to each other. Branched-chain amino acids (Leu, Val, Ile) and aromatic amino acids (Tyr, Phe) were found in higher concentrations in faecal water of IBS patients compared to HC, as were glucose, formate and (tentatively) orotate. Other unidentified spectroscopic signatures are yet to be identified; these include resonances from sugar-like compounds found higher in HC. No differences were observed for fatty acids butyrate and propionate, nor for acetate, lactate, succinate and glutamate.
Conclusion: Spectroscopic profiling of faecal water shows differences between IBS patients and HC in terms of the metabolic profile, indicating altered intraluminal gut metabolic activity in IBS.
Perspective: Additional analyses will be performed to study differences between IBS subtypes, the relation between GI symptoms and metabolic profiles, and the correlation between faecal microbiota compositions and faecal water metabolites. This method has the potential to identify biological pathways related to IBS phenotype and its pathophysiology.
Disclosure: Nothing to disclose

P1063 PROTEASE ACTIVATED RECEPTOR-2 INDUCES IMMUNE ACTIVATION AND VISCERAL HYPERSENSITIVITY IN POST-INFECTIOUS IRRITABLE BOWEL SYNDROME

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Introduction: Protease-activated receptor-2 (PAR-2), a G-protein-coupled receptor of mast-cell tryptase and trypsin, is highly expressed in the intestine. Role of PAR-2 in the pathogenesis of abdominal pain in irritable bowel syndrome (IBS) is not well defined.
Aims and Methods: We aimed to investigate the role of PAR-2-mediated visceral hypersensitivity by using a post-infectious IBS (PI-IBS) mouse model. *T. spiralis*

infected PI-IBS mouse model was used. Fecal serine protease activity and intestinal mast cells were evaluated. PI-IBS mice received intraperitoneally PAR-2 antagonist (FSLLRY-NH2) or normal saline, and control mice received intracolonically PAR-2 agonist (SLIGRL-NH2) or normal saline. Intestinal permeability was assessed by urine lactulose/mannitol ratio, and colonic expressions of PAR-2 and tight junction (TJ) proteins were examined by Western blot. Intestinal immune profile was assessed by measuring Th (T helper) 1/Th2 cytokine expression. Visceral sensitivity was evaluated by abdominal withdrawal reflex (AWR) in response to colorectal distension (CRD).
Results: Mice infected with *T. spiralis* developed visceral hypersensitivity after 8 weeks. PI-IBS mice had higher AWR scores for all levels of distention (20, 40, 60, and 80 mmHg) and lower pain and volume thresholds compared to the control mice (all $P < 0.05$). Colonic PAR-2 expression (19.54 ± 6.4 vs. 0.23 ± 0.1, $P = 0.03$) as well as fecal serine protease activity (127.2 ± 39.1 U/mg vs. 25.6 ± 15.8 U/mg, $P = 0.02$) and intestinal mast cell counts (19.1 ± 2.7 vs. 2.8 ± 0.7, $P < 0.001$) were elevated in PI-IBS compared to the control mice. Decreased colonic TJ proteins (occludin: 0.45 ± 0.16 vs. 4.89 ± 2.26, $P = 0.009$; ZO-1: 0.48 ± 0.23 vs. 1.94 ± 1.06, $P = 0.015$) expression, increased lactulose/mannitol ratio (0.35 ± 0.04 vs. 0.15 ± 0.03, $P = 0.001$), and elevated colonic Th1/Th2 cytokine ratio (3.5 ± 0.4 vs. 1.4 ± 0.1, $P = 0.001$) were observed in PI-IBS compared to the control mice. Administration of PAR-2 agonist in control mice demonstrated similar changes observed in PI-IBS mice, while PAR-2 antagonist normalized intestinal hyper-permeability (0.15 ± 0.02 vs. 0.35 ± 0.04, $P = 0.001$), led a trend towards decreased Th1/Th2 ratio (2.4 ± 0.3 vs. 3.5 ± 0.4, $P = 0.07$) and reduced visceral hypersensitivity (decreased AWR scores and higher pain and volume thresholds) in PI-IBS mice.
Conclusion: PAR-2 activation induces intestinal hyper-permeability leading to immune activation and visceral hypersensitivity in PI-IBS mouse model. PAR-2 plays an important role in the pathogenesis of PI-IBS.
Disclosure: Nothing to disclose

P1064 THE MODERATING IMPACT OF PAIN AETIOLOGY ON THERAPEUTIC CHANGE IN COGNITIVE-BEHAVIOURAL THERAPY FOR CHRONIC PAIN

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Introduction: Chronic relapsing and remitting pain is a central feature of common gastrointestinal disorders including both functional (e.g. irritable bowel disorder) and organic (e.g. Crohn's disease) disorders. The role of aetiology in chronic pain is not well understood. One approach to classifying chronic pain disorders is to consider whether the condition has an identifiable pathophysiology or not. Hence the use of the terms organic and functional conditions, respectively. In addition, the contemporary treatment of chronic pain has highlighted the importance of psychological therapies, such as Cognitive Behavioural Therapy (CBT). Recent work by the eCentreClinic has developed transdiagnostic CBT models for chronic pain which should make organic versus functional aetiology irrelevant.
Aims and Methods: The aim of the present study is to determine whether pain-related treatment outcomes are moderated (altered) by a functional or organic pain aetiology, among individuals undergoing CBT for chronic pain. The possibility of transdiagnostic, aetiology-independent therapy opens the potential for efficacious and cost-effective pain relief for patients.
The present study is a secondary analysis of data collected from an internet-delivered pain management program, known as The Pain Course. Participants pain aetiology was identified as functional or organic, via interview and self-reported data provided. A formal test of moderation was undertaken via analysis of covariance in which all dependent variables (pain disability, pain intensity, pain self-efficacy, pain acceptance, fear avoidance, depression and anxiety). The interaction between treatment group (active CBT or Control) and pain condition classification (organic or functional), were used as the independent variables.
Results: N = 471 participants engaged in a 5 week trail of CBT for chronic pain. Between group differences of both the active CBT and waitlist control, for functional or organic status, age, gender, mean pain duration and average number of painful sites were non-significant. All dependent variables were not moderated by a functional or organic status (pain disability: $F(1, 417) = 0.012$, $p = 0.91$, pain intensity: $F(1, 417) = 3.68$, $p = 0.06$, pain self-efficacy: $F(1, 417) = 0.10$, $p = 0.75$, pain acceptance: $F(1, 417) = 3.14$, $p = 0.08$, fear avoidance: $F(1, 416) = 0.02$, $p = .89$, depression: $F(1,417) = 3.14$, $p = 0.08$ and anxiety: $F(1, 417) = 1.75$, $p = 0.19$).
Conclusion: The present study identifies that the therapeutic change experienced by participants undergoing CBT for chronic pain is not altered by the presenting aetiology being organically driven. This reinforces a biopsychosocial formulation of those experiencing persistent pain, independent of the driving stimuli. Future research should identify further predictors of treatment responses which optimize outcomes and reduce the overall financial costs associated with chronic pain.
Disclosure: Nothing to disclose

P1065 HOW THE PLACEBO EFFECT PLATEAUS: PREDICTORS OF THE SHAPE OF PLACEBO RESPONSE IN IBS-C

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Introduction: Placebo effects are common in clinical trials. In IBS specifically, approximately 40% of patients experience a placebo effect. While previous research has demonstrated some predictors of placebo response, limited research to date has investigated how placebo effects change over time, and what factors predict this changing pattern of response.
Aims and Methods: This study aimed to establish (1) the specific shape of the time course of the placebo effect over a 12-week clinical trial, and (2) the predictors of this time course.
Data were obtained from 599 women enrolled in the placebo arm of a phase-III clinical randomized control trial. Daily measures of abdominal pain (rated on a 1–10 scale) and number of complete spontaneous bowel motions (CSBMs) were used as outcomes throughout the 12-week period. Latent growth curve models were fitted to identify the specific shape of the time course of the placebo effect.
Results: A quadratic curve was the best fit for placebo trends in both pain and CSBM; that is, across the 12-week period, there was, on average, an initial decrease in symptoms, which on average plateaued around week 5. For that reason, the model chosen required two components: one which captured the initial improvement in symptoms at week 1 of the trial (the linear term), and the other which measured the extent to which the improvement plateaus over time (the quadratic term). Models showed significant between-individual variability in both the linear and quadratic terms for both outcomes, which indicates that there is individual variability in the rapidity of the initial improvement, and also when the improvement begins to plateau.
For the pain outcome, predictors of greater initial decrease in pain (the linear term), but subsequent plateau of pain relief (quadratic term), included higher average baseline pain, abnormal baseline stool form, no history of migraine or drug hypersensitivity, a history of asthma, and experiencing early adequate pain relief.
For the CSBM outcome, predictors of greater initial increase in CSBMs (linear term), but subsequent plateau of CSBM increase (quadratic term), were a history of asthma and experiencing early adequate pain relief. (See Table 1.)
Conclusion: The quadratic shape of the placebo response demonstrated that, over 12 weeks, many individuals experience an early peak, which subsequently plateaus. These results show that abdominal pain at baseline, medical history and stool form influence the extent and shape of the placebo response. The placebo response for pain appears to be more dependent upon symptom severity, whereas the placebo response for CSBMs seems more independent of patient factors. Understanding which individuals experience a less stable placebo response, and which symptom outcomes are more affected by patient factors, can potentially help both researchers and clinicians in comparing active therapy effects with placebo effects, as well as better understand mechanisms underlying the placebo effect.

Pain Outcome

Predictor	Linear unstandardized beta (standard error)	Linear standardized beta	Quadratic unstandardized beta (standard error)	Quadratic standardized beta
Abdominal pain last day of baseline	0.030 (0.014)*	0.231	−0.002 (0.001)	−0.181
Average abdominal pain at baseline	−0.058 (0.017)***	−0.381	0.003 (0.001)*	0.251
Normal stool consistency at baseline	0.103 (0.055)	0.092	−0.012 (0.004)**	−.139
History of Migraine	0.087 (0.040)*	0.106	−0.006 (0.003)*	−0.100
History of Asthma	−0.139 (0.050)**	−0.136	−0.006 (0.003)*	−0.149
History of Drug hypersensetivity	0.100 (0.037)**	−0.131	−0.008 (0.003)**	−0.149
Early pain relief (week 3)	−0.116 (0.031)***	−0.186	0.008 (0.002)**	0.163
CSBM Outcome				
History of Asthma	.101 (.055)	0.103	−0.010 (0.004)*	−0.138
Early pain relief (week 3)	0.086 (0.034)**	0.142	−0.007 (0.003)*	−0.158

*P < 0.05 **P < 0.01 ***P < 0.001.
[Table 1. Predictors of pain and CSBM placebo trends.]
Disclosure: Nothing to disclose

P1066 LACK OF EVIDENCE FOR A LINK BETWEEN INTESTINAL MAST CELLS, SYMPTOM PROFILE AND MUCOSAL BARRIER INTEGRITY IN IRRITABLE BOWEL SYNDROME

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Introduction: Although previous studies show conflicting results, colonic mast cell (MC) accumulation and increased proportions of MC in close proximity to intestinal nerves have been proposed to be associated with more severe Irritable Bowel Syndrome (IBS) symptoms, altered intestinal barrier properties and visceral hypersensitivity.

Aims and Methods: This study aimed to determine if IBS patients displayed an altered MC profile compared with healthy subjects and if MC profiles correlated with IBS symptoms, barrier integrity or visceral sensitivity.

Biopsies from the sigmoid colon (25–35 cm from the anus) were collected from a Swedish cohort of IBS patients meeting the ROME III criteria and from healthy subjects. Mucosal MC profile was determined using anti-tryptase antibody, immunofluorescence and blinded quantification with a computer-assisted analysis system. The IBS Severity Scoring System (IBS-SSS), Gastrointestinal Symptom Rating Scale-IBS (GSRS-IBS), Visceral Sensitivity Index (VSI) and Hospital Anxiety and Depression Scale (HADS) questionnaires were used to evaluate the symptom profile. Expression of mucosal barrier proteins CLD-1, MUC, TJP1 and OCLN was measured with Real-time quantitative PCR and normalised to housekeeping genes 18S, POLR2YA and RPLPO. Fecal serine protease activity was detected using azocasein or tryptase substrate protease assays and AEBSF inhibitor. Visceral sensitivity was determined with a rectal barostat test. Univariate analyses, hierarchical cluster analysis (HCA) and multivariate orthogonal partial least squares-discriminant analysis (OPLS-DA) were performed. Data are presented as median (25th-75th percentiles).

Results: This study included 43 IBS patients (30 females; 32 (25–44) years) of subtypes IBS-C (n = 9), IBS-D (n = 18), IBS-nonCnonD (n = 16), and with IBS-SSS total score of 269 (196–365), and 20 healthy subjects (14 females; 27 (24–38) years). Total HAD scores were 13 (9–19) in IBS patients and 7 (3–13) in healthy subjects ($p = 0.0002$). MC frequencies were 2 (0–6) cells in IBS patients and 3.5 (1.1–9.1) cells in healthy subjects ($p = 0.26$, univariate analysis). MC in close proximity to nerve fibres were 0 (0–20) % in IBS patients and 3.1 (0–17.6) % in healthy subjects ($p = 0.76$). There were no differences between the different IBS subtypes concerning MC numbers and location. HCA identified two distinct groups among IBS patients, based on MC numbers and location. These groups were characterized by higher MC numbers and proportions of MC in close proximity to nerves (MC high), or by lower MC numbers and proportions of MC in close proximity to nerves (MC low). Univariate analysis showed no differences in total IBS-SSS, VSI and HAD scores between MC high and MC low IBS patient groups. OPLS-DA showed that MC high and MC low groups could not be discriminated with regards to IBS symptoms (GSRS, IBS-SSS, HAD and VSI) or barrier properties (mucosal expression of CLD-1, MUC, TJP1 and OCLN, and activity of fecal serine proteases). Finally, parameters of visceral sensitivity were equivalent in MC high and MC low groups when investigated by OPLS-DA.

Conclusion: This study was not able to identify any differences in mast cell frequencies, or proportions of mast cells in close proximity to nerves, between IBS patients and healthy subjects. Furthermore, there were no links between mast cell profile to individual or global IBS symptoms, expression levels of barrier proteins or degree of visceral sensitivity in IBS patients. These findings indicate that quantity and location of mucosal mast cells are factors not involved in the pathophysiology of IBS.

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P1067 SEXUAL DYSFUNCTION AND IMPACT OF IRRITABLE BOWEL SYNDROME IN PATIENTS AND SPOUSES

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Introduction: Although not a life-threatening disease, irritable bowel syndrome (IBS), associating abdominal pain with transit disorders, can alterate the quality of life (QoL) in all its domains. Studies in the USA have shown that the disease can alter sexuality in two-thirds of patients and sometimes have repercussions on the partner.

Aims and Methods: Our goal was to determine in a French cohort of patients the prevalence of possible sexual dysfunction and its links with IBS characteristics, as well as the partner burden. This online study was conducted among members of the French Association of Patients Suffering from IBS (APSSII). For IBS members, demographic data and IBS characteristics were noted: disease duration, transit subtype, severity (IBS-SSS), QoL, and state of depression and anxiety (HAD score). Study of sexual dysfunction was performed using the Female Sexual Function Index score (FSFI) in women (19 questions, 6 domains, abnormal if <26.55, score 2- 36) and the International Index of Erectile Function (IIEF) in men (15 questions, 5 domains, abnormal if <26). The partner burden was evaluated among partners of IBS members participating in the study: age, sex, burden assessment questionnaire (ZBI, Zarit et al.[1]) includes 22 items (score 0–88; severe if >60; i.e. studies have shown an average score of 32.9 for dementia and 18.5 for terminal cancer stage) and a validated 7-questions Relationship Scale were completed.

Results: (mean ± SD) 257 patients (73.2% F), mean age 46.3 ± 16.15 years, with a disease duration of 7.5 ± 9.8 years were included. Transit subtypes were: IBS-D 33.7%; IBS-C 21.4% and IBS-M 42.9%. A colonoscopy was performed in 85.7% of participants and 66.9% had an employment at the time of the survey. Among IBS participants, 33.5% of women were menopausal; 5.8% of men had prostate surgery; 62.6% had at least minimal physical activity, 2% had diabetes, 11.4% had hypertension, 6.6% took beta blockers, and 30% antidepressants and/or anxiolytics. According to HAD score 61% of IBS participants had anxiety and 24.7% depression. The IBS-SSS score was 301 ± 94 (minimal in 10%, moderate in 38%, severe IBS in 51%); the fatigue score was 46.68 ± 13.03. The IBS-QoL score was 60.9 ± 17.8 with sexual sub-score of 48.31 ± 33.5. Sexual dysfunction was present in 67.5% of women and 53.3% of men with erectile dysfunction that was moderately severe in 38.3% and severe in 20%. In women, sexual dysfunction was related neither with IBS-SSS nor with HAD score, but only with IBS-QoL sexuality subscore, bloating (IBS-SSS), employment, physical activity, spousal status. In men, no relationship was found with sexual dysfunction and other characteristics.

Forty-seven partners of IBS participants, mean age 44.65 ± 14.38 years (Men 63.8%) had also responded to the survey. The average Zarit's burden score was 23.6 ± 16.68 (The burden was absent in 50%, mild in 36.8%, moderate in 10.5% and severe in 2.6%), and relationship scale was 3.2 ± 0.6. There was no correlation between ZBI and IBS-SSS but a negative correlation between ZBI and relationship scale ($r = -0.337$; $p = 0.039$).

Conclusion: In this survey of IBS participants, with 50% of severe IBS, a sexual dysfunction was present in 2/3 of women and a moderately severe to severe sexual and erectile dysfunction in more than one in two men. This study also confirms a partner burden in half of them that was not correlated with disease severity may be because of the strength of the relationship.

Disclosure: Nothing to disclose

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P1068 ADHERENCE WITH LOW FODMAPS DIET IN IRRITABLE BOWEL SYNDROME: ARE EATING DISORDERS THE MISSING LINK?

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Introduction: The low FODMAP diet has emerged as an option for the treatment of irritable bowel syndrome (IBS). One major challenge of this dietary treatment is the need to restrict a range of foods and high levels of adherence are required for effective outcomes. Preliminary findings suggest an association between eating disorder (ED) and the risk of developing IBS. We hypothesised that high adherence to this diet is associated with an increased risk of eating disorder behaviour.

Aims and Methods: We report a single-centre study in the IBS patient population at University College London Hospital (UCLH). 233 consecutive patients (186 female) who commenced a low FODMAP group programme for IBS (Rome III or IV). Self-reported diet adherence at the end of the 6-week programme was measured. At baseline, participants completed the SCOFF questionnaire (a validated 5-item screening tool for EDs) and the IBS-symptom severity score (IBS-SSS).

Results: The SCOFF questionnaire identified 54 (23%) patients at an increased risk of ED behaviour. Overall, 95 (41%) participants were diet-adherent at 6 weeks (defined as adhering to low FODMAP foods for $>75\%$ of intake), with significantly greater adherence in identified ED individuals (57%). The highest adherence rate was in the IBS-D subtype (51%) and the lowest rate in IBS-C(10%). There was no significant relationship between IBS symptom severity and either adherence or ED severity

Conclusion: In our IBS patient cohort greater adherence to a low FODMAPs diet is associated with greater risk of eating disorder behaviour. The implications of our study are for clinicians to be aware of the risks associated with following a restrictive diet in the context of the prevalence of EDs in IBS patients. It is

important low FODMAP dietary advice to the general IBS population includes an explanation of the psychological risks of following restricted diets.
Disclosure: Nothing to disclose

P1069 IRRITABLE BOWEL SYNDROME, CHRONIC FATIGUE AND PAIN IN A NORWEGIAN PRIMARY CARE POPULATION

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Introduction: Irritable bowel syndrome (IBS) is a common condition with a pooled global prevalence of 11%. The prevalence varies depending on the year and geographic location of the study, method for data-collection and the criteria used (1). In 2016 the new Rome IV criteria for the diagnosis of IBS were announced (2). No studies on the prevalence of IBS based on the Rome IV criteria have been published, but it has been reported that Rome IV criteria will identify a smaller patient population with more severe IBS compared to the previous Rome III criteria (3).
Several studies have shown an overlap of IBS with other syndromes and symptoms, such as chronic fatigue, fibromyalgia, and widespread pain (4). Mostly, these studies are small, with patients in secondary or tertiary care.
Aims and Methods: The aims of this study were to estimate the prevalence of IBS according to Rome IV criteria in a primary care population, and to establish the association with chronic widespread pain and fatigue.
During the sixth year of their studies, all medical students at the University of Bergen have a four-week placement in general practice. Each student was asked to distribute a one-page questionnaire to 20 consecutive patients aged 18 and above who visited the practice. The data collection for this study took place in the fall of 2017 and winter of 2018.
The main outcome was IBS based on questions composed to fit Rome IV criteria. Secondary outcomes were the symptoms 'chronic fatigue' based on the two questions from Chalder's Fatigue Questionnaire that corresponded best with chronic fatigue in the control group of a previous study (4), and 'pain'-based on questions about back pain and muscular pain. Explanatory variables were age, sex, education and country of birth.
Results: The response rate was 83% (1926/2307). The mean age was 49.7 years, 63.1% of the respondents were female, and 9.3% were born outside Norway.
The overall prevalence of IBS was 5.9% (107/1817), 7.4% among women and 3.3% among men (relative risk (RR) 2.3, 95% confidence interval (CI) 1.4–3.6). Patients with IBS were younger than those without IBS (41.9 vs. 49.5 years, $p < 0.001$). IBS status was not associated with level of education or country of birth.
The prevalence of chronic fatigue was 23.7% (421/1777) and of pain 20.0% (355/1775). IBS was associated with both these outcomes. Among patients with IBS 51.9% also reported chronic fatigue (RR 2.44, 95% CI 1.98–2.99) and 41.9% reported chronic pain (RR 2.40, 95% CI 1.87–3.08).
Conclusion: The prevalence of IBS in Norwegian primary care was 5.9%. IBS was associated with younger age and being female, and a high proportion of patients with IBS also reported chronic fatigue or pain.
Disclosure: Nothing to disclose

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P1070 THE SOCIOECONOMIC BURDEN OF IRRITABLE BOWEL SYNDROME IN A DUTCH POPULATION

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Introduction: Irritable Bowel Syndrome (IBS) is a highly prevalent functional disorder that carries a substantial socioeconomic burden due to increased healthcare utilization and productivity losses. Actual data on this topic for the Dutch situation is lacking.
Aims and Methods: This study aimed 1) to determine the socioeconomic cost of IBS and 2) to identify sociodemographic and clinical characteristics associated with direct and indirect costs in a Dutch IBS population.
Baseline data from patients enrolled in the PERSUADE trial (peppermint oil versus placebo) was used. IBS patients (ROME IV), aged between 18 and 75 years old, were included via primary and secondary/tertiary care recruitment or self-referral and completed questionnaires regarding demographics and life style, symptom severity, Quality of Life, and anxiety and depression. Direct and indirect health related costs were measured using the iMTA/Trimbos Medical Cost Questionnaire (MCQ, recall period 3 months) and Productivity Cost Questionnaire (PCQ, recall period 4 weeks) respectively. Costs were calculated by multiplying resource use by the cost price per resource unit, adopting reference prices derived from the Dutch guidelines for cost calculations in health care. The friction cost method was applied for the determination of long term absenteeism costs. Data regarding short-term absenteeism was extrapolated to estimate costs for a 3-month period.
Results: 111 patients (86% female, mean age 33 years old; Sd 13) were included in the current analysis. Data was highly skewed. Table 1 shows the total direct and indirect costs.

Category	Total direct and indirect costs, sum in € (%); mean (Sd)
N = 111	
Absenteeism	45.619 (39.8); 205 (1.150)
Mental health care	13.622 (11.9);123 (329)
Outpatient consultation	11.439 (10); 122 (329)
Physiotherapy	8.775 (7.7); 79 (142)
Diagnostics or treatment without hospitalization	7.931 (6.9); 36 (268)
Impaired unpaid work	5.291 (4.6); 48 (135)
General Practice	5.270 (4.6); 48 (58)
Hospitalization	3.416 (3.0); 31 (249)
Medication	3.345 (2.9); 30 (45)
Other costs	9.794 (8.6); 12 (77)
Total	114.513 (100); 1031 (2022)

N.B.: other costs comprise of i.e. costs for ER (emergency room) and ambulance, dietary advice, domestic help, etc.
[Total direct and indirect health related costs.]
Mean total direct costs for a period of 3 months were +/− €573, Sd €999 (median €285; IQR €74–689). Visits to mental health care providers and outpatient visits (to a physician other than psychiatrist) contributed most to these direct costs (22% and 18% respectively), followed by physiotherapist consultations (14%). Depression symptom scores were positively associated with direct costs (B €108, $P < 0.00$; CI 51–165). Mean total indirect costs for 3 months were +/− €459, Sd €1608, but were caused entirely by a subgroup of 31 patients. In this subgroup (87% female, mean age 34 years old; Sd 11), mean indirect costs were €1642, Sd €2735 (median €729; IQR €286–1924). Indirect costs were primarily related to absenteeism.
Conclusion: Both direct and indirect costs lead to a substantial socioeconomic burden in a Dutch IBS population. Mental health care and absenteeism appear to be important driving factors of costs in these patients.
Disclosure: The PERSUADE trial is funded in part by WillPharma.

P1071 STRONG EVIDENCE SOMATISATION MEASURES BASED ON SYMPTOM CHECKLISTS ARE MORE REFLECTIVE OF PSYCHOLOGICAL RATHER THAN PHYSICAL HEALTH: IMPORTANT CONSEQUENCES FOR GASTROENTEROLOGY RESEARCH AND PRACTICE

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Introduction: Functional gastrointestinal disorders (FGIDs) have been strongly associated with psychological disorders, including somatisation (1). Somatisation in gastrointestinal (GI) research is typically defined as a physical expression of psychological distress and a number of scales are commonly used to measure it, including somatic symptom checklists (SSCLs) (2) and measures centred around psychological distress [e.g. DSM]. Some of these have been criticised as not truly measuring somatisation as they can be confounded with actual organic co-morbidities, especially in the absence of clinical examination or structured interview (3). Consequently neither researchers nor clinicians can be certain whether they reflect psychological distress or somatic illness burden.
Aims and Methods: We aimed to determine whether somatisation as measured through an SSCL was primarily driven by measures of psychological state or measures of physical health in a large, longitudinal study of women's health.

Two waves (3 and 4) of data collected from the cohort born 1973–1978 of the Australian Longitudinal Study of Women's Health (n = 4368) (4) were analysed to determine whether somatisation as measured in one wave was better predicted by psychological traits or physical health and lifestyle three years earlier. The same analysis was repeated cross sectionally to determine whether the SSCL was more influenced by concurrent psychological state or physical health. To reduce optimism bias in model development predictors were chosen based on Bayesian Information Criterion (BIC) rather than conventional tests.

Results: As shown in the table below, almost the same number of psychological and physical health measures were found to be longitudinal predictors of SSCL. However the psychological predictors accounted for approximately twice as much of the variance in SSCL as did physical health predictors. Cross-sectionally, a much larger list of concurrent physical health predictors were identified (Table) and slightly fewer psychological predictors were involved. However the variance in SSCL explained by concurrent psychological predictors was again approximately twice the variance explained by physical health and lifestyle predictors.

Conclusion: Despite being a list of potential health complaints, the SSCL utilised in this large, population-representative longitudinal study of women appears to be more a reflection of psychological distress than physical health.

Predictor	Longitudinal	Cross-sectional
SEIFA (SES)	−.04 (.02)	n/a
CESD (depression)	.125 (.025)	.088 (.026)
Stress	.147 (.019)	.139 (.019)
SF-36 mental	−.173 (.025)	−.279 (.025)
Satisfaction w GP	−.032 (.014)	n/a
Experienced violence	n/a	.020 (.013)
SF-36 physical	−.256 (.020)	−.343 (.020)
Major illness	.051 (.014)	.040 (.013)
medications for nerves	−.014 (.014)	n/a
Other medication	−.038 (.014)	n/a
Non-prescribed medications	.077 (.014)	053 (.013)
Low v high alcohol intake	.015 (.013)	n/a
Smoking: ex v never	n/a	.011 (.014)
Smoking: current v never	n/a	.020 (.014)
Marijuana: ever v never	n/a	.021 (.015)
Other drugs: ever v never	n/a	.041 (.016)
Exercise: moderate v low	n/a	.0046 (.014)
Exercise: high v low	n/a	.032 (.014)
Other exercise	n/a	.032 (.014)
R^2 (total)	.188	.249
R^2 (psych)	.138	.174
R^2 (physical)	.068	.098

[Table. Predictors of somatisation score. Psychological variables italicised. Cell entries are coefficient (SE).]

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P1073 PREVALENCE AND IMPACT OF SELF-REPORTED VERSUS ROME IV CRITERIA-BASED IRRITABLE BOWEL SYMPTOMS IN THE GENERAL POPULATION

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Introduction: The symptom-based diagnostic criteria for IBS have recently been revised in the Rome IV consensus. In a tertiary care cohort, compared to Rome III, Rome IV identifies a subgroup with more severe symptoms, co-morbidity and quality of life impact (Vork 2018). On the other hand, with rising public awareness of IBS, self-diagnosis and self-management are likely to increase as well. The prevalence and impact of Rome IV-based IBS versus self-diagnosed IBS was compared in the general population.

Aims and Methods: An internet panel filled out an online survey on bowel symptoms and their impact. Questions addressed demographics, IBS symptoms based on Rome IV criteria, their frequency, and their impact on healthcare utilization and daily activities.

Results: A representative internet panel of 1,012 subjects, which reflected the Belgian population in terms of educational level, professional activity, and regional distribution, completed the online survey. Rome IV IBS criteria were fulfilled by 5.5% of the Belgian population who were younger and more likely to be female (7% of women vs. 3.9% of men, 42.4 ± 1.9 vs. 45.4 ± 0.5 years, $p \leq 0.05$). Thirty-seven percent had consulted a physician for IBS symptoms (27% primary care, 15% a specialist) over the last year, with an average of 41 ± 2.2 doctor visits per patient; colonoscopy was performed in 12% and radiological examination in 15%. Rome IV IBS subjects reported as a consequence of their symptoms bothersome fatigue (88%), irritability (85%), insomnia (65%), anxiety (69%), loss of appetite (69%), depressive mood (54%), shame (58%), staying home from social activities (54%), anger (54%) and interference with ability to work (27%). Sixty-one percent of these subjects were employed, and 7% reported absence from work due to IBS symptoms, leading to 14 days of absence from work due to bowel symptoms over the last year.

Based on a brief description of the condition, 17.6% of the population self-identified as suffering from IBS ($p < 0.001$ compared to Rome IV), and these were more likely to be female, but without significant age difference (28.2% of women vs. 14.9% of men, $p = 0.0003$, 45.7 ± 0.9 vs. 45.1 ± 0.5 years, NS). Concordance with the Rome IV criteria was only 17%. Thirty-two percent had consulted a physician over the last year (27% primary care, 13% a specialist; NS compared to Rome IV); colonoscopy was performed in 11% and radiological examination in 14% (NS compared to Rome IV). Subjects self-reporting with IBS attributed to these symptoms a major impact on daily life through associated fatigue (83%), irritability (83%), insomnia (65%), anxiety (59%), loss of appetite (61%), depressive mood (54%), shame (49%), staying home from social activities (50%), anger (40%) and interference with ability to work (24%). Sixty-seven percent of these subjects were employed and 19% reported absence from work due to bowel symptoms, generating a total of 134 days over the last year.

Conclusion: In the general population, the prevalence of self-reported "IBS" is three-fold higher than the prevalence of IBS according to Rome IV criteria and the concordance is very low. In the general population, compared to those fulfilling Rome IV criteria, self-reported IBS is associated with similar or higher impact on healthcare utilization, quality of life, and ability to work.

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P1074 DOES BLINDING AFFECT THE OUTCOME OF FRUCTOSE BREATH TESTING IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS?

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Introduction: The fructose breath test is widely used for the investigation of fructose intolerance and malabsorption as contributing factors to symptoms of functional gastrointestinal disorders (FGID). Additionally, it is useful in predicting responders to a dietary reduction of fermentable sugars (low FODMAP diet)(1). Patients with FGID are, however, well known to have high placebo response susceptibility. As the breath test is normally applied in open fashion, it is unknown what the contribution of knowledge of the substrate is to the test outcome.

Aims and Methods: The aim of this single-centre, placebo-controlled prospective trial was to compare the outcome of breath tests when fructose is given in open versus blinded fashion in successive patients with FGID. Identical breath tests were performed in randomized sequence at least one week apart with either a) water (neutral placebo), b) artificial sweetener (Assugrin®: cyclamate/saccharine, sweet placebo), c) fructose given double-blind or d) fructose given open. Breath samples were collected in 30 male and female patients with FGID (defined by Rome III criteria, mean age 29 ± 9 years) for measurement of hydrogen and methane concentrations, and GI symptom intensities (abdominal bloating, flatulence, fullness, nausea, diarrhoea, abdominal cramps or pain, borborygmi, and gastroesophageal reflux) were each scored on a 3-point Likert scale for 5 hours after substrate ingestion. Patients were not selected based on symptom or gas responses. The areas-under-the-curve (AUC) of the individual and aggregate GI symptom scores and of the breath hydrogen and methane concentrations were compared between substrate arms.

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Table: Baseline-corrected means and standard deviations are shown.

	water	fructose open	fructose blind	artificial sweetener	p-value across all arms (Dunn's test, Bonferroni corrected)
AUC GI aggregate symptom score	1.42 ± 5.17	6.47 ± 9.04	4.37 ± 8.27	1.81 ± 3.98	0.01
AUC hydrogen concentration	−8.92 ± 18.94	23.39 ± 50.16	20.44 ± 53.09	−6.05 ± 26.12	0.002
AUC methane concentration	−1.16 ± 4.54	8.83 ± 21.74	5.32 ± 13.10	0.08 ± 9.22	0.02

Results: There were no significant differences between the open fructose and blinded fructose arms in the AUCs of any of the individual or aggregate GI symptom scores (see Table). However, the AUCs of the aggregate GI symptom scores were greater following open fructose than water ($p = 0.003$). There were no significant differences in the AUCs of either hydrogen or methane concentrations between open and blinded fructose breath tests, but hydrogen gas concentration AUCs were greater following open and blinded fructose than after water and artificial sweetener (all $p < 0.05$). A similar trend towards higher methane breath gas concentrations following open and blinded fructose than after water and artificial sweetener was seen. Blinding was maintained very effectively, as only 5 of 120 (4%) treatment substrates were attributed correctly by the patients.
[Baseline-corrected means and standard deviations are shown.]
Conclusion: The absence of significant differences in symptom scores and gas concentrations between breath tests with fructose given open or blinded clearly indicates that clinical breath testing can be performed in open fashion in patients with FGID. The comparisons of GI symptoms and breath gas concentrations between the neutral and sweet placebos and the fructose arms are marked by wide variability due to the inclusion of patients across the entire spectrum of responses, i.e. with and without fructose intolerance or malabsorption.
Disclosure: Sponsored by Forschungsstftung Hirslanden, Zurich, Switzerland.

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P1075 BLOATING IN A LARGE OUTPATIENT POPULATION: DISCHARGE OR INVESTIGATE?

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Introduction: Bloating is a common presenting complaint and affects approximately up to 20% of the population, though objective abdominal distension only occurs in half of the cases. It can have a significant impact on the patient's everyday activities. Its severity may vary from transient without the need for treatment, to severe and debilitating symptoms that cause multiple outpatient clinic visits or even to the emergency department. However, its evaluation and management may be difficult, thus necessitating multiple medical appointments and investigations.
Aims and Methods: The aims of this study were to determine the prevalence of this symptom among patients presenting to a gastroenterology out-patient clinic and the pathologies that were diagnosed in this group of patients. This was a retrospective analysis of patients presenting to a single consultant gastroenterology secondary care out-patients clinic (2013–2015) where one of the symptoms was bloating. The clinical case notes and investigations (blood tests, faecal calprotectin, radiology and endoscopic procedures) were reviewed.
Results: From an overall cohort of 840 patients, 256 patients with bloating (73.4% females) were identified. The mean patient age was 42.4 (SD +/− 14.1) years. The mean time of follow up for these patients was 47.5 months (range: 20.5–71.3).
Other symptoms were: abdominal pain (73.8%), dyspepsia (32%), nausea (14.8%), vomiting (4.7%), bleeding pr (7%), change in bowel habit to diarrhoea (29.7%), change in bowel habit to constipation (17.6%) and weight loss (9%),
In 9.4% of patients the following pathologies were diagnosed: coeliac disease ($n = 6$), small bowel intussusception ($n = 1$); renal cell carcinoma ($n = 2$); endometrial carcinoma ($n = 1$); hypothyroidism ($n = 2$); ulcerative colitis ($n = 5$); small bowel Crohn's disease ($n = 3$); microscopic colitis ($n = 2$); unclassified inflammatory bowel disease ($n = 2$). All malignancies occurred in patients above the age of 50 years.
Conclusion: This data demonstrates that bloating contributes to a significant patient load in an out-patient setting as 30.5% of patients had this symptom. Routine blood investigations, a faecal calprotectin and abdominal ultrasonography are initial baseline investigations that should be considered in all such patients as approximately 10% of these patients had significant pathologies diagnosed.
Disclosure: Nothing to disclose

P1076 EFFECTS OF *ALOE BARBADENSIS* MILL. EXTRACT ON SYMPTOMS AND FAECAL MICROBIOTA PROFILE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: *Aloe barbadensis* Mill. has been suggested to reduce symptoms in patients with irritable bowel syndrome (IBS).
Aims and Methods: We aimed to determine the effects of a commercially available *Aloe barbadensis* Mill. (Aloe) extract AVH200®, on symptoms and fecal microbiota in patients with IBS, in a randomized, double-blind, placebo-controlled study. After a 2 week screening period, 173 patients with IBS according to the ROME III criteria, were randomized to active treatment ($n = 91$) (250 mg aloe extract, 60 mg ascorbic acid and inulin) or placebo ($n = 82$) (60 mg ascorbic acid and inulin), for 4 weeks. Patients completed IBS Symptom Severity Scoring (IBS-SSS) questionnaires on a weekly basis. Response was defined as a reduction of IBS-SSS ≥ 50, compared with baseline. Faecal samples were collected before and after the intervention from 52 patients and microbiota composition was evaluated by GA-map™ Dysbiosis Test of 54 DNA probes targeting ≥ 300 bacteria which were analyzed with Orthogonal Projections to Latent Structures Discriminatory Analysis (OPLS-DA) implementing a VIP cut-off of 0.7. Statistical analysis were carried out using non-parametric tests.
Results: In total, 160 IBS patients completed the study. The overall severity of IBS symptoms was reduced in patients receiving active treatment ($n = 84$; 242 (199–291) vs. 218 (138–281), $P < 0.001$) and placebo ($n = 76$; 236 (171–289) vs. 197 (126–258), $P < 0.001$) comparing baseline vs. end of intervention, without difference between the groups ($P = 0.61$). However, a reduction in overall symptom severity was recorded in diarrhea predominant patients (IBS-D) receiving active treatment ($n = 21$; 273 (196–330) vs. 226 (101–308), $P = 0.003$) but not placebo ($n = 22$; 229 (138–259) vs. 196 (118–238), $P = 0.07$), without difference between the groups ($P = 0.21$). Further, pain severity, pain frequency, bloating and daily life were similarly reduced in both groups (data not shown). However, bowel habit was improved by active treatment (70 (52–88) vs. 60 (41–81), $P = 0.001$), but not placebo (70 (46–85) vs. 66(46–80), $P = 0.17$), although without difference between the two groups ($P = 0.43$). The frequency of responders did not differ between active treatment ($n = 27$, 32%) and placebo ($n = 31$, 41%) ($P = 0.26$).
In the active treatment group, faecal microbiota profiles differed between responders ($n = 10$) and non-responders ($n = 14$) both before ($R2 = 0.96$, $Q2 = 0.55$) and after intervention ($R2 = 0.94$, $Q2 = 0.73$). The abundance of *Akkermansia muciniphila* was higher in responders than non-responders before (65.5 (35.8–187.3) vs. 3.5 (1–44), $P = 0.03$) but not after the intervention (54 (14.5–226.8) vs. 23 (1–106.78), $P = 0.32$). In the placebo group, the fecal microbiota profiles of responders ($n = 12$) and non-responders ($n = 16$) did not differ before or after the intervention.
Conclusion: Aloe extract and placebo were similarly effective in reducing overall symptoms of IBS patients, but a tendency towards better effect of aloe extract were seen in IBS-D patients. Further, faecal microbiota profiles may help predict IBS patients' responsiveness to aloe extract.
Disclosure: Presenting Author – Bani Ahluwalia is employed by Calmino Group AB while carrying out her Industrial PhD studies at the University of Gothenburg.

P1077 EFFICACY AND SAFETY OF ELUXADOLINE IN IBS-D PATIENTS WHO REPORT INADEQUATE SYMPTOM CONTROL WITH PRIOR LOPERAMIDE USE: A PHASE 4, MULTICENTER, MULTINATIONAL, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLINDED STUDY (RELIEF)

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Introduction: Irritable bowel syndrome with diarrhea (IBS-D) is a functional gastrointestinal disorder with limited treatment options. We evaluated the efficacy and safety of eluxadoline, an FDA-approved mixed μ-opioid receptor (OR) and κ-OR agonist and δ-OR antagonist compared to placebo in IBS-D patients

who reported inadequate symptom control with prior use of loperamide, an over-the-counter μ-OR agonist.
Aims and Methods: Adults with IBS-D (Rome III criteria) who reported inadequate symptom control subsequent to loperamide use within the preceding 12 months were randomized 1:1 to placebo or eluxadoline 100 mg twice daily taken with food for 12 weeks. Patients recorded daily IBS-D symptoms, including worst abdominal pain (WAP) on a 0 to 10-point scale and stool consistency (evaluated by Bristol Stool Score [BSS]). The primary efficacy endpoint was the proportion of composite responders, defined as patients who met daily composite response criteria (WAP improvement by ≥40% **AND** BSS score <5 or absence of bowel movement accompanied by ≥40% WAP improvement compared to baseline) for at least 50% of treatment days, and had ≥60 days of diary entries over the 12-week treatment period
Results: 346 patients were enrolled. The majority (70%) were female, and mean age was 44 years. A significantly greater proportion of patients receiving eluxadoline achieved the primary composite responder endpoint compared to placebo (22.7% [39/172] vs. 10.3% [18/174]; p = 0.0022). Additionally, a higher proportion of patients achieved the secondary endpoints of improvements in stool consistency (27.9% [48/172] vs. 16.7% [29/174]; p = 0.0119) and WAP (43.6% [75/172] vs. 31.0% [54/174]; p = 0.0174) with eluxadoline than placebo, respectively. Throughout the 12-week study, a greater proportion of eluxadoline patients met the monthly composite responder endpoint compared with placebo (Weeks 1–4: 14.0% vs. 6.9%, p = 0.0330; Weeks 5–8: 26.7% vs. 14.9%, p = 0.0063; Weeks 9–12: 30.8% vs. 16.7%, p = 0.0018). A comparable number of patients reported treatment-emergent adverse events (TEAEs) with eluxadoline (124 events; 37.4% [64/171]) and placebo (112 events, 35.3% [61/173]). More patients discontinued treatment due to TEAEs with eluxadoline compared with placebo (10 vs. 3). No treatment-related serious AE was reported.
Conclusion: Eluxadoline appears safe, effective, and well tolerated for treating IBS-D symptoms in patients who report inadequate symptom control with prior loperamide use.
Disclosure: This study was funded by Allergan plc. Darren Brenner is a consultant and speaker for Allergan plc. Catherine Gutman is an employee of Allergan plc. Esther Jo is an employee of Allergan plc.

P1078 MULTIDISCIPLINARY SHARED MEDICAL APPOINTMENTS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS: PRELIMINARY RESULTS OF A NON-PHARMACOLOGICAL PILOT STUDY

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Introduction: Functional gastrointestinal disorders (FGIDs) are prevalent and resource consuming. Biopsychosocial interventions have proven useful for symptom control. Shared medical appointments have been successfully used in other diseases to reduce waiting times, limit costs and increase patient satisfaction, but their use in FGIDs is still limited. No specific multidisciplinary programmes have been developed for FGIDs.
Aims and Methods: A multidisciplinary (Gastroenterology, Dietetics, Psychiatry) approach was used in a group of patients diagnosed with FGIDs attending shared medical appointments. Efficacy of a series of non-pharmacological interventions (dietary modifications, psychoeducation, stress and anxiety control) over a 4-month period was assessed on several health indicators (presence and intensity of gastrointestinal (GI) and psychological symptoms, drug use) and a dietary journal. (Table 1: time course of the intervention).
Results: 25 patients have been included so far. 80% were women. Mean age was 46.2 years (range 29–68). Initial diagnoses were, as per the ROME IV criteria (1, 2): 36% irritable bowel syndrome, 12% functional diarrhoea, 32% functional abdominal distension, and 88% dyspepsia. 96% of patients attended at least one formative session. The severity of the GI symptoms (3) improved from a baseline score of 324.8 ± 16.7 points (severe) to 104 ± 28.4 (mild) (p < 0.00005). Adherence to low fodmap diet was good (7.3 ± 1.4 vs 1.4 ± 1.1 servings of high fodmap foods per day, p = 0.025). A trend towards a reduction in waist circumference (97.4 ± 8.9 vs 92.8 ± 8.3 cm, p = 0.076) in the absence of significant changes in body mass index suggests an improvement in abdominal bloating. The number of drug groups used during the 6 months prior to the intervention was 2.7 ± 0.4, and it was reduced to 0 ± 0 (p = 0.0037). Baseline anxiety and depression scores (4) were within the pathological and borderline range respectively and did not improve significantly after the intervention (11.4 ± 0.8 vs 10.2 ± 2.3 points for anxiety; 7.2 ± 1.1 vs 6.6 ± 2.8 for depression).
Conclusion: A multidisciplinary shared medical appointment approach to implement non-pharmacological measures in the treatment of FGIDs is useful to alleviate GI symptoms in these patients. A stronger psychological intervention might be needed for adequate control of anxiety. A dietary reintroduction phase is currently being implemented to tailor the individual needs and prevent nutritional deficits. A 6 and 12-month post intervention assessment will be needed to see whether improvement persists.
Disclosure: Nothing to disclose

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P1079 HYPNOTHERAPY FOR IRRITABLE BOWEL SYNDROME: THE PATIENT'S PERCEPTION

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Introduction: Numerous studies have shown that hypnotherapy (HT) improves the symptoms of irritable bowel syndrome (IBS) using clinical outcome measures. In light of the increasing interest in capturing the patient's perception of their illness and treatment, it was felt it would be helpful to record how patients perceive the hypnotherapeutic process, on which there is currently little information.
Aims and Methods: In addition to measuring symptom change, we have recently started to record the patient's perception of hypnotherapy for their IBS, including their expectations, and now report the results for the first 50 patients.
50 consecutive IBS patients (38 females and 12 males, age range 18–76) attending for hypnotherapy were asked to complete questionnaires recording their IBS symptom severity (IBS SSS), quality of life, non-colonic symptoms, anxiety and depression before and after treatment. In addition, they completed questionnaires detailing their perception of HT, other people's perception of HT and their expectations about the efficacy of HT. Their perceptions about the hypnotherapeutic process were assessed quantitatively and also qualitatively using patient descriptions. Furthermore, the analysis compared the characteristics of responders and non-responders.
Results: 39 out of 50 patients (78%, P < 0.001) responded to treatment (50 point or more reduction in IBS SSS), which is exactly consistent with our previously published data. Pain scores, non-colonic symptoms, quality of life, anxiety and depression also significantly improved after HT (all P < 0.001). When asked how patients felt before treatment, 52% of responses portrayed hypnotherapy negatively compared to 3% after treatment. The relatives and doctors of patients were generally supportive of HT although one cognitive behavioral therapist advised against it. In responders, 19 patients (48.7%) expected hypnotherapy to be effective prior to starting it, whereas in non-responders, 7 (64%) expected treatment to be successful. Interestingly, 9 of 11 non-responders (82%) considered treatment worthwhile despite no significant effect on their symptoms. This may be because 46 patients (92% of all patients) had found HT helped them with other issues, such as dealing with stressful situations or poor sleep.
Conclusion: Although initially being perceived negatively, hypnotherapy significantly improved symptoms and resulted in other benefits not related to the gastrointestinal system. Interestingly, those with greater expectation about treatment did not seem to do quite so well, suggesting that high expectations are not necessary for a good outcome.
Disclosure: Nothing to disclose

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Table 1: Intervention timecourse.

Week 1	Week 2	Week 3	Weeks 4–7	Week 8	Weeks 9–11	Week 12	Weeks 13–15	Week 16
Session 1: Getting to know FGIDs.		Session 2: Low FOODMAP diet.		Session 3: Drugs in FGIDs.		Session 4: Healthy diet.		Session 5: Laughter workshop.
Relaxation techniques.		Relaxation techniques.		Relaxation techniques.		Relaxation techniques.		Relaxation techniques.

P1080 RANDOMIZED CLINICAL TRIAL: EFFECT OF BIO-25 ON MICROBIOTA COMPOSITION OF PATIENTS WITH DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME

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Introduction: The pathogenesis of IBS is multifactorial and not completely understood. Epidemiological observations have demonstrated the development of IBS symptoms following disruption of the individual 'normal' microbiota and multiple studies have described differences between the microbiome in IBS patients and healthy cohorts. While probiotic therapy for IBS is the subject of intense investigation, its mechanisms of action are not clear.

Aims and Methods: We aimed to evaluate the impact of a multispecies probiotic on the enteric microbiota composition in women with diarrhea-predominant irritable bowel syndrome (IBS-D) and to determine whether these effects are associated with changes in IBS symptoms or inflammatory markers.

In this double blind, placebo-controlled study, Rome III IBS-D women completed a two-week run-in period. Eligible women were then assigned at random to a probiotic capsule (BIO- 25) or an indistinguishable placebo, twice daily for 8 weeks. IBS symptoms and stool consistency were rated daily by visual analogue scales and the Bristol stool scale. High-sensitive C-reactive protein was tested at baseline and 4 and 8 weeks. Fecal calprotectin and microbial composition (diversity and taxa) were tested at baseline and 8 weeks. Microbial sequencing of the 16S rRNA was performed using the pyrosequencing platform. Data was analyzed to compare patients who responded to treatment and those who did not using QIIME and Linear discriminate analysis with effect size estimation (LEfSe).

Results: One-hundred and seventy-two IBS-D patients were recruited, and 107 eligible patients were allocated to the intervention (n = 54) or placebo (n = 53) group. Compared to placebo, BIO-25 did not result in significant fecal microbial alterations, except for higher *Lactobacillus* levels in the BIO-25 group (P = 0.002). Among patients receiving BIO-25, the prevalence of specific microbial groups at baseline was predictive of the response to probiotic therapy: higher proportions of *Bilophila* at baseline were associated (P = 0.003) with symptomatic relief (clinical response) and higher proportions of *Hemophilus* (P = 0.01), *Enterobacter* (P = 0.05), *Slackia* (P = 0.03), *Faecalibacterium* (P = 0.03) *and Odoribacter* (P = 0.05) were associated with a decrease in CRP/calprotectin levels (inflammatory response) compared to the non-responders (Table 1).

Parameter	Genus	Non-responders	Responders	P-value
Bristol stool scale		n = 39	n = 11	
	Bilophilia	0.0006	0.0022	0.02
Abdominal pain reduction		n = 30	n = 21	
	Bilophilia	0.0014	0.0025	0.03
hs-CRP		n = 32	n = 15	
	Haemophilus	0.0013	0.0027	0.01
	Enterobacter	0.0006	0.0026	0.05
	Slackia	0.0006	0.0016	0.03
Fecal calprotectin		n = 25	n = 15	
	Faecalibacterium	0.076	0.088	0.03
	Odoribacter	0.0018	0.0027	0.05
	Ruminococcus	0.132	0.111	0.01
	Lactococcus	0.0014	0.0002	0.02

[Table 1 – Proportions of fecal bacterial genera associated with IBS response to the probiotic Bio-25].

Conclusion: This study provides insights into potential microbial composition tools for the identification of female IBS-D patients who may respond to probiotic therapy. Additional studies should be performed with other probiotic agents to replicate these findings.

Disclosure: Nothing to disclose

P1081 STRUCTURED PATIENT GROUP EDUCATION VERSUS STRUCTURED PATIENT EDUCATION VIA THE INTERNET FOR PATIENTS WITH IBS: A RANDOMIZED, CONTROLLED TRIAL

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Introduction: Structured patient group education (IBS School), has previously been evaluated and found efficacious for symptom improvement in patients with irritable bowel syndrome (IBS) (Ringstrom et al 2012). In this randomized controlled study we compared the effects with a similar education provided via the internet. We hypothesized that patient education provided via the internet would give effects comparable to patient education in a group format.

Aims and Methods: The study population consists of IBS patients >18 years, referred to our unit to participate in the IBS School. Patients were included in blocks of 20 and were then randomized 1:1 to IBS School in group-format or via Internet. A total number of 120 patients were included in the study (57 in the group condition and 63 in the internet condition). The IBS school in group-format consisted of three, two-hour sessions held once per week with eight to ten patients in each group. A nurse and a dietician lead the sessions. At the first session, general information was provided about IBS, symptoms, pathophysiology and treatment options. At the second session, food-related issues were discussed and at the third session the effects of other life style factors like stress, physical activity and relaxation were discussed. The participants in the Internet group received texts in a stepwise fashion over the three weeks, with the same information that were covered in the group condition. The patients were also able to communicate reflections and questions concerning the written information with the nurse and the dietician via e-mail. They were also encouraged to attend a closed online forum where they had the opportunity to discuss and reflect over information material from the last week with other patients. GI symptom severity (IBS-SSS and GSRS-IBS), GI-specific anxiety (VSI), self-rated disease knowledge (VAS 0–100 score), anxiety and depression (HADS) were assessed with validated questionnaires at baseline and 6 months after the intervention.

Results: For the primary endpoint, the IBS-SSS, 90 patients (75%) had provided follow-up data. Taken together, both groups showed significant improvement of GI symptoms, measured with the IBS-SSS ($p < .001$) and GSRS-IBS ($p < .001$), respectively, but there were no differences between the groups (p = . 30 and p = .73, respectively). Both groups showed improvement in GI-specific anxiety ($p < .001$), self-rated disease knowledge ($p < .001$), and anxiety (p = .005). There were no differences between the groups in any of these outcomes (p = .31, p = .87, and p = .46, respectively). There was no overall improvement in symptoms of depression (p = .54) and no differences between the groups (p = .93). See Table 1 for means and standard deviations for the two groups at the assessment points.

Conclusion: This study demonstrates that patient education for patients with IBS can both be delivered in traditional group format and over the internet with significant improvements in GI symptom severity, GI-specific anxiety, general anxiety, and self-rated disease knowledge and with comparable effects between the two education formats.

	Baseline		6- months follow-up	
Outcome	Group	Internet	Group	Internet
IBS-SSS	297.5 (103.4)	288.9 (77.3)	243.3 (102.2)	246.1(101,1)
GSRS-IBS	51.3 (14.3)	50.4 (10.3)	45.1(14.5)	43.5 (13.5)
VSI	40.3 (20.0)	39.2 (18.8)	34.2 (20.8)	30.8 (18.5)
Knowledge (VAS 0–100)	48.3 (21.8)	40.9 (22.6)	71.5 (17.2)	66.0 (19.0)
HADS (Depression)	8.2 (4.3)	7.6 (4.4)	7.4 (4.9)	6.2 (4.2)
HADS (Anxiety)	5.3 (3.9)	5.0 (4.2)	4.9 (3.5)	4.9 (3.7)

[Table 1 ***Outcome:*** *Mean (SD)]*

Disclosure: Nothing to disclose

P1082 USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE BY PATIENTS WITH ROMA IV CRITERIA FOR IRRITABLE BOWEL SYNDROME: A SINGLE-CENTER ITALIAN SURVEY

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Introduction: Complementary and alternative medicine (CAM) is an emerging option for irritable bowel syndrome (IBS), whose features have been recently revised by the Rome IV criteria.

Aims and Methods: The study was conducted to evaluate the impact of CAM in IBS patients as assessed by the Rome IV criteria. Consecutive patients referring for IBS were re-evaluated according to the Rome IV criteria. Demographic features and characteristics potentially associated with the use of CAM were collected. A validated, self-administered, survey questionnaire dealing with CAM and patients' level of knowledge, motivation, perception, and information seeking-behavior toward the use of CAM was analyzed. Multivariate logistic regression analysis was performed in order to identify predictors of CAM use among participants.

Results: Among 156 patients claiming IBS, 137 (88%) met the Rome IV criteria and 62 of them (45%) were CAM users. Biologically based therapy was the most chosen CAM (78%). Mind-body interventions and homeopathy account for the 11% and 5% of preferences, respectively, while none had ever used energy therapies. Significant risk factors (adjusted odd ratio, 95% confidence interval) for the use of CAM were female gender (7.22, 2.31–22.51), higher BMI (1.16, 1.02–1.33), not having children (0.25, 0.07–0.95), and a good knowledge of CAM (4.46, 1.73–11.45). Only 19% of patients used CAM due to medical advice, while 34% of them indicating media, such as television and newspapers, as a source, and 24% citing the internet. Over half (51%) thought it was a ''more natural'' approach, 25% were motivated because of the lack of therapeutic options offered by traditional medicine, while 24% expressed apprehension towards adverse drug reactions. Even though a minority of patients (16%) had full satisfaction from CAM, 81% of users would repeat the CAM experience for their IBS symptoms.

Conclusion: In a native local resident setting of IBS patients from southern Italy, the Rome IV criteria confirmed their specificity in diagnosing IBS, compared to the Rome III criteria. The widespread use of CAM in IBS, the patients' belief in its safety, and their vocation to re-use it, suggest that knowledge of health-care providers and patient education should be improved.

Disclosure: Nothing to disclose

P1083 THE MEANING OF BILE ACIDS AND VIOLATIONS OF MICROBIAL METABOLISM IN THE COLON IN THE PATHOGENIC MECHANISM OF DIARRHEA IN PATIENTS THAT SUSTAINED CHOLECYSTECTOMY OR RESECTION OF THE SMALL INTESTINE

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Introduction: Cholecystectomy and resection of the small intestine result in increased risk of bile acid diarrhea development due to a large amount of bile acids (BA) entering the colon. Long-term presence of BA in the colon may result in violation of microbiota composition and inflammation of its mucous membrane.

Aims and Methods: The aim of this work is to evaluate the influence of BA on colon microbiocenosis in patients with chronic diarrhea that had cholecystectomy or and resection of the small intestine.

18 patients with chronic diarrhea were studied that had cholecystectomy (group 1), as well as 20 patients with post-resection short small intestine syndrome (group 2). Daily BA excretion was determined in the feces of all patients with the help of spectrophotometric enzymatic analysis. Metabolic activity of colon microflora was evaluated according to the content of short-chain fatty acids (SCFA) – acetic, propionic, butyric (Bu), valeric, caproic acids and their isoforms in coprofiltrates. SCFA were identified by gas-liquid chromatography.

Results: In group 1 patients, average daily BA content in feces amounted to 564.5+ 116.3 mg/day, in group 2 patients – 1,674.8+440.1 mg/day, $p < 0.012$. In both groups, daily BA excretion with feces considerably exceeded the norm (50–200 mg/ day), $p < 0.001$. The data obtained confirmed the leading role of BA in diarrhea development in these patients. Metabolomic study of the large bowel microbiocenosis showed pronounced reduction in metabolic activity of colon microflora in the examined patients. Average values of total SCFA concentration (TSCFA) made up 4.11 + 1.81 mg/g vs norm 10.6 + 0.23 mg/g, $p < 0.005$. In this case, the value of TSCFA in the 1st group was somewhat higher – 4.79 + 0.63 mg/g than in the 2nd group – 3.61 + 0.27 mg/g (NS). The analysis showed true correlation level between the TSCFA and daily BA excretion: $r = -0.42$, $p = 0.05$. Special attention is drawn by reduced concentration of butyrate (Bu conc.) and its share (%Bu) in the total concentration of metabolites. It reached 1% with the norm of 16% in 61% of the studied patients. It is butyrate that shows high correlation with BA concentration: Bu conc. – BA conc. $r = -0.49$, $p = 0.03$; %Bu – BA conc. $r = -0.52$. $p = 0.02$.

Conclusion: The reason for diarrhea development in patients that had cholecystectomy or resection of the small intestine is high BA concentration in the colon. Besides, BA considerably suppress bacterial metabolism in the colon. Butyrate-producing bacteria suffer the most. As butyrate is an energy substrate for colonocytes, disease chronization may entail progressing dystrophy of colon mucosal epithelium.

Disclosure: Nothing to disclose

P1084 PSYCHOLOGICAL MORBIDITY AND IMPACT ON THE QUALITY OF LIFE OF BENIGN ANORECTAL DISORDERS

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Introduction: Benign anorectal disorders (BADs) are very common, with associated symptoms that may have a significant impact on the quality of life.

Aims and Methods: The aim of the study was to evaluate the prevalence of anxiety/depression symptoms and quality of life (QOL) in patients with BADs. Single-center prospective study that included consecutive patients with BADs evaluated at the Coloproctology outpatient clinic and a group of healthy volunteers (blood donors). Psychological morbidity was assessed using the Hospital Anxiety and Depression Scale (HADS) questionnaire, including anxiety (HADS-A) and depression (HADS-D) subscales. A HADS score greater than 8 was considered abnormal. The QOL was evaluated using the *Short Form (36) Health Survey* (SF36), summarized in a physical (PCS) and mental (MCS) component score (with lower scores representing a lower QOL).

Results: Fifty-one participants (31 patients and 20 healthy volunteers) were included, 59% women, with a median age of 52 years (IQR 38–62). There were no differences between the two groups regarding gender ($p = 0.250$) but the control group was younger (median 45 vs. 59 years, $p = 0.002$) and had a higher education (high school 55% vs. 26%, $p = 0.044$). The main BADs were hemorrhoids (32%), pruritus ani (29%) and anal fissure (19%). More than one BAD was present in 23% of patients. Compared with controls, patients with BADs had higher mean scores of HADS-A (10 ± 4 vs. 4 ± 3, $p < 0.001$) and HADS-D (7 ± 4 vs. 2 ± 3, $p < 0.001$). In the BADs group the proportion of patients with abnormal scores of HADS-A (77% vs. 10%, $p < 0.001$) and HADS-D (47% vs. 10%, $p = 0.012$) was significantly greater than in controls. Mean scores of PCS (46 ± 10 vs. 54 ± 5, $p < 0.001$) and MCS (31 ± 22 vs. 48 ± 17, $p = 0.004$) were lower in the BADs group. In the subanalysis of the BADs group the presence of pruritus ani was significantly associated with a higher HADS-A score (13 ± 5 vs. 9 ± 4; $p = 0.013$) and lower MCS (16 ± 20 vs. 35 ± 20; $p = 0.031$). The presence of more than one BAD showed a tendency for a lower PCS (39 ± 7 vs. 48 ± 10; $p = 0.057$) and MCS (16 ± 15 vs. 34 ± 22; $p = 0.06$) but it did not reach statistical significance.

Conclusion: Bening anorectal disorders are associated with a considerable prevalence of anxiety/depression symptoms and a negative impact on quality of life. A high degree of suspicion of an undiagnosed BADs-associated psychological disorder may be important, in order to allow for a timely and adequate therapeutic approach.

Disclosure: Nothing to disclose

P1085 ANATOMICAL AND FUNCTIONAL FEATURES OF THE INTERNAL RECTAL PROLAPSE DETERMINED WITH 3D ENDORECTAL ULTRASONOGRAPHY AND HIGH-RESOLUTION ANORECTAL MANOMETRY. AN OBSERVATIONAL CASE-CONTROL STUDY

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Introduction: Approximately half of constipated patients suffer from obstructed defecation. Obstructed defecation syndrome (ODS) is the inability to empty the rectum satisfactorily during defecation and is well defined in the Rome IV. Internal Rectal Prolapse (IRP), a full-thickness intussusception of the rectum, often associated with rectocele, plays an important role in the pathophysiology of ODS. Furthermore, there are scarce data on rectal anatomical evaluation and its relationship with a possible impairment of rectal function.

Aims and Methods: The aim was to investigate whether any correlation between rectal wall thickness (RWT) and rectal pressure (RP), determined by means of 3D endorectal ultrasound (EUS) and high-resolution anorectal manometry (HRAM), can offer new insights in the pathophysiology of patients with ODS caused by IRP.

Patients with ODS caused by IRP were selected. Healthy volunteers (HVs) served as controls and to define normal data. Standardized clinical questionnaire were administered. Subjects underwent 3D EUS to measure RWT and HRAM to measure pushing endorectal pressure (PEP), and recto-anal gradient. Total rectal wall volume (TRWV) was calculated; 3 TRWV grades were defined according to HVs percentile. Relationships between clinical score, HRAM features and TRWV were investigated.

Results: We enrolled 35 ODS patients and 25 HVs. HVs showed 68.45 cm3 median TRWV value, mean PEP was 51.2+-6.4 mmHg, mean recto-anal gradient was 20.1+-5.8 mmHg. Patients showed a marked decrease in TRWV (median 57.32 cm3, $p < 0.001$ vs HVs). Three patients had normal TRWV, 22 had mild pathological TRWV ($p < 0.001$), and 10 had severe pathological TRWV ($p < 0.001$), Table 1. Patients had a significantly decrease in mean PEP and recto-anal gradient (35.0+-3.90 mmHg, $p < 0.001$ and 10.2+-0.8 mmHg, $p < 0.001$). Eight patients had normal PEP, 22 had slightly hypotonic PEP ($p < 0.05$) and 5 had markedly hypotonic PEP ($p < 0.001$). A linear correlation was found between patients with a markedly reduced TRWV and those with a markedly hypotonic PEP (r 0.8).

Conclusion: This study suggested that patients with ODS can have a reduced muscular function of the rectal wall, leading to a decreased pushing ability during defecation. HRAM and 3D endoanal ultrasound should be performed in the ODS assessment, in the effort to better understand anatomic-functional profile and employ the best patient-tailored approach.

	Healthy Volunteers N. 25 mean ± SD (IQR)	Patients N 35 mean ± SD (IQR)	P Value
Level I 8 cm from anorectal ring			
Anterior	0.5 ± 0.06 (0.5–1.4) cm	0.4 ± 0.04 (0.5–1.1) cm	<0.05
Posterior	0.48 ± 0.06 (0.5–1.4) cm	0.38 ± 0.04 (0.5–1.1) cm	<0.05
Level II 5 cm from anorectal ring			
Anterior	0.51 ± 0.02 (0.4–0.8) cm	0.32 ± 0.04 (0.2–0.8) cm	<0.001
Posterior	0.48 ± 0.01 (0.4–0.8) cm	0.32 ± 0.02 (0.2–0.8) cm	<0.001
Level III 2 cm from anorectal ring			
Anterior	0.31 ± 0.04 (0.4–0.8) cm	0.17 ± 0.02 (0.3–0.6) cm	<0.001
Posterior	0.29 ± 0.03 (0.4–0.8) cm	0.17 ± 0.02 (0.3–0.6) cm	<0.001
Total Rectal Wall Volume			
25th–75th percentile	68.45 (65–70) cm^3	65.78 (63–71) cm^3 (N.3)	N.S.
5th – <25th percentile		55.29 (53–57) cm^3 (N.22)	<0.05
<5th percentile		45.40 (43–47) cm^3 (N.5)	<0.001

[Table 1. Assessment of anterior and posterior rectal wall thickness (RWT) at different levels by 3D endorectal ultrasound in healthy volunteers and in patients]
Disclosure: Nothing to disclose

P1086 FAECAL INCONTINENCE IN TYPE 2 DIABETICS: COMPARISON WITH NON DIABETIC HEALTHY INDIVIDUALS AND ANALYSIS OF RELATED FACTORS

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Introduction: Faecal incontinence is a complaint that some type 2 diabetic patients frequently refer[1,2]. The factors involved with are not well known.
Aims and Methods: The aim of this study was to compare the frequency of faecal incontinence between type 2 diabetic patients and non diabetic healthy individuals and to analyse some factors involved in this perturbation in diabetics.
A questioner of Gastrointestinal Symptoms Rating Scale was performed to 140 type 2 diabetics and 132 non diabetic healthy individuals, matched by age and gender.
Results: The frequency of faecal incontinence in diabetics vs. non-diabetics was 14.3% vs. 3.1%, $p<0.01$. According to the severity, the frequency of faecal incontinence between diabetics vs. non diabetics was the follow: minor symptoms, 3.6% vs. 2.3%; moderate symptoms, 7.9% vs. 0.8%; severe symptoms, 2.1% vs. 0.0%; very severe symptoms, 0.7% vs. 0.0%, $p=0.03$.
When analysing the frequency of faecal incontinence in diabetics according to the disease duration, ≤10 years vs. >10 years the results was 9.5% vs. 24%, $p<0.01$. The symptoms severity was also significantly higher in diabetics with more than 10 years of disease, $p=0.01$. In diabetic patients, age, gender and glycaemia control did not influence the frequency and severity of faecal incontinence.
Conclusion: 1- Faecal Incontinence is more frequent and more severe in type 2 diabetics than non diabetic healthy individuals. 2- Diabetes duration influences the frequency and the severity of faecal incontinence. 3- Age, gender and glycaemia control did not influence the frequency and the severity of faecal incontinence in diabetic patients.
Disclosure: Nothing to disclose

Reference

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2. Strid H et al. *Nephrol Dial Transplant*. 2002; 17: 1434–9.

P1087 EFFECTS OF BIOFEEDBACK THERAPY ON CLINICAL AND MANOMETRIC PARAMETERS IN PELVIC FLOOR DYSFUNCTIONS

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Introduction: Patients with pelvic floor dysfunctions may benefit of biofeedback therapy (BFT), before considering surgical treatment for coexisting anomalies. The efficacy of BFT has been reported to be an effective treatment of fecal incontinence (FI) and dyssynergic defecation (DD).
Aims and Methods: To evaluate the effect of BFT in patients with pelvic floor dysfunctions. The population referred to the outpatient Unit of Gastroenterology of two Italian Hospitals, in Rome and Milan, included 125 patients (M 16%, F 84%), mean age 64 ± 17 s.d. (range 16–95 year) with DD (74.4%) and FI (25.6%). All patients received behavioural treatments such as anal sphincter exercises/pelvic floor muscle training with 8 sessions of BFT, in a 3-month period. Clinical presentation (history, symptom profile and severity) and anorectal physiological evaluation (digital examination, manometry, rectal sensory testing, balloon expulsion test) were performed before and after BFT. Improvement of resting/squeezing pressure and reduction in laxatives therapy were considered as clinical improvement of FI and DD, respectively.
Results: In the FI group (F 94%), 44% of patients reported a complete resolution of symptoms, 53% had a considerable improvement, 3% no effect. Resting pressure increased from 42 ± 28 s.d. mmHg to 53 ± 17 s.d. mmHg after BFT, squeezing pressure from 96 ± 28 mmHg to 117 ± 24 mmHg; the rectal volume for first sensation from 37 ± 12ml to 34 ± 11ml.
In the DD group (F 81%), 41% of patients reported a complete resolution of symptoms, 52% considerable improvement, 7% had no effect. Resting pressure and rectal volume for first sensation were normal at baseline (73 ± 21 mmHg and 41 ± 30 ml, respectively). Before BFT, 46% of patients had no complete relaxation straining, 68% had a failure of balloon expulsion test (EBT). After BFT, 69% of patients had a complete relaxation during straining and 84% were able to expel the balloon.
Conclusion: BFT is considered an effective treatment for DD and FI and is widely used. Our data confirm the ability of BFT to improve manometric parameters and clinical symptoms of pelvic floor dysfunctions.
Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00

Oesophageal, Gastric and Duodenal Disorders II – Hall X1

P1089 PREVALENCE OF AUTOIMMUNE GASTRITIS IN AUTOIMMUNE DISEASES: A POPULATION STUDY BASED ON A NON-INVASIVE TEST

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Introduction: Autoimmune gastritis (AG) is a chronic disease in which anti-parietal cell antibodies cause an inflammatory damage to the gastric mucosa, leading to parietal cell atrophy, reduction of the acid secretion and consequently, hypergastrinemia. Although it is generally associated with few symptoms or none at all, it represents a precancerous condition that warrants an appropriate follow-up due to the increased risk of developing gastric adenocarcinoma and neuroendocrine neoplasms.
Aims and Methods: The aim of the study was to evaluate the prevalence of the following autoimmune diseases in the general population: Hashimoto's thyroiditis (HT), celiac disease (CD), rheumatoid arthritis (RA), psoriatic arthritis (PA), Sjögren's syndrome (SS) and vitiligo (VI), and to assess cases of patients with multiple autoimmune diseases.
The secondary aim was to investigate in these patients the prevalence of chronic atrophic AG through a non-invasive method, and to evaluate its usefulness for the diagnosis of AG in patients affected primarily by a different autoimmune disease. The study was performed at a tertiary regional hospital and patients affected by the mentioned autoimmune conditions were enrolled through the specific diagnosis code, according with Italian Health System rules, obtaining a population sample of 5291 patients (4299 F, mean age 51.9 ± 17.6); 609 of them (532 F, mean age 52.4 ± 14.3) underwent a non-invasive evaluation of gastric functionality through the serum dosage of pepsinogen I (PGI) and gastrin-17 (G-17) (Biohit Oyj, Finland). Accordingly to literature, patients were considered affected by gastric atrophy when PGI < 30 μg/l and G-17 > 7 pmol/l.
Results: The overall prevalence of the six studied autoimmune diseases in the population sample was 2.84% (1.85% for HT, 0.30% for CD, 0.40% for RA, 0.26% for PA and 0.06% for SS); the prevalence of VI wasn't assessable for incomplete data. Among the 609 patients evaluated in the study, 22 were affected by more than one autoimmune disease: 7 HT+CD (5 F, mean age 41.1 ± 8.3), 4 HT+VI (3 F, mean age 49.3 ± 21.7), 4 HT+PA (4 F, mean age 59.1 ± 11.9), 3 HT+RA (3 F mean age 62.8 ± 7.7), 1 HT+SS (1 F, 44.4 y.o.), 1 RA+PA (0 F, 75.2 y.o.), 1 RA+SS (1 F, 42.4 y.o.) and 1 HT+CD+SS (1 F, 43.1 y.o.).

Gastric atrophy was found in 97 patients (15.9%); only patients affected by CD didńt show cases of atrophy, neither as a single disease, neither in association.
Conclusion: Atrophic gastritis is more frequently found in patients with autoimmune diseases compared to the general population. The serological evaluation of PGI and G-17 can be a useful non-invasive method for the assessment of the presence of chronic atrophic AG in asymptomatic patients affected by autoimmune diseases.
Disclosure: Nothing to disclose

P1090 GASTRIC FUNCTION MARKERS: BECAUSE ANTIBODIES ARE NOT ENOUGH IN THE EVALUATION OF AUTOIMMUNE GASTRITIS

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Introduction: Autoimmune gastritis (AG) is a chronic disease that affects the corpus-fundus of the stomach, and is characterized by the development of two types of auto-antibodies: anti-parietal cells antibodies (APCA) and anti-intrinsic factor antibodies (AIFA). The hypergastrinemia that ensues as a consequence of gastric cell destruction and hypochlorhidia increase the risk of adenocarcinoma and neuroendocrine tumors; an early diagnosis and an appropriate follow-up are therefore warranted. AG is usually diagnosed using a combination of APCA positivity and histological criteria. However, the latter is an invasive and costly method, and lacks an evaluation of gastric function.
Aims and Methods: The aim of this study was to assess the usefulness of two serological gastric function markers, pepsinogen I (PGI) and gastrin-17 (G-17), in association with APCA determination, in the evaluation of AG.
A cohort of patients with autoimmune diseases who, as part of our tertiary hospital protocol, underwent routine upper endoscopy with histological evaluation (two antral, one angularis, and two corpus biopsies) for the exclusion of autoimmune gastritis, were considered for this study. All patients were also evaluated from a functional standpoint, with the non-invasive determination of serum pepsinogen I (PGI) and gastrin-17 (G-17). Cut-off values of PGI < 30 µg/l and G-17 > 7 pmol/l were considered diagnostic for atrophic gastritis of the stomach body and fundus. APCA dosage was also performed in all patients, and a title of $> 1/80$ was considered positive.
Results: A total of 237 patients (F = 205, mean age = 54.6 ± 14.8 years) were included in the study. Stomach body atrophy was histologically determined in 97 patients (AG group). PGI and G-17 were significantly reduced in patients with body mucosal atrophy (PGI mean value 16.63 ± 15.38; G-17 mean value 88.66 ± 99.78), with respect to patients without this histological feature (non-AG group) $p < 0.0001$. APCA were more frequently found in the AG group (87/97, 89.69%) than in the non-AG group (78/140, 55.71%) ($p < 0.0001$).
Conclusion: The positivity of APCA in patients with autoimmune diseases is considerable even in the absence of histological and functional features of AG. On the other hand, histological damage well correlates with impaired gastric function. Thus, a gastric function evaluation including determination of PGI and G-17 could be a useful and cost-effective method for early stomach body atrophy, especially in asymptomatic patients without indication for performing upper endoscopy. Finally, an evaluation of the isolate presence of APCA is inadequate and should be integrated with gastric functional markers (PG I and G-17) that adequately reflect both disease presence and severity.
Disclosure: Nothing to disclose

P1091 INCREASED DEEP INTRAEPITHELIAL LYMPHOCYTE INFILTRATION OF THE STOMACH CORPUS AS A CLUE OF AUTOIMMUNE ATROPHIC GASTRITIS

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Introduction: It is known that increased intraepithelial lymphocyte (IEL) infiltration of gastric mucosa may be associated with active coeliac disease and *Helicobacter pylori* (HP)-induced gastritis. However, there are no data regarding lymphocytic infiltration of the gastric corpus in patients suffering from autoimmune atrophic gastritis (AAG), an organ-specific disease where T-lymphocytes have a major pathogenic role.
Aims and Methods: We aimed at assessing the number of CD3 and CD8-positive IELs infiltrating the gastric corpus mucosa of patients affected by AAG, in comparison to healthy controls (HC). Patients with HP-induced gastritis and untreated coeliac disease (UCD) were studied as positive controls. We evaluated sections from paraffin-embedded biopsies of gastric corpus of 8 patients with severe AAG (mean age 54 ± 12 years, F:M ratio 2:1), 9 HC (mean age 52 ± 14 years, F:M ratio 1.5:1), 8 patients with HP-induced gastritis (mean age 42 ± 7 years, F:M ratio 1:1) and 6 patients with CD at diagnosis (mean age 32 ± 16 years, F:M ratio 1:1). CD3- and CD8-positivive IELs were evaluated through immunoperoxidase staining, counted *per* 100 epithelial cells. IELs count was divided in superficial (glands apex) and deep (glands crypt).
Results: In the gastric corpus of AAG patients, both deep CD3-positive IELs (mean 12.8 ± 3.5) and deep CD8-positive IELs (mean 13.7 ± 3.9) were significantly ($p < 0.01$) higher in comparison to those of HC (mean 4.9 ± 1.2 and 5.5 ± 2.5, respectively), those of HP-induced gastritis (mean 4.1 ± 2.1 and 3.1 ± 0.8, respectively), and those of UCD (6.8 ± 3.6 and 4.7 ± 1.4, respectively). Regarding superficial IELs count, no statistical differences were seen among the four groups for both CD3- and CD8-positive cells (complete data shown in Figure). None of the patients fulfilled the criteria of lymphocytic gastritis (i.e., IELs > 25/100 cells).
Conclusion: We here described an increased deep IEL infiltration of the stomach corpus of AAG patients as compared to both negative and positive controls. This feature should raise the suspicion of AAG even in the absence of anti-parietal cell antibodies and may be ascribed as a peculiar feature of this condition. Further data are needed in order to confirm this hypothesis.
Disclosure: Nothing to disclose

P1092 GASTRIC MUCOSAL DAMAGE INDUCED BY ETHANOL CAN BE IMPROVED BY CAFFEIC ACID IN RATS

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Introduction: Peptic ulcer is one of the most common gastrointestinal diseases. Excessive ethanol ingestion results in gastritis characterized by mucosal edema, subepithelial hemorrhages, cellular exfoliation, and inflammatory cell infiltration. Caffeic acid is a natural phenolic compound found in many plants and present in diets as part of fruits, vegetables, tea and wine. It has been reported to have broad spectrum of bioactive activities including antidiabetic, antihypertensive, antioxidant, immunomodulatory, anti-inflammatory and neuroprotective properties.
Aims and Methods: Aim of the study is to investigate the anti-ulcerative effects of caffeic acid on ethanol induced ulcer model and to determine the pathways that are involved in action mechanism of caffeic acid. Following a 18-h starvation period, ulcer was induced in Sprague-Dawley rats (250–300g) by intragastric administration of absolute ethanol while control group received saline. 60 minutes before ulcer induction, rats were treated with either 1 ml 10% tween-80 as vehicle or caffeic-acid (100, 250 or 500 mg/kg dissolved in 1ml vehicle, per oral). 250 mg/kg of caffeic acid was found to be most efficient dose. To elucidate the roles of nitric oxide (NO) and cholinergic pathway, 10 mg/kg L-NAME or 1 mg/kg atropine was administered 30 minutes before 250 mg/kg of caffeic acid treatment to ulcer induced rats. All rats were decapitated 60 minutes after ulcer induction and stomach samples were scored macroscopically, and analyzed for myeloperoxidase activity (MPO; index of tissue neutrophil infiltration), malondialdehyde (MDA; an end product of lipid peroxidation) and glutathione (GSH; a key antioxidant) levels. Student's t-test was used for statistical analyses. Values of $p < 0.05$ was regarded as significant.
Results: Ethanol administration resulted in an increase in macroscopic damage scores ($p < 0.001$) and only 250 mg/kg caffeic acid treatment reduced macroscopic damage score significantly ($p < 0.05$). In addition, increased gastric MDA levels ($p < 0.001$) and MPO ($p < 0.01$) activity with concomitant decrease in GSH levels were measured with the ulcer induction. Treatment with 250 mg/kg caffeic acid decreased MDA levels ($p < 0.05$). Both 250 mg/kg and 500 mg/kg caffeic acid treatment decreased MPO activity ($p < 0.05$) while gastric GSH was replenished ($p < 0.05$ and $p < 0.01$, respectively). Administration of atropine before 250 mg/kg caffeic acid elevated the reduced MDA levels ($P < 0.05$). Furthermore, increased GSH levels by caffeic acid decreased by L-NAME administration ($P < 0.05$).
Conclusion: Results showed that caffeic acid ameliorates the ethanol-induced gastric mucosal damage by preventing neutrophil infiltration, tissue damage derived from lipid peroxidation and endogenous anti-oxidant GSH depletion. Moreover, caffeic acid may display these effects via NO and/or cholinergic pathway. Future studies are needed to investigate the mechanism of anti-ulcerative effects of caffeic acid as a therapeutic agent.
Disclosure: Nothing to disclose

P1094 GASTRIC MICROBIOTA ALTERATION FOLLOWING ERADICATION OF *H. PYLORI*

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Introduction: The human gastric microbiota studies are mainly focused on *H. pylori* (HP) infection, and few studies focused on bacteria other than HP. Moreover, the results of these studies are controversial. Bik et al. reported that

the human gastric flora was not affected by HP infection. On the other hand, Maldonado-Conteras et al. reported that HP infection increased the rate of Proteobacteria in the human stomach, and decreased the rate of Firmicutes.
Aims and Methods: The aim of this study is to clarify the composition of the gastric bacterial flora using the next generation sequencer and the changes in gastric microbiota composition before or after HP eradication.
Between December 2012 and July 2016, 24 patients who underwent upper gastrointestinal endoscopy before and after HP eradication were enrolled. Stomach body and antrum biopsy specimens were collected using upper gastrointestinal endoscopy. Bacterial DNA was extracted and purified from the collected samples by the complex enzyme method. After PCR amplification of the 16S rRNA gene V1-2 region of the extracted DNA, barcode sequencing was carried out using Miseq (Illumina) which is a high-speed sequencer. The stomach bacterial flora was clarified through the informational analysis of the obtained sequence data by using Operational Taxonomic Unit (OTU) analysis.
Results: Twelve pairs of samples obtained from the antrum before and after *HP* eradication and seventeen pairs of the stomach body samples were PCR amplifiable and analysis was performed thereafter. There were many kinds of bacterial species other than HP in the gastric environment. In antrum, average OTU is 120.9 and 118.3 before and after eradication, respectively. In gastric body, average OTU is 90.9 and 123.8 before and after eradication, respectively. HP eradication was associated with a significant increase of α-diversity in gastric body microbiome in Shannon's diversity and there was no significant difference in α-diversity of antrum microbiome between before and after eradication. Principal coordinates analysis (PcoA) of weighted and unweighted Unifrac distances of both gastric body and antrum microbiome were significantly different between before and after HP eradication based on Permutational Multivariate Analysis of Variance. While HP is the most dominant species before HP eradication in both gastric body (64%) and antrum (24%), *Streptococcus mitis,* which is the second dominant bacteria before HP eradication, became the most dominant bacteria species after eradication. The population of many bacteria species were increased and the population of some bacteria species were decreased after HP eradication compared to before the eradication.
Conclusion: There were a lot of bacterial species in the gastric environment. HP eradication changes the gastric microbiota dramatically.
Disclosure: Nothing to disclose

P1095 *HELICOBACTER PYLORI* ANTIBODY AND PEPSINOGEN TESTING FOR PREDICTING GASTRIC MICROBIOME ABUNDANCE

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Introduction: Although the high-throughput sequencing technique is useful for evaluating gastric microbiome, it is relatively expensive and requires gastric mucosal samples (or juice). Therefore, we aimed to develop a predictive model for gastric microbiome using serologic testing.
Aims and Methods: This study was designed to further analyze the Hanyang University Gastric Microbiome Cohort, which was originally established to investigate gastric microbial distribution according to the intragastric environment. We obtained the relative abundance of nitrosating/nitrate-reducing bacteria or type IV secretion system (T4SS) protein gene-contributing bacteria, IgG anti-*Helicobacter pylori* (HP) antibody, and pepsinogen (PG) levels.
Results: We included 57 and 26 participants without and with HP infection, respectively. The relative abundance of nitrosating/nitrate-reducing bacteria was 4.9% and 3.6% in the HP(-) and HP(+) groups, respectively. The relative abundance of T4SS protein gene-contributing bacteria was 20.5% and 6.5% in the HP(-) and HP(+) groups, respectively. The relative abundance of both nitrosating/nitrate-reducing bacteria and T4SS protein gene-contributing bacteria increased exponentially as PG levels decreased. In the multivariable analysis, advanced age (only for nitrosating/nitrate-reducing bacteria), a negative IgG anti-HP antibody result, low PG I and II levels, and high Charlson comorbidity index were associated with a high relative abundance of nitrosating/nitrate-reducing bacteria and T4SS protein gene-contributing bacteria. Adjusted coefficient of determination (R^2) was 53.7% and 70.0% in the model for nitrosating/nitrate-reducing bacteria and T4SS protein gene-contributing bacteria, respectively.
Conclusion: Negative results of IgG anti-HP antibody and low PG levels were associated with a high abundance of nitrosating/nitrate-reducing bacteria and T4SS protein gene-contributing bacteria.
Disclosure: This work was supported by the research fund of Hanyang University (HY-2017).

P1096 CHARACTERIZATION OF MUCOSAL AND FLUID MICROBIOME ACROSS STAGES OF GASTRIC CARCINOGENESIS

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Introduction: Recently a complex microbiota has been uncovered within the stomach and the mucosal microbiota dysbiosis is associated with gastric cancer (GC). However, the alterations of mucosal microbiota among stages of GC are inconsistent in different studies. It is also not uncertain the role of fluid bacteria in this process and its difference with mucosal microbiota.
Aims and Methods: The aim of this study was to perform a comparative analysis of the microbiome in both luminal and mucosal niches along the histological stages of gastric tumorigenesis. We performed 16S rRNA gene sequencing of gastric mucosal samples from 179 patients including 61 superficial gastritis (SG), 54 intestinal metaplasia (IM) and 64 GC, as well as gastric fluid samples from 96 patients of the same cohort including 42 SG, 26 IM and 28 GC, to determine their alterations across stages of GC.
Results: The composition of gastric mucosal microbiome was different from fluid with lower bacterial diversity. *Helicobacter pylori* (*H. pylori*) which were observed to dominate the mucosal community strikingly influenced the overall microbial structure in the stomach that correlated with its abundance. Microbial dysbiosis was shown in mucosa rather than fluid during the progression of GC. Three enterotypes were identified in gastric mucosa with compositional and functional differences and the changes along disease stages varied between enterotypes. The specific taxa consistently altered in IM and GC were identified in each enterotype and their effect for discriminating GC from SG was validated.
Conclusion: The detailed analysis of the whole gastric microbiome along carcinogenesis demonstrated for the first time that the dysbiosis of mucosal instead of luminal bacteria was associated with GC. The characteristic profiles of gastric mucosal enterotypes in GC development suggest that the potential necessity of enterotype classification before evaluating the correlation between gastric microbiota and GC.
Disclosure: Nothing to disclose

P1097 COMPREHENSIVE ANALYSIS OF HISTOLOGICAL MICRORNAS OF PANCREATIC CANCER COLLECTED BY EUS-FNA

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Introduction: The microRNA is a small RNA molecule whose full length is 18–25 bases, whose biological roles are to regulate its expression by binding to and disrupting target messenger RNA in cells. Recently, it has been reported that these miRNA are involved in metastasis and expression of various cancers. The aim of this study was to comprehensively analyze the extracted miRNA of cancer tissue obtained by EUS-FNA, which was performed for the definite diagnosis of pancreatic cancer, and to identify miRNA targets related to prediction of metastasis, grade, and prognostic factors.
Aims and Methods: The subjects were 51 patients (21 men and 30 women) with invasive ductal adenocarcinoma diagnosed histologically by EUS-FNA (written informed consent was obtained with approval from the hospital ethics committee). The observation period was from April 2013 to February 2018. MiRNAs extracted from tissues collected by EUS-FNA performed for definitive diagnostic purposes was comprehensively analyzed using a microarray tip equipped with 2555 molecules. MiRNAs comparisons were made using the following three areas of clinical features, clinical stage, sites of recurrences and metastases, and prognoses. The miRNAs of candidates for defining clinical pathology was identified using statistical methods such as cluster analysis.
Results: 1. We identified miRNAs (oncogenic miRNA) with increased expression and miRNAs (tumor suppressor genotype miRNAs) with decreased expression in the Stage IV group with distant metastases compared with the Stage I-III groups. 2. There were the increase and decrease of the genes which seemed to correlate in miRNAs and recurrence position of the postoperative recurrence patients. 3. Median survival in cumulative survival rates (Kaplan-Meir Methods) was calculated, and microRNA with significant differences were identified by comparing survival greater than or less than the median survival time between the groups.
Conclusion: In this study, we identified a miRNAs that may define the clinical features of invasive ductal carcinoma of the pancreas by comprehensively analyzing the miRNAs obtained by EUS-FNA. Functional analysis of these miRNAs was used to evaluate their potential as biomarkers for early detection of pancreatic cancer, progression of metastasis, evaluation of therapeutic effects, and prediction of prognosis.
Disclosure: Nothing to disclose

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P1098 ALTERATIONS IN GUT MICROBIOTA COMPOSITION DURING AGING

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Introduction: The gut microbiota have been considered to play an important role in health. Meanwhile aging is a degenerative process that accompanied by a number of diseases and poor health, such as atherosclerosis, dementia, or

cancer. Several researchers have reported that gut microbiota were closely related with aging in recent years. However, the distinct species of age-related changes in microbiota composition remains unexplored.
Aims and Methods: The present study was conducted to deepen our knowledge on the relationship between the composition of the gut microbiota and host's age. 116 healthy adults were enrolled for this study in Hangzhou. The 116 healthy adults were divided into 3 groups: young group (n = 36, 20–34 years, 27.89 ± 3.37), middle-aged group (n = 53, 35–55 years, 45.58 ± 5.70) and elderly group (n = 27, ≥56 years, 63.00 ± 5.52). Feces were collected and stored at -80°C, total bacterial DNA was extracted from all samples. The fecal microbiota of the 116 samples was characterized by Illumina sequencing of the V3-V4 region of the bacterial 16S rRNA gene.
Results: No significant difference was observed among the three groups with regard to baseline characteristics. Among the detected gut microbes, the chao index was decreased in middle-aged and elderly groups compared with young group, which represents the community richness. The Shannon index was also decreased with aging, which shows the community diversity. Moreover, the genera *Prevotella*, *Paraprevotella*, *Veillonella* and *Klebsiella* were enriched with aging. The genera above were mostly the source of common infection. However, the genera *Phascolarctobacterium*, *Faecalibacterium*, *Bifidobacterium*, *Streptococcus*, *Dorea* and *Bilophila* were negatively correlated with age, some of which were well known as beneficial to the gut health. Meanwhile, the presence of *Faecalibacterium prausnitzii*, *Dorea formicigenerans* and *Bifidobacterium longum* were negatively correlated with age, which has a significant difference. The three specific species above were known to have anti-inflammatory or protective properties in gastrointestinal tract.
Conclusion: These results suggested the evolving microbial-host associations and relations across the lifespan of a human being. Furthermore, we proved that the microbiota aimed at improving healthy outcomes were decreased with aging. On the other hand, the opportunistic bacteriums were elevated with aging.

Species	Young group (%)	Middle-aged group (%)	Elderly group (%)	P value
Faecalibacterium prausnitzii	5.23 ± 5.67	3.41 ± 3.92	2.63 ± 2.66	0.04653*
Roseburia faecis	5.02 ± 6.13	1.94 ± 2.77	3.00 ± 3.72	0.01333*
Blautia obeum	0.25 ± 0.39	0.27 ± 0.52	0.08 ± 0.74	0.02314*
Bifidobacterium longum	0.22 ± 0.35	0.18 ± 0.43	0.07 ± 0.16	0.00597*
Dorea formicigenerans	0.12 ± 0.20	0.11 ± 0.27	0.04 ± 0.05	0.03381*
Bifidobacterium adolescentis	0.10 ± 0.25	0.05 ± 0.26	0.08 ± 0.32	0.00157*

[Comparison of gut microbiota at species level]
Disclosure: Nothing to disclose

P1099 COMPARISON OF RISK SCORING SYSTEMS FOR PATIENTS PRESENTING WITH ACUTE UPPER GASTROINTESTINAL BLEEDING (AUGIB): AN ITALIAN MULTICENTRE PROSPECTIVE STUDY

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Introduction: Several risk assessment scores have been developed to predict mortality, need for hospital intervention, rebleeding for patients with acute upper gastrointestinal bleeding. The Rockall score has been widely used and it has been suggested that the PNED score and AIMS65 are superior to it. The Glasgow Blatchford (GB) score seems useful in identifying very low risk patients not needing of endoscopic treatment but is often considered for predicting death.
Aims and Methods: To compare the four risk assessment scores to predict mortality and rebleeding in acute upper gastrointestinal bleeding. Clinical, biochemical, endoscopic and treatment delivered data on patients consecutively hospitalized for AUGIB were collected from January 1st 2014 to December 31st 2015. Haemorrhage-related death was defined as any event occurring within 30 days for patients with non-variceal bleeding and 42 days for those with variceal bleeding. Rebleeding was endoscopy proved and defined as new episode of hematemesis after index endoscopy, melena or hematochezia after normalization of the color of feces, tachycardia (> 110 m/min) or hypotension (PA <90 mmHg) in absence of any plausible cause, hemoglobin (HB) fall >2gr/dl following two stable HB scores, HB fall >3gr/dl in 24 hours associated with melena or hematochezia. Comorbidity and its clinical seriousness was evaluated by ASA scores.
Results: A total of 3324 patients were included; males were 67.8% and their mean age was 68.1 ± 15.7. The source of bleeding was non-variceal in 2,764 (83.1%) and variceal in 560. Comorbidities were present in 79.8% of the patients; at admission, mean Hb value was 9.2 ± 2.6; 7.6% had hemodynamic instability, 59.3% of the patients received al least one transfusion (Nr.1972) Overall mortality (variceal and non-variceal) was 223 patients (6.7%.) and overall rebleeding was 6.2%. PNED score showed the best area under the receiver operating characteristic curve (AUCROC) 0.80 [cl.95% 0.77–0.84] for predicting death compared with the Rockall score 0.68 [c.l.95% 0.64–0.72], GB score 0.69 [c.l.95% 0.65–0.73] and AIMS65 score 0.61 [c.l.95% 0.57–0.65] all P < 0.001 see figure. The PNED score (AUCROC: 0.79 [c.l.95% 0.77–0.82]) showed the best performance also for the prediction of rebleeding (chi2 = 44.53 p < 0.000) (Rockall score 0.68 [c.l.95% 0.64–0.72]; GB 0.69 [c.l.95% 0.65–0.73]; AIMS65 0.61 [c.l.95% 0.57–0.65]).
Conclusion: The PNED score is accurate and superior to other scores for the prediction of death and rebleeding.
Disclosure: Nothing to disclose

P1100 COMPARATIVE EFFICACY AND SAFETY OF INTERVENTIONS FOR PRIMARY PREVENTION OF VARICEAL BLEEDING: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: We conducted a network meta-analysis to compare efficacy and safety of interventions for primary prophylaxis of esophageal variceal bleeding
Aims and Methods: We searched Medline, Embase, Cochrane Library and grey literature sources through October 2017. We included randomised controlled trials (RCTs) that compared non-selected betablockers (NSBB) (propranolol, nadolol), carvedilol, isosorbide-5-mononitrate (ISMN), endoscopic variceal ligation (EVL), either alone or combined, to each other for the prevention of first variceal bleeding. Efficacy outcomes were incidence of variceal and upper gastrointestinal bleeding, incidence of bleeding related and all-cause mortality. Safety outcomes included incidence of any adverse event (AE) and discontinuation rate due to AE. We combined direct and indirect evidence through multivariate random-effects network meta-analyses and relative ranking of treatments was assessed using surface under the cumulative ranking (SUCRA) probabilities. We also estimated Predictive intervals (PrI), which indicate the interval within which the relative effect of a future study is expected to be, in order to facilitate interpretation of the results in the light of the magnitude of heterogeneity. We assessed quality of evidence using GRADE criteria.
Results: We included 36 RCTs (3859 patients). Low quality of evidence suggested that EVL (OR 0.55; 95% *CI* 0.39–0.78, SUCRA: 69%) and carvedilol (OR 0.48; 95% CI 0.26–0.87, SUCRA: 80.1%) reduced significantly the risk of first variceal bleeding compared to NSBBs (SUCRA: 23.8%). However, the advantage was not retained when predictive intervals were included in analysis. Combined therapy of EVL and NSBBs (SUCRA: 76.8%) did not demonstrate significant improvements in rates of variceal bleeding compared to monotherapy with EVL (OR 0.87, 95%CI 0.37–2.06), carvedilol (OR 1.00, 95%CI 0.37–2.75) or NSBBs (OR 0.48, 95%CI 0.21–1.13). ISMN was inferior compared to other interventions in incidence of variceal bleeding. EVL (OR 0.70, 95%CI 0.50–0.97) was superior to NSBBs in terms of upper gastrointestinal bleeding but predictive intervals were wide, extending to both sides of "no effect" line. Compared to each other none of the interventions either alone or in combination showed superiority in terms of bleeding related mortality and all-cause mortality (low and very low quality of evidence). Incidence of any adverse events did not differ among interventions (low quality of evidence). Combination therapy of NSBBs and ISMN showed higher rates of discontinuation due to AE compared to most interventions.
Conclusion: EVL, NSBBs, carvedilol and combination of EVL plus NSBBs are equally effective in primary prophylaxis of upper gastrointestinal bleeding in patient with esophageal varices. Any differences among interventions were imprecise with low confidence in our estimates. Combination of NSBBs and ISMN had also beneficial effect but there are safety concerns.
Disclosure: Nothing to disclose

P1102 EFFECT OF GASTROPROTECTIVE AGENTS ON PREVENTING UPPER GASTROINTESTINAL BLEEDING IN PATIENTS RECEIVING DIRECT ORAL ANTICOAGULANTS: A RETROSPECTIVE MULTICENTER STUDY

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Introduction: Direct oral anticoagulants (DOACs) are effective in the prevention and treatment of thromboembolism; however, they are associated with upper gastrointestinal bleeding (UGIB). In this study, we evaluated the efficacy of gastroprotective agents (GPAs) in reducing the risk of UGIB in patients receiving DOACs.
Aims and Methods: We retrospectively reviewed the medical records of 2076 patients who received DOACs for the prevention or treatment of thromboembolic events between January 2008 and July 2016. A cumulative incidence analysis using the Kaplan-Meier method was performed to determine the rate of UGIB and its association with GPAs administration.
Results: Of the 2076 patients, 360 received GPAs. Over the follow-up period (1160 person-years), 1 patient in the GPA group (0.7 per 100 person-years) and 29 patients in the non-GPA group (2.8 per 100 person-years) developed UGIB ($P = 0.189$). In the multivariate analysis, UGIB was associated with older age (hazard ratio [HR], 1.041; $P = 0.048$), a history of peptic ulcer or UGIB (HR, 5.931; $P < 0.001$), and concomitant use of antiplatelet agents (HR, 3.121; $P = 0.014$). GPAs administration did not reduce the risk of UGIB (HR, 0.200; $P = 0.116$). However, based on the subgroup analysis of 225 patients with concomitant use of antiplatelet agents or a history of peptic ulcer or UGIB, the GPA group (0 per 100 person-years) showed reduced incidence of UGIB compared with the non-GPA group (11.3 per 100 person-years) ($P = 0.065$).
Conclusion: Routine use of GPAs for UGIB is not mandatory in patients receiving DOACs. However, GPAs could reduce the risk of UGIB in patients receiving DOACs, who are at a high risk.
Disclosure: Nothing to disclose

P1103 DEVELOPMENT OF A NEW SCORE TO PREDICT MORTALITY AND INTERVENTION IN UPPER GASTROINTESTINAL BLEEDING. THE HA(MA)SH SCORE

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Introduction: There has been a special interest in the development of scores to establish patients' risk of death and need for intervention in an early phase after upper gastrointestinal bleeding (UGIB). However, some of them such as Glasgow-Blatchford score (GBS), are troublesome to calculate, whereas others such as Rockall score need an endoscopy to be completed. Recently, AIMS65 changed the paradigm, shifting to a simple type of score, easy to use and applicable.
For these reasons, provided that the most important decision to make in the ER is whether an immediate intervention is needed, we decided to develop a score centered in this outcome, as well as in mortality.
Aims and Methods: The database was built with information of consecutive UGIB patients admitted to the "Virgen de las Nieves" University Hospital emergency room over 48 months from January 2013 to January 2017. All patients received upper endoscopy, and information regarding patients' demographic data, comorbidities, current medications, clinical presentations, hemodynamics, laboratory test results on admission, and endoscopic findings were collected. An univariate and multivariate analysis were performed, looking for individual odds ratio for every risk factor. After this analysis, we built a score weighting the relative risk of every factor, and giving to values above or below the cutoff point 1 or 2 points depending on their individual odds ratio. The score was tested both for mortality and for two composite endpoints, considering interventions (Endoscopic intervention, surgery or 30 days mortality) or any given intervention (the before mentioned plus transfusions). Comparison between curves were performed by means of the Hanley and McNeill Method.
Results: The score was validated in our database of 547 patients (367 males; aged 64.14 ± 16.4). Factors included in the multivariate analysis after achieving significance in the univariate analysis for any intervention or death were: Impaired mental status, Albumin < 2.5 g/dL, Systolic blood pressure < 90 mmHg, Hematemesis, Hemoglobin < 10 g/dl; and ASA score > 2.
Our score, denominated HAH(MA)S (Hematemesis, ASA score > 2, Hemoglobin < 10, Altered mental status, albumin < 2.5 and systolic blood pressure < 90) gives two points to the variables inside the brackets and one to the rest, performed for death prediction better than AIMS65 (AUC 0.776 vs 0.751; $p < 0.05$), Glasgow-Blatchford score (GBS) (0.736; $p < 0.05$) and postendoscopic Rockal score (0.754; p = n.s.) in our series (Figure 1). Regarding intervention, it was slightly better than AIMS65 (AUC 0.654 vs. 0.627; p = n.s.) and GBS (AUC 0.623; p = ns). When considering every intervention (adding red cells transfusions) there were no differences between the HA(MA)SH and GBS scores, but there were between both ones and AIMS65 ($p < 0.005$) (AUC: HA(MA)SH 0.792; GBS 0.811; AIMS65 0.706). With a HAH(MA)S = 0 no patient died and only 3% required intervention.
Conclusion: The HA(MA)SH score can be an option for risk assessment in the Emergency Room. Although still far from perfect, it points towards simpler and more clinically based scores, provided that the Glasgow-Blatchford score is somehow troublesome to calculate and the AIMS65 is not optimal predicting interventions. Previous to its external validation, de HA(MA)SH score seems a very promising option.
Disclosure: Nothing to disclose

P1104 THE STATISTICAL COMPARISON OF ENDOSCOPIC PROCEDURE AND TRANSARTERIAL EMBOLIZATION FOR HEMORRHAGE CAUSED BY DUODENAL ULCER

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Introduction: Endoscopic procedure is performed for active duodenal ulcer hemorrhage. But if endoscopic hemostasis fails, transarterial embolization (TAE) or operation are additionally selected. We made statistical analysis for the feature between the group which only endoscopic procedure are performed (endoscopy group) for duodenal ulcer and the group which interventional radiology is additionally performed (TAE group).
Aims and Methods: From April 2005 to December 2017, 141 patients with hemorrhage of benign duodenal ulcer are admitted in our hospital. The patients were divided into two group retrospectively, endoscopy group and TAE group. We made statistical analysis for laboratory data (Alb, Hb, Plt, PT—INR) at initial diagnosis, number of endoscopic treatment, the amount of blood transfusion, comorbid disease, and 30-day mortality.
Results: Of 141 patients, 129 patients (91.5%) were success in only endoscopic procedure. 11 patients (7.8%) were underwent TAE additionally, 2 patients (1.4%) were underwent operation. 109 patients (77.3%) were male, the mean age was 62.8 year-old, range 21 to 97 years.
Based on the results of t-test for laboratory data at initial diagnosis, Alb and Hb in TAE group was statistically lower than in endoscopic group ($P < 0.05$). In addition, the number of endoscopic examination was larger ($P < 0.05$). In terms of comorbid disease, hemodialysis was risk factor in TAE group. Then we performed logistic regression analysis to identify cut-off value for Alb, Hb and times of endoscopic exam. The cut-off value were Alb = 2.3, Hb = 8.3, times of

endoscopy was twice. Sensitivity was 84.5%, 48.8%, 94.6% respectively, and specificity was 54.5%, 81.8%, 63.6% respectively.
Conclusion: This study may show the opportunity to select TAE for patients who were difficult to control duodenal ulcer hemorrhage with endoscopic procedure. Alb, Hb at initial diagnosis, number of endoscopic exam after the admission, and comorbid disease of hemodialysis might be predictable value for TAE treatment for duodenal hemorrhage.
Disclosure: Nothing to disclose

P1105 A RETROSPECTIVE SINGLE-CENTRE REVIEW OF HEMOSPRAY® IN GI BLEEDING

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Introduction: Upper GI bleeding can have a poor outcome in the absence of haemostasis. Hemospray is an inorganic powder that creates an adhesive barrier over the bleeding site and has been used as an adjunct to conventional endotherapy in high-risk non-variceal, and more recently variceal bleeds.
Aims and Methods: We wished to review Hemospray ® use in NHS Tayside and assess clinical outcome. From the endoscopy database we identified Hemospray ® use between January 2014 and October 2017. We recorded demographics, indication, co-morbidities, Blatchford score, endoscopic findings and therapy, haemostasis and 30-day mortality.
Results: We identified 49 applications in 46 patients (M22:F24, mean age 68.4 years, range 30–91). Indications were primary acute GI bleeding (87.8%) and bleeding post endoscopic procedure [12.2%]. 11 patients had liver disease and 6 malignancy (2 pancreatic, 2 oesophageal, 1 hepatoma, 1 haematological).
The mean Blatchford score was 10.96 (range 2–19) and was >6 in 86.3%.
In 100% of cases immediate haemostasis was achieved.
Overall 30 day mortality was 10.9% (5/46 patients) only 1 death was directly related to GI bleeding (oesophageal stent erosion into a sub-mucosal vessel).
Overall 30 day haemostasis in those surviving was 79.6%.
Hemospray ® Application by site is shown below (Table 1).
In 12 cases, at the discretion of the endoscopist, Hemospray ® was used as monotherapy; these applications and the associated 30-day haemostasis is also displayed in the table.
In the three cases of oesophageal varices this was used as a salvage measure in the setting of massive haematemsis. In one case the patient was palliated and re-bled at day 6 but died beyond 30 days. In the other two cases Hemospray ® provided a bridge to either TIPSS or endoscopy with banding 24 hours later – neither patient re-bled.
In 2 duodenal cases the patients were electively sent for interventional radiology despite immediate haemostasis.
30 day haemostasis in the monotherapy group was 91.7%.
Conclusion: We have shown our centres experience with Hemospray ®. It provides effective immediate haemostasis from a range of causes of GI bleeding when used either in combination or as monotherapy. We have also had success when used in massive variceal haemorrhage as a bridge to other adjunct therapy such as interventional radiology. Longer term haemostasis has been shown to be better than in similar cohorts.
Disclosure: Nothing to disclose

P1106 IS TOPICAL TRANEXAMIC ACID EFFECTIVE IN UPPER GI BLEEDING?

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Introduction: Non-variceal upper gastrointestinal bleeding (NVUGIB) is the most common emergency that gastroenterologists encounter. The aim of this study is evaluating effect of topical Tranexamic Acid via endoscopic procedure for control of NVUGIB.
Aims and Methods: In this study, 100 eligible patients with NVUGIB enrolled and divided to two equal groups: In control group the ulcer underwent epinephrine injection plus Argon Plasma Coagulation as the standard treatment. In second group, topical Tranexamic Acid solution spraying was added to standard treatment (intervention group). Estimated blood loss volume, blood transfusion volume, hemoglobin, blood pressure, heart rate, need to second endoscopy, mortality rate, need to surgery, hospitalization duration was evaluated in both groups and the differences expressed statistically.
Results: The mean average ages of intervention and control groups were 62.8 ± 19.6 and 63.1 ± 17.8 yrs. respectively. Demographic features were not different between two groups. Estimated blood loss, need to transfusion, hospitalization duration and re-bleeding were significantly lower in intervention group (p -value <0.05). Eight patients (16%) in the intervention group and 17 (34%) in control group had re-bleeding and underwent re-endoscopy ($p = 0.038$). Mortality rate, need for surgery and drug effectiveness regarding the ulcer location (duodenum or stomach) had no statistically significant differences in two groups (P-value >0.05).
Conclusion: Topical tranexamic Acid is a useful additive treatment to control NVUGIB and prevent re-bleeding. Therefore it can be used in addition to the standard treatment.
Disclosure: Nothing to disclose

P1107 CLINICAL COURSE AFTER HEMORRHAGE IN PATIENTS TAKING DOAC AND SIGNIFICANCE OF GASTROINTESTINAL BLEEDING

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Introduction: Several direct oral anticoagulants (DOAC) have been developed to prevent cardiogenic thrombosis in patients with non-valvular atrial fibrillation. The major adverse effect of DOACs is hemorrhage, and the gastrointestinal tract is one of common sites of involvement. However, clinical course after gastrointestinal bleeding (GIB) during DOAC therapy have not been fully elucidated. This retrospective cohort study was conducted to investigate the course after hemorrhagic events during DOAC therapy. The significance of GIB was also evaluated.
Aims and Methods: First, all 662 patients prescribed dabigatran, rivaroxaban, apixaban, or edoxaban between April 2011 and November 2015 were listed. Their medical charts were reviewed to examine whether any hemorrhagic events developed from the day of initial prescription until the end of August 2017. Regarding 126 patients with hemorrhage, the cause of bleeding was identified to clarify the clinical significance of GIB. Additionally, the course after bleeding was investigated until the end of March 2018, if available. Finally, after excluding 30 patients with insufficient description or lack of data, 96 patients were selected as subjects.
Results: Of hemorrhagic events occurred during DOAC therapy, GIB was identified in 38 patients (2.8%/year), majority of which were clinically relevant GIB (Bleeding Academic Research Consotium type 2 or above). Regarding 96 patients with follow-up data, observational period was 157 patients-year. Of these, 11 minor bleeding occurred (7%/year) including 2 GIB, 1 anorectal bleeding and 1 small intestinal bleeding, and no serious bleeding was seen. On the other hand, 2 major thrombotic events developed during observation (1.3%/year); 1 cerebral infarction and 1 acute arterial occlusion. Both patients developed GIB initially and had stopped taking anticoagulants after bleeding because of the fear for re-bleeding.

Abstract No: P1105
Table 1

	Oesophageal (Variceal)	Oesophageal (Non Variceal)	Gastric (Variceal)	Gastric (Non Variceal)	Duodenal	Colonic
Total Applications of Hemospray	6	16	4	7	14	2
Immediate Haemostasis	100% (6)	100% (16)	100% (4)	100% (7)	100% (14)	100% (2)
30 Day Haemostasis	83.3% (5)	75% (12)	50% (2)	100% (7)	85.7% (12)	100% (2)
Applications where Hemospray was used as Monotherapy	3/6 (50%)	6/16 (37.5%)	0/4 (0%)	1/7 (14.3%)	2/14 (14.3%)	0/2 (0%)
Monotherapy 30 Day Haemostasis	2/3 (66%)	6/6 (100%)	–	1/1 (100%)	2/2 (100%)	–

Conclusion: GIB is common and serious adverse event during DOAC therapy. However, once GIB occurred, it seemed important for clinicians to continue anticoagulant therapy.
Disclosure: Nothing to disclose

P1108 ENDOSCOPIC EXPLORATORY VARICES DEVASCULARIZATION FOR THE TREATMENT OF ACUTE ESOPHAGEAL VARICEAL BLEEDING IN PATIENTS WITH CIRRHOSIS

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Introduction: The principal goal of band ligation is to strangulate and finaly obliterate the perforating veins connecting varices to extraesophageal collaterals. But the patients still face the risk of rebleeding after endoscopic treatment. We hope to find a more effective way in preventing early rebleeding.
Aims and Methods: We aimed to evaluate the effect of EEVD (Endoscopic Exploratory Varices Devascularization) for acute esophageal variceal bleeding in patients with cirrhosis.
In the retrospective study, we compared endoscopic exploratory varices devascularization and endoscopic band ligation in 75 patients with cirrhosis (Child-Pugh score range from 7–12 points) and esophageal variceal bleeding. 46 patients underwent EEVD, and 29 did band ligation. We compared the mean time to recurrence between EEVD group and band ligation group. And the presence of the varices measured by Computed tomographic angiography (CTA) at different time points and under different conditions (before performent of EEVD; at least 24 hours after performent of EEVD into hemodynamically stable patients; 2 weeks after performent of EEVD).
Results: The number of esophageal varices in 46 patients were significantly more before performent of EEVD than at least after 24 hours. The results at least 24 hours later and after 2 weeks were similar, no newly gastroesophageal varices were observed. The number of gastric varices appears to decrease after EEVD. Mean bleeding recurrence time after EEVD was significantly longer (7.63 ± 3.63 months) than band ligation (5.60 ± 2.39 months, $P < 0.05$).
Conclusion: 1. The results show the effectiveness of varices occlusion by EEVD for gastric varices and the esophageal varices originated from them.
2. EEVD may delayed the occurrence of variceal rebleeding by thrombosis of the potential varices, compared to band ligation.
Disclosure: This technology is based on the pioneering method of Professor Li Ping, who is from Depatrment of Gastroenterology, BeiJing DiTan Hospital, Capital Medical University, BeiJing, China.

P1109 EFFICACY AND SAFETY OF OCTREOTIDE FOR THE TREATMENT OF SEVERE RECURRENT GASTROINTESTINAL BLEEDING IN HEREDITARY HEMORRHAGIC TELANGIECTASIA: RESULTS OF A PROSPECTIVE PHASE II MULTICENTER CLINICAL TRIAL

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Introduction: Hereditary hemorrhagic telangiectasia (HHT) is a genetic disease that leads to vascular malformations in multiple organs. Approximately 25% of the HHT patients have symptoms of gastrointestinal (GI) bleeding with iron deficiency anaemia as a consequence. Endoscopic argon plasma coagulation is the first-line therapy, but often not a long-term solution due to recurrent bleeding and the impossibility to treat all GI lesions. Therefore, current treatment focuses on managing anaemia with blood transfusions, which is associated with multiple hospital visits, admissions, and a significant burden for the patients and healthcare.
Aims and Methods: The aim of this study is to investigate the efficacy and safety of octreotide as a treatment for severe gastrointestinal bleeding in patients with HHT. We initiated an open-label, phase II, prospective, non-randomized, multicenter clinical trial. Patients with HHT and transfusion dependency (≥2 units blood and/or intravenous iron in the 6 months prior to inclusion) and prior attempt for endoscopic treatment were included between December 2016 and September 2017. Octreotide LAR 20 mg monthly was administered for 6 months. The primary outcome was response to treatment, defined as complete responder (no need for blood, iron and APC during the study period), partial responder (decrease in need for blood or iron) or non-responder (no decrease in need for blood and iron). Follow-up was until one month after the end of treatment.
Results: Nine patients, with a mean age of 56.9 years (SD 7.5) and of which 5 were men, were enrolled. Eight patients (89%) were partial responder with a reduction in iron and/or blood transfusions. None of the patients were complete responder and one patient was a non-responder (11%). The overall mean difference in units of blood transfusions decreased with 6 units, from 21 (SD 32.6) in the six months prior to study inclusion to 15 (SD 28.5) during the treatment period. Intravenous iron decreased with 1.1 from 6 units (SD 7.3) at baseline to 4.9 units (SD 8.5) during the treatment period. Due to the small sample size and wide variation, both treatment effects were not statistically significant (i.e. blood transfusion $p = 0.33$, intravenous iron $p = 0.35$). As secondary outcome the epistaxis severity score decreased not statistical significant from baseline 4.7 to 3.8 ($p = 0.19$). One patient stopped octreotide treatment after three months due to complaints of dizziness. Other side-effects were graded as non-serious, grade I adverse events: abdominal discomfort for less than two days after injection ($n = 4$), light colored stool ($n = 1$). Eight of the nine patients chose to continue octreotide therapy after the end of study, because they experienced improvement of quality of life.
Conclusion: Octreotide is safe and seems to be effective in reducing the number of iron and blood transfusions in HHT patients with gastrointestinal bleeding. Further research in a larger number of patients in a well-controlled study is needed to investigate if there is a clinical relevant effect of octreotide.
Disclosure: Nothing to disclose

P1110 THE DETERMINATION OF NOVEL ANGIOGENIC FACTORS IN SMALL BOWEL ANGIODYSPLASIA

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Introduction: Small bowel angiodysplasias (SBAs) account for 50% of cases of obscure gastrointestinal bleeding and due to delays in diagnosis and ineffective treatments are associated with high levels of morbidity and mortality. The development of effective treatments for SBA is impeded by a limited knowledge of the pathophysiology, and the lack of any specific therapeutic targets. We have previously presented our work outlining abnormalities in the Angiopoietin pathway (Angiopoietin 1 and 2) in both tissue and serum of patients with SBA compared to controls, however as angiogenesis is controlled by the interaction between a multitude of pro and anti-angiogenic factors this is likely to only be the tip of the iceberg in identifying a future therapeutic target for SBA.
Aims and Methods: Serum samples were collected from patients with a definite diagnosis of SBA by capsule endoscopy and from controls with no history of overt gastrointestinal bleeding who had undergone panendoscopy and capsule endoscopy to outrule bleeding, and were not anaemic. Using a commercially available human angiogenesis antibody array profiler kit (R&D systems) the relative levels of 55 angiogenesis related proteins was measured using near infrared fluorescence detection. Based on the detection of possibly significant factors identified by this putative assessment, quantitative assessments of three factors – Endostatin, TIMP1 (metallopeptidase inhibitor-1) and Platelet derived growth factor (PDGF) AA were measured using commercially available ELISA antibody array kits (R&D systems) in a larger group of patients and controls. Samples were measured in duplicate and the median relative level and mean level of each factor was then compared between SBA patients and controls using a Mann Whitney U test, with a p value of < 0.05 considered to be statistically significant.
Results: An initial assessment using the 55 antibody array assay was performed in 13 samples (7 SBA patients and 6 controls). Significantly lower levels of 4 factors were found in patients with SBA vs controls including: Angiopoietin-1 ($p < 0.004$), Platelet derived growth factor (PDGF) AA ($p < 0.009$), Endostatin ($p < 0.03$) and TIMP1 (metallopeptidase inhibitor-1) ($p < 0.04$). Quantitative ELISA assessments of serum levels of PDGF-AA, Endostatin and TIMP1 in 20 SBA patients and 20 controls were then performed. As outlined in the table, SBA patients had significantly lower levels of TIMP1 ($p < 0.003$) and higher levels of Endostatin ($p < 0.004$) than controls (Table 1 shows the mean level of each factor). No differences were detected in levels of PDGF-AA.

	Endostatin ng/ml	TIMP1 ng/ml	PDGF-AA pg/ml
SBA n = 20	579.63 (208.92–909.39)	425.10 (134.34–616.30)	31170.91 (410.19–66117.12)
Controls n = 20	357.21 (123.26–554.25)	566.75 (374.20–808.92)	41323.51 (2586.39–70024.52)
p value	0.0035	0.0028	0.1247

[Table showing mean values of each factor for SBA patients and controls]
Conclusion: This assessment has revealed two previously unidentified factors possibly associated with SBA formation, which will be useful in directing further cellular based work to elucidate the pathophysiology of SBA. Endostatin and TIMP1 are both angiogenesis inhibitors. Elevated serum levels of Endostatin have been associated with a number of vascular malignancies and hypoxia driven conditions such as chronic kidney disease and peripheral vascular disease which are also associated with SBA. TIMP1 is a regulatory protein inhibiting metalloproteinases with an important role in extracellular matrix composition and healing. The identification of both Endostatin and TIMP1 as potential

drivers of SBA warrants further investigation and may yield exciting advances in the diagnosis and treatment of SBA.
Disclosure: Nothing to disclose

P1111 ENHANCED EXPRESSION OF HUMAN HERPES SIMPLEX VIRUS 1 DERIVED MICRO RNA IN LOWER ESOPHAGEAL SPHINCTER MUSCLE USING BIOPSY SAMPLES UNDER PER-ORAL ENDOSCOPIC MYOTOMY

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Introduction: Esophageal achalasia is a rare chronic progressive disease characterized by incomplete lower esophageal sphincter (LES) relaxation. The disease occurs due to Auerbach plexus degeneration. Viruses and autoimmune disorders have been suggested as the cause of the disease; however, the exact cause remains unknown. Micro RNA (miRNA) is a single-stranded RNA that controls gene expression and plays a crucial role in many biological phenomena. In 2016, per-oral endoscopic myotomy (POEM) for esophageal achalasia was developed and became covered by health insurance. To identify the cause of achalasia, we conducted biopsies sampling from the circular muscle layer of LES during POEM and undertook a comprehensive analysis of miRNA expression patterns.
Aims and Methods: We conducted biopsies sampling from the LES of esophageal achalasia cases during POEM. As controls, we conducted biopsies sampling from the LES of operative cases in which the esophagogastric junction was excised and had no abnormal esophagus motility. Following RNA extraction, a microarray analysis was conducted (Agilent Technology). We quantified miRNA thought to have fluctuation over 2-fold based on the microarray with SYBR Green real time PCR using Exiqoṅs locked nucleic acid (LNA) primers (11 achalasia cases, 6 controls). We investigated correlations with diverse clinical factors.
Results: The expression of human herpes virus 1 (HSV-1) derived hsv1-miR-H1-3p ($p<0.05$) and hsv1-miR-H18 ($p<0.05$) was significantly prominent in achalasia patients. No clear relationships were observed with expansion type, expantion level, or disease duration. Furthermore, esophageal mucosal biopsy did not reveal the HSV-1 derived miRNA in either achalasia or control groups.
Conclusion: Considering miRNA genes constitute a latency associated transcript (LAT) and influence herpes virus pathogenicity, enhanced expression of miRNA derived from neurotropic HSV-1 in the achalasia LES implies a causal relationship.
Disclosure: Nothing to disclose

P1112 JIANPILIQI FORMULA RESTORES DUODENAL MUCOSAL INTEGRITY AND SUPPRESSES LOW-GRADE INFLAMMATION IN A RAT MODEL OF FUNCTIONAL DYSPEPSIA

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Introduction: Chinese medicine Jianpiliqi formula has shown strong therapeutic effects in the treatment of functional dyspepsia (FD). However, little is known about the underlying molecular basis. Recent reports have demonstrated that impaired duodenal mucosal integrity and low-grade inflammation contribute to the pathogeneses of FD.
Aims and Methods: FD was induced by stimulating rats via tail clamping that simulates pathological change of FD as determined by visceral sensitivity and gastric compliance. FD rats were randomly divided into two groups, which received saline or the Jianpiliqi formula in the drinking water for 7 days.
Results: We found that Jianpiliqi formula restored duodenal epithelial integrity and suppressed low-grade inflammation. Ussing chamber analysis showed an increase in transepithelial electric resistance in Jianpiliqi-treated FD rats as compared to the control FD rats. Western blotting further showed that the expression of tight junction proteins occludin and claudin-1 were increased by Jianpiliqi formula. Moreover, Jianpiliqi formula ameliorated the production of tumor necrosis factor alpha (TNF-α) and interferon gamma (INF-γ) in duodenal mucosa as determined by ELISA. Mast cells acts as a key effector in stress-induced mucosal injury and inflammation. We observed that the number of mast cells was significantly increased in FD rats compared to the healthy rats as indicated by immunofluorescence staining. Importantly, treatment by Jianpiliqi formula significantly negated the increase in mast cell number in duodenum of FD rats. A concurrent decrease was also found in the mRNA expression of tryptase and PAR-2 that activate proinflammatory pathways leading to low-grade inflammation and high permeability.
Conclusion: The therapeutic effect of Jianpiliqi formula on FD is at least partially through the improvement of duodenal mucosal integrity and the attenuation of low-grade inflammation in the duodenum by suppressing the mast cell-mediated tryptase-PAR-2 signaling pathway. Our findings highlight the molecular basis of Jianpiliqi formula-based treatment of FD in human patients.
Disclosure: Nothing to disclose

P1113 MANOMETRICS CHARACTERISTICS OF OESOPHAGEAL MOTOR ACTIVITY IN TYPE 2 DIABETICS WITH COMPLAINTS OF CONSTIPATION: COMPARISON WITH DIABETICS WITHOUT CONSTIPATION

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Introduction: Some studies support that there is a significant overlap between the different functional disorders of the digestive tract.
Aims and Methods: The aim of this study was to compare oesophageal motor characteristics between type 2 diabetics with and without constipation.
Oesophageal manometry was performed in 16 diabetic individuals with complaints of constipation and 20 without constipation. Glycaemic control was similar. Waves were evaluated in the 3 thirds of the oesophagus (P1 = upper, P2 = middle, and P3 = distal). Results are in mean ± standard error.
Results: In constipated vs. non-constipated diabetics, wave distribution was as follows: peristaltic waves, $85.54 \pm 3.85\%$ vs. $91.45 \pm 2.32\%$, $p = 0.16$; simultaneous waves, $3.50 \pm \%1.19\%$ vs. $0.93 \pm 0.28\%$, $p = 0.015$. The percent of no transmitted waves and of retrograde waves between groups were similar. Wave amplitude did not reveal significant differences between groups. Wave duration (sec.) in constipated vs. non-constipated was as follow: P1-P2, 4.76 ± 0.67 vs. 4.15 ± 0.53, $p < 0.47$; P2-P3, 7.24 ± 0.93 vs. 4.90 ± 0.47, $p < 0.017$ and P1-P3, 6.71 ± 1.20 vs. 3.37 ± 0.42 $p = 0.013$. Velocity duration (cm/s) registered in constipated vs. non-constipated was: P1-P2, 2.93 ± 0.64 vs. 4.03 ± 0.58, $p < 0.21$; P2-P3, 3.42 ± 0.67 vs. 5.07 ± 0.51, $p < 0.05$ and P1-P3, 2.69 ± 0.58 vs. 4.27 ± 0.37, $p < 0.01$.
Conclusion: (1) Simultaneous oesophageal waves were significantly more frequent in constipated diabetics. (2) Wave duration was significantly higher within the middle and distal oesophagus of constipated diabetics. (3) Wave velocity was significantly higher within the middle esophagus of non-constipated individuals. (4) Constipated individuals have some differences in esophageal motility when compared with non-constipated individuals.
Disclosure: Nothing to disclose

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P1114 IS THERE A ROLE OF INTERSTITIAL CELLS OF CAJAL FOR GASTRIC SLOW WAVE PATTERNS DURING GASTRIC ELECTRICAL STIMULATION

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Introduction: Gastric electrical stimulation (GES), which has been reported to have therapeutic potentials for gastroparesis. However, effective application methods of GES on stomach is not defined. The interstitial cells of Cajal (ICC) are recognized as mediators of neuromuscular transmission in the gastrointestinal tract and as pacemakers involved in the modulation of gastrointestinal motility. We aimed to investigate the efficacy of GES according to distribution of ICC in various gastric lesions of porcine models.
Aims and Methods: The study was performed in healthy fasted weaner pigs surgically implanted with gastric serosal electrodes and endoscopically applied electrodes. The experiment consisted of a 10-minute baseline, a 10-minute GES, and a 10-minute recovery. Acquisition of gastric electrical signals was performed before, during, and after electrical stimulation. A multi-channel recorder (Acknowledge 4.4, MP150; Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity throughout the study. Immunohistochemical labelling of interstitial cells of Cajal was performed using an anti-Kit antibody.
Results: The number of c-kit (+) cells appeared to be 12.13 ± 6.02 in the fundus, 18.93 ± 11.93 in the body, and 23.04 ± 6.86 in the antrum when observed at high-power magnification. Electrogastrogram recordings demonstrated that elevated frequency amplitude ratio with increased density of c-kit (+) cells during gastric electrical stimulation.
Conclusion: Intensity and distribution of interstitial Cells of cajal in gastrointestinal tract might affect gastric slow wave patterns during electrical stimulation.
Disclosure: Nothing to disclose

P1115 HOW CAN WE MEASURE ACID SECRETION IN THE SINGLE PATIENT? A VALIDATED NON-INVASIVE SURROGATE TEST COMPARED WITH MAXIMAL ACID OUTPUT IN 600 PEOPLE

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Introduction: Direct measurement of gastric acid production is out of order in clinical practice but many GI symptoms are claimed to be related with acid disorders andempirically cured. Hypochlorhydria is associated with precancerous conditions such as chronic atrophic gastritis (CAG). Acid measurement with non-invasive methods (pepsinogens) is supported by international guidelines. Their correlation with the gold standard invasive method (aspiration test) is unknown.

Aims and Methods: This study aimed to assess the efficacy of Pepsinogen I (PGI) and Gastrin 17 (G17) both in hyposecretory and hypersecretory status, as well as in heathy patients, in comparison with the gold standard. Serum PGI and G17 were measured in 600 pts (M/F = 426/176, mean age 44.2 years) with upper GI symptoms, undergoing EGD. Basal acid output, B.A.O. (n.v. 1–5 mEq/h), and maximal acid output, M.A.O. (n.v. 5–25 mEq/h), have been determined through a nasogastric tube respectively in basal condition and after pentagastrin stimulation (i.m. 6 mcrg/kg). All measurements were made off-therapy.

Results: The correlation between M.A.O. and PGI was statistically significant ($R = 0.876$, $p < 0.0001$), as well as the correlation B.A.O.-PGI ($R = 0.0567$, $p < 0.01$). The relationship between M.A.O. and G17 was inverse ($R = -0.579$ $p < 0.001$). In 344 patients (M/F = 284/60) affected by duodenal ulcer, with M.A.O. >25 mEq/h, the correlation between M.A.O. and PGI was high ($R = 0.646$, $p < 0.0001$) as well as the comparison PGI-BAO ($R = 0.234$, $p < 0.0001$) and G17-MAO ($R = -0.247$, $p < 0.0001$). In 64 pts (M/F = 30/34) affected by CAG with M.A.O. <5 mEq/h, the correlation M.A.O.-PGI was statistically significant ($R = 0.357$, $p < 0.004$).

The PGI-B.A.O. relationship showed $R = 0.234$, ($p < 0.115$) and G17-M.A.O. inverse $R = -0.309$ ($p < 0.013$). In 192 control pts (M/F = 112/80) with negative EGD and M.A.O.> 5 mEq/h and <25 mEq/h, the correlation between M.A.O. and PGI was confirmed ($R = 0.617$, $p < 0.0001$) as well as the comparison PGI-B.A.O. ($R = 0.212$, $p < 0.0004$) and G17-M.A.O. ($R = -0.454$, $p < 0.0001$).

Conclusion: PGI and G17 have been separately reported as significantly related to M.A.O. and B.A.O. in different clinical conditions. The correlation coefficient between serum markers and invasive test varied depending on the diagnosis, but it was always statistically significant. The simple value of PGI resulted able to identify the presence of a normal acid secretion. In gastric cancer screening and clinical practice measuring both serum PGI and G17 levels provides a non-invasive method to identify hypoclorhydria.

Disclosure: Nothing to disclose

P1116 INTERNATIONAL CONSENSUS CONFERENCE ON DUMPING SYNDROME DIAGNOSIS AND MANAGEMENT

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Introduction: Dumping syndrome (DS) is a common complication of gastric/esophageal surgery including under-diagnosed/-treated early and late symptoms. Clinical recommendations for its diagnosis and management are lacking.

Aims and Methods: Thus, we initiated a Delphi consensus process with international multidisciplinary experts to generate such recommendations.

We defined the scope, proposed statements, and searched electronic databases by a systematic literature surveyavailable on a online access point. A Delphi consensus process (80% agreement threshold) byGRADE (Grading of Recommendations Assessment, Development and Evaluation) was used to categorize the quality of evidence and strength of recommendations.

Results: Consensus (>80% agreement) was reached for 52 of 62 statements. The panel agreed on a simple definition of DS, recognizing its impact on quality of life.

There was agreement on the pathophysiological relevance of rapid passage of nutrients to the small bowel, but not on decreased gastric volume capacity in generating DS.

Symptom recognition is crucial in DS diagnosis but the usefulness of questionnaires like Sigstad's questionnaire for diagnosis and assessement of therapeutic response is not established. Arts' questionnaire can discriminate early from late DS symptoms. The modified oral glucose tolerance test is considered useful for DS diagnosis while gastric emptying tests are not for diagnosis confirmation (low sensitivity and specificity).

Dietary intervention is the agreed first step in DS treatment, while lying down after meals and dietary supplements increasing foods viscosity were not agreed upon.

Pharmacological treatment was agreed for the management of DS not responding to diet. Acarbose is effective for late DS symptoms only. Somatostatin analogues are the preferred treatment for patients with well established DS non-responding to diet and/or acarbose. Short-acting formulations are more effective than long-acting ones for symptom-control although repeated injections limit their long-term use.

In refractory DS treatment, continous enteral feeding via jejunostomy can be a valid alternative and gastric tube enteral feeding can be useful for DS after Nissen fundoplication only.

Surgical reintervention should be considered in DS non-responding to dietary and/or pharmacological interventions (best results achieved with gastric bypass reversal and gastric pouch restriction). No agreement was reached on the efficacy of partial pancreatectomy for management of refractory hypoglycemia.

Conclusion: This multidisciplinary international consensus process generated key clinical recommendations for definition, diagnosis and treatment of DS in clinical practice.

Disclosure: Nothing to disclose

P1117 EFFICIENCY AND SAFETY OF ENDOSCOPIC DILATION OF THE PLUMMER-VINSON RING

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Introduction: The Plummer Vincent syndrome (PVS) or Kelly Paterson is a rare entity defined by the association of higher dysphagia, iron deficiency anemia and a fibrous ring of the cervical esophagus. Although correction of sideropenia may improve these symptoms, endoscopic dilatation of the oesophageal diaphragm is often necessary. The main objective of our work is to analyze the results of endoscopic treatment and then to study the epidemiological, clinical and endoscopic characteristics of PVS

Aims and Methods: We included in this study study of 77 cases of PVS collected in our unit between September 2005 and April 2018. All patients underwent martial treatment and endoscopic dilation of the esophageal ring with Gillard Savary Bougies or hydrostatic balloon under or without scopy. Other session (s) of dilatation was performed in case of recurrence of dysphagia and/or oesophageal stenosis under sedation with propofol.

Results: 11,373 upper gastrointestinal endoscopies were performed, including 184 in the context of PVS, over a period of 13 years (1,6%)

A total of 77 patients with PVS were included, including 66 women (85.7%) and 11 men (14.3%). The average age was 39 (range: 16–78 years). All patients presented dysphagia and anemic syndrome. The anemia found in all patients was iron deficient, the mean hemoglobin level was 9.5 g/dl and ferritinemia 10 µg/l. High gastrointestinal endoscopy was performed in all patients; 74 cases (96%) had a single ring while 3 patients had 2 rings (3.9%). Only one patient (1.3%) had 3. All our patients underwent endoscopic dilation with an average of 1.5 dilations with Savary Gillard's bougies in 70 cases (91%) and balloons of dilation in 4 cases (5.2%). No cases of perforation were noted after dilatation. The clinical, biological and endoscopic evolution was favorable; no case of malignant degeneration was noted with a mean follow-up of 31.5 months.

Conclusion: Management of PVS is based on endoscopic dilatation and martial supplementation. Our experience confirms that endoscopic dilation is effective, well tolerated and safe.

Regular endoscopic monitoring is required despite endoscopic dilatation because the PVS is a premalignant condition

Disclosure: Nothing to disclose

P1118 ENDOSCOPIC TREATMENT OF LARGE GASTRIC PHYTOBEZOARS WITH A SIMPLE HANDMADE BEZOARATOME

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Introduction: Big phytobezoars can not be effectively fragmented by using conventional endoscopic equipments such as basket and snare.

Aims and Methods: We aimed to present the efficacy of a special designed handmade bezoarotome in fragmenting big bezoars. The study was conducted on patients who underwent endoscopic treatment of big gastric phytobezoars at ourcenter within the last 3 years by using a handmade bezoarotome. The handmade bezoarotome was designed by using the sheath and handle of a mechanica llithotriptor used for fragmentation of common bile duct stones during endoscopic retrograde cholangiography and a guidewire. A large snare was created by inserting a folded guidewire through the sheathand it was inserted through the working channel of a gastroscope in order to capture phytobezoars. Later on the snare was squeezed by using the handle and the phytobezoars were fragmented into small pieces as much as possible by repeated procedures. Patients were adviced to drink cola or pineapple juice after the procedure. The endoscopic sessions were repeated every 3 days if necessary.

Results: The study group included 37 patients (16 female, mean age: 57.6 (33–81)). Predisposing factors were type II diabetes mellitus in 13 patients and subtotal gastrectomy in 5 patient. Epigastric pain was the most common symptom (73%). The mean size of the maximum diameter of the bezoars were 81mm (60–100). Seven patients had more than one bezoar. Bezoars were effectively fragmented in all of the patients with relief of symptoms and no side effects, other than one (2.7%) who developed intestinal obstruction following treatment and required surgery. The mean number of thesessions were 1.53(1–3) and the mean total endoscopy procedure time was 14.24+6.12 minutes.

Conclusion: Handmade bezoarotome is a simple and feasible equipment which can be effectively used in the treatment of big gastric phytobezoars.

Disclosure: Nothing to disclose

P1119 EFFECT OF INTRACOLONIC GAS ON GASTRIC TONE AND SATIETY IN PATIENTS WITH CONSTIPATION PREDOMINANT IRRITABLE BOWEL SYNDROME AND DYSPEPTIC SYMPTOMS

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Introduction: Interaction between stimuli at different segments of the intestine is critical to maintain gut homeostasis. In patients with functional gut disorders, overlap between symptoms referred to different segments of the intestinal tract is common, but the underlying mechanisms are not completely understood.

Aims and Methods: We aimed to determine the effect of increased volume of colonic contents on gastric motor responses and satiety in patients with constipation predominant irritable bowel syndrome (IBS-C) and concomitant dyspeptic symptoms.

In ten healthy subjects (4 women and 6 men, age range 20–36 years) and 11 patients with IBS-C and concomitant dyspeptic symptoms (10 female and 1 male; age range 33- 67 years), gastric motor responses and satiety were studied in 2 different days: 1) during colonic gas filling with a non-absorbable gas mixture infused at 24 ml/min for 40 min (Total 960 ml), and 2) during sham infusion of gas into the colon for 40 min. During colonic gas filling, gastric tone was continuously recorded using an electronic barostat, and abdominal perception was registered from 0–6 using a graded questionnaire at 10-min intervals. At the end of colonic filling a satiety test was performed each study day by ingestion of Nutridrink 100 ml/min up to maximal tolerance.

Results: In healthy subjects, colonic gas infusion was associated to a progressive increment in gastric tone (gastric tone increment 65 ± 32 ml greater than during sham infusion; $p < 0.05$), but induced no increment in perception of abdominal symptoms (mean score 1.4 ± 0.4; NS vs score 1.7 ± 0.3 during sham infusion). By contrast, in patients with IBS-C colonic gas infusion was not associated to gastric contraction (gastric tone increment -15 ± 21 ml greater than during sham infusion; $p < 0.05$ vs healthy controls), but induced significant perception of abdominal symptoms (mean score 2.6 ± 0.1; $p < 0.05$ vs health during gas infusion), an effect that was not observed during sham infusion (1.7 ± 0.3; $p < 0.05$ vs real gas infusion; NS vs healthy controls). The nutridrink test revealed a minor decrease in the maximal volume tolerated after colonic gas infusion in healthy subjects (860 ± 94 ml; NS vs 940 ± 70 ml after sham infusion), whereas in IBS-C patients the maximal volume ingested was significantly smaller when the colon was filled with gas (491 ± 58 ml; $p < 0.05$ vs health), but remained similar to healthy controls after sham gas infusion (791 ± 87 ml; $p < 0.05$ vs gas infusion, NS vs sham infusion in health).

Conclusion: In patients with IBS-C and concomitant dyspeptic symptoms, increments in the volume of the colonic contents produce abdominal symptoms that are associated to early satiety and a reduction in the tolerance to ingestion of nutrients. These effects suggest that dietary and pharmacological advice to treat IBS-C, should consider avoidance of substances that increase the volume of colonic contents, especially in those patients with concomitant dyspeptic symptoms.

Disclosure: Nothing to disclose

P1120 EVALUATION OF THE EFFECT OF ITRACONAZOLE, A POTENT CYP3A4 INHIBITOR, ON THE PHARMACOKINETICS OF A SINGLE ORAL DOSE OF TAK-906, A PERIPHERALLY-SELECTIVE D_2/D_3 DOPAMINE RECEPTOR ANTAGONIST

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Introduction: Gastroparesis is characterized by delayed gastric emptying in the absence of mechanical obstruction. There is an unmet need for novel treatment options for gastroparesis owing to the safety concerns of existing therapies. For example, domperidone, a peripherally-selective dopamine D_2/D_3 receptor antagonist, is approved in some countries for short-term antiemetic and prokinetic therapy. However, the US FDA has not approved domperidone because of the risk of QT interval prolongation leading to torsade de pointes. The prolongation is amplified by inhibition of an enzyme in its primary metabolic pathway, CYP3A4.[1] This phase 1 study evaluated the pharmacokinetics (PK) and safety of TAK-906, a novel peripherally-selective D_2/D_3 dopamine receptor antagonist, in the presence and absence of a potent CYP3A4 inhibitor, itraconazole.

Aims and Methods: This was a phase 1, single-sequence, open-label, two-period crossover trial in healthy volunteers (NCT03161405). On day 1, period 1 (3 days), eligible individuals received a single oral dose of TAK-906 25 mg. During period 2 (6 days), individuals received itraconazole 200 mg once daily on days 1–5; they also received a single oral dose of TAK-906 25 mg 1 hour after the itraconazole dose on day 4. There was a minimum washout period of 4 days between the TAK-906 dose on day 1 of period 1, and the beginning of period 2. Blood samples were collected at protocol-specified times following TAK-906 dosing during both periods to assess PK. The following safety assessments were performed throughout the study: AE and vital signs monitoring, physical examinations and triplicate ECG measurements. The QT effects (placebo-corrected, change-from-baseline QTcF [ΔΔQTcF]) of TAK-906 at the geometric mean peak exposure (C_{max}) in the presence and absence of itraconazole were predicted using a linear mixed-effects model. The primary objective was to evaluate the effect of itraconazole on the PK of TAK-906. The secondary objective was to assess the safety and tolerability of TAK-906 in the presence and absence of itraconazole.

Results: A total of 12 men with a median age of 33.0 years were included in the study. Compared with administration of TAK-906 alone, co-administration of TAK-906 with itraconazole increased total systemic exposure to TAK-906 (area under the concentration-time curve from zero to infinity [$AUC_{0-\infty}$]) by 1.28-fold (90% CI: 1.10, 1.49) and C_{max} by 1.98-fold (90% CI: 1.64, 2.39; Table 1). ΔΔQTcF of TAK-906 alone (C_{max}: 9.53 ng/mL) and TAK-906 with itraconazole (18.0 ng/mL) were estimated to be 1.31 milliseconds (90% CI: -0.39, 3.01) and 1.54 milliseconds (90% CI: -0.15, 3.24), respectively. There were no AEs in period 1, and two mild AEs in period 2 considered unrelated to TAK-906 (swelling of the face prior to TAK-906 dosing and constipation after dosing). During the study, there were no deaths, and no AEs led to treatment discontinuation. No clinically significant abnormalities were observed in vital signs, ECGs (including QT interval), physical examinations, haematology and chemistry parameters or urinalysis.

Conclusion: Compared with TAK-906 alone, co-administration of itraconazole with TAK-906 increased the C_{max} of TAK-906 by 1.98-fold and $AUC_{0-\infty}$ by 1.28-fold, indicating that TAK-906 is not a sensitive CYP3A4 substrate. The cardiovascular safety concerns associated with domperidone are unlikely to be elicited by TAK-906 under similar conditions.

Analyte	PK parameter	Geometric mean ratio[a]	90% CI of geometric mean ratio[a]
TAK-906	$AUC_{0-\infty}$ (h*ng/mL)	1.28	1.10, 1.49
	C_{max} (ng/mL)	1.98	1.64, 2.39

[a]Ratio = test:reference (test, geometric mean of TAK-906 25 mg with itraconazole 200 mg; reference, geometric mean of TAK-906 25 mg alone). $AUC_{0-\infty}$, area under the concentration-time *curve* from time zero to infinity; C_{max}, geometric mean peak exposure; PK, pharmacokinetic.

[T1: Summary of the PK parameters of TAK-906 after administration of a single oral dose of TAK-906 25 mg in the presence and absence of itraconazole]

Disclosure: C Chen, W Zhang, M Baratta and M Rosario are employees of Takeda Development Center Americas, Inc. R Jenkins and M Bari are employees of Takeda International UK, Ltd.

Reference

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P1121 SIGNIFICANT DECREASE IN INTEGRATED RELAXATION PRESSURE OF THE UPPER ESOPHAGEAL SPHINCTER FOLLOWING PNEUMATIC DILATATION OF LOWER ESOPHAGEAL SPHINCTER FOR ACHALASIA

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Introduction: Upper esophageal sphincter (UES) abnormality has been associated with achalasia and shown to be predictive of inferior response to treatment in these patients. UES function following pneumatic dilatation (PD) of the lower esophageal sphincter (LES) for achalasia has not been accessed. This study's objective is to investigate change in UES function following PD of LES for achalasia.
Aims and Methods: A Retrospective analysis of high resolution manometry (HRM) data regarding LES and UES function, before and after PD for achalasia. Continuous variables are presented as median (interquartile range-IQR).
Results: From June 2011 until December 2017, 116 patients underwent PD for achalasia, preceded by HRM in our center. Thirty-three of them had a HRM performed before and after the procedure. Median age of patients was 66.2 (IQR 18) years, 55% men. 76% had type 2 achalasia. Median LES integrated relaxation pressures (IRP) before and after PD were 21.9 mmHg (IQR 16.2) and 10.7 mmHg (IQR 10.7) respectively ($P < 0.001$). Similar UES mean-basal pressure and relaxation duration were observed at baseline compared to post-PD, 53.0 mmHg (IQR 47.8) vs. 49.0 mmHg (IQR 53.5) and 808 msec (IQR 386) vs. 746 msec (472) respectively ($P > 0.5$). Nevertheless, median UES IRP decreased by more than 65%, 3.8 mmHg (IQR 5.1) vs. 1.3 mmHg (IQR 5.0), ($P = 0.013$).
Conclusion: PD for achalasia was associated with a significant decrease in lower and upper esophageal sphincter IRPs. The pathophysiologic mechanism behind UES IRP decrease and its significance in the setting of PD of LES is unclear and mandates further investigation.
Disclosure: Nothing to disclose

P1122 PER ORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA: TIME FOR CLINICAL PRACTICE GUIDELINES? A EUROPEAN MULTICENTER SURVEY

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Introduction: POEM is an established, safe and successful treatment of esophageal motor disorders. Although the procedural aspects seem validated, the pre-procedural evaluation, the indications, and the follow-up remain heterogeneous. Considering the growing place of POEM, it appears necessary to build European Clinical Practice Guidelines. As first step, our objective was to assess the clinical practice in various European expert centers.
Aims and Methods: French and European centers performing POEM routinely were identified, and were proposed to complete (one/center) an online survey about their current practice in the management of achalasia, divided in 4 parts: 1/ Pre-procedure evaluation; 2/ Indications; 3/ Detailed procedural technique; 4/ Follow-up (including post-operative treatment, clinical and paraclinical tests).
Results: Twenty-one centers responded, 13 from France, 8 from Spain, Switzerland, England, Italy and Belgium. There is a mean of 1.5 operator/center [1–3], mostly gastroenterologists (86%), performing a mean of 28 POEM/year [8–70]. Fellows are trained in 43% of them and the estimated learning curve was 11 +/− 7 cases. The pre-operative clinical assessment includes Eckardt score in 100% of the cases and BMI in 62%. The paraclinical assessment includes an EGD in all the cases as well as a high resolution manometry (HRM). POEM is indicated in first intention in 100% of centers for Chicago type III achalasia, 81% for type I, and 76% for type II. POEM is also indicated as first treatment in 95% of centers after failure of Heller, 81% if high Eckardt score and young men, and 67% in patients >80 years-old. In case of previous dilation, 45% of centers indicate POEM after one session of any diameter. The two main contra-indications are paraneoplastic achalasia (71%) and systemic diseases (52%). Regarding pre-operative care, patients have liquid diet in 67% of centers, 1.8 days before the POEM [1–5] and are fasting 12 hours before. Aspirin is stopped in 29% of centers (100% of AVK and antiplatelets).
The patients are always hospitalized in conventional unit. Procedures are always performed with general anesthesia and intubation, in supine position in 90% of centers. Patients are curarized in 62% and receive antibiotic prophylaxis in 86%. A regular endoscope is used in 90% of the cases, always with CO2. The most used knife is the Triangle (Olympus, Japan) for tunneling (n = 9/21) and the myotomy (n = 12/21). The operators use one device in 62% of centers and CoaGrasper in 76%. In achalasia, the tunnel is posterior (86%) with a mean tunnel length of 13.6cm [10–17]. The myotomy is anterograde in 81% of centers, only on the circular fibers in 86%, with mean length of 10cm [6–15]. The mean number of clips is 5.3 [4–7], equally distributed in terms of size. The mean procedure time is 55 min [25–100].
Post-operatively, patients resume liquid diet from POD 1 in 81% of the cases, normal diet from POD 4 in 71% of the cases. 43% of the centers discharge patients at POD 1, but the mean hospital stay after POEM is 2.2 days [1–5]. Patients have oral PPI in 100% of centers, resume antiplatelets after 3 days and anti-coagulants after 6 days. The median of reevaluation is 3 months, including Eckardt score (100%) and BMI (76%). A HRM is routinely performed in 52% of the centers. Patients are followed annually in most of the cases (71%).
Conclusion: Despite its growing place in the treatment of esophageal motor disorders, the policy of management differs in few points among European expert centers. A Delphi method could be used to propose European Clinical Practice Guidelines for POEM practice.
Disclosure: Nothing to disclose

P1123 LONG-TERM EFFICACY OF PERORAL ENDOSCOPIC MYOTOMY FOR PATIENTS WITH ACHALASIA: A 4-YEAR FOLLOW-UP STUDY

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Introduction: Peroral endoscopic myotomy (POEM) is an excellent endoscopic treatment for achalasia (AC). Short-term studies are ample but long-term studies are few. This study aimed to evaluate the long-term efficacy of peroral endoscopic myotomy for patients with achalasia.
Aims and Methods: A total of 115 patients (median age 45 years; interquartile range 34–57) with AC who underwent POEM at the First Affiliated Hospital of ZheJiang Chinese Medical University with a median follow-up of 36 months were enrolled in this study. Eckardt score and the lower esophageal sphincter pressure changes were analyzed, and gastroesophageal reflux was observed.
Results: During the final follow-up, the median Eckardt score reduced from 7.5 ± 1.9 preoperatively to 2.2 ± 1.3 ($P < 0.001$). Treatment success after 12, 24, 36, and 48 months was observed in 90.4% [confidence interval (CI) 85.7–95.0], 89.3% (CI 84.5–94.0), 87.7% (CI 82.3–93.1), and 80.8% (CI 72.7–88.9) of patients, respectively. A total of 16 (13.9%) failures occurred. Four patients were nonresponders (failure within 3 months), nine were early recurrence (between 3 months and 3 years), and three were late recurrence (after 3 years). Further, 21 (23.1%) patients had symptoms of reflux during the 2-year follow-up. Only one patient with new-onset reflux symptoms was added during the subsequent 2-year follow-up. Moreover, 71 (61.7%) patients underwent gastroscopy after POEM, and 13 (18.3%) patients were diagnosed with reflux esophagitis.
Conclusion: POEM is safe and effective for treating AC and has a better long-term effect.
Disclosure: Nothing to disclose

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P1124 LONG BREAKS IN PERISTALTIC INTEGRITY SEEN IN FRAGMENTED AND FAILED SWALLOWS ON ESOPHAGEAL HIGH-RESOLUTION MANOMETRY (HRM) PREDICT ABNORMAL REFLUX BURDEN BETTER THAN WEAK CONTRACTION VIGOR

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Introduction: The spectrum of esophageal body hypomotility on high resolution manometry (HRM) includes fragmented, weak and failed sequences, the latter two are considered ineffective. The Chicago Classification (CC) 3.0 criteria for diagnosis of fragmented peristalsis and ineffective esophageal motility (IEM) are based on consensus 50% thresholds of fragmented and ineffective sequences respectively. Objective proportions and type of hypomotile sequences predicting abnormal esophageal reflux burden are incompletely understood.

Aims and Methods: Our aim was to evaluate thresholds of fragmented, weak and failed esophageal sequences on HRM that predict abnormal acid exposure time (AET) and mean nocturnal baseline impedance (MNBI) on ambulatory pH-impedance monitoring performed off acid suppressive therapy. Clinical data, HRM and ambulatory pH-impedance studies performed on patients with persisting reflux symptoms were reviewed from six centers (5 in Europe and 1 in US) for this preliminary report. Incomplete studies, achalasia, esophageal outflow obstruction and prior foregut surgery were exclusions. HRM studies were analyzed according to CC 3.0, using distal contractile integral (DCI) to designate fragmented (DCI > 450 mmHg.cm.s with breaks > 5 cm on 20 mmHg isobaric contour), weak (DCI 100–450 mmHg.cm.s) and failed (DCI < 100 mmHg.cm.s) sequences. Total AET > 6% and MNBI < 2292 ohms defined abnormal reflux metrics on pH-impedance testing. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated to determine likelihood of abnormal reflux metrics with varying proportions of fragmented, weak and failed sequences, using normal HRM studies (10 intact sequences with DCI > 450 mmHg.cm.s) for comparison.

Results: Of 351 patients (52.1 ± 0.8 yr, 67%F), 61.5% presented with typical symptoms. AET > 6% was found in 103 (29.3%), and MNBI < 2292 ohms in 217 patients (61.8%). Compared to normal HRM, ≥50% fragmented peristalsis had OR 3.6 (CI 1.3–9.8, p = 0.01) in predicting abnormal AET, and OR 3.7 (CI 1.2–11.8, p = 0.03) in predicting abnormal MNBI. Both AET and MNBI were significantly abnormal with > 70% fragmented sequences compared to ≤80% (AET 8.8 ± 1.5% vs 4.5 ± 0.6%, MNBI 1225 ± 193 vs 2232 ± 87 ohms, p < 0.05 for each). IEM as currently defined by CC 3.0 also predicted abnormal AET (OR 2.4, CI 1.3–4.4, p = 0.009), and abnormal MNBI (OR 2.3, CI 1.3–4.2, p = 0.006). When weak and failed sequences within IEM were separately analyzed, ≥50% weak sequences did not predict abnormal AET (OR 1.9, CI 0.8–4.2, p = 0.14) but predicted abnormal MNBI (OR 3.8, CI 1.6–9.1, p = 0.002); > 70% weak sequences resulted in numerically higher AET (5.0 ± 1.1% vs. 4.5 ± 0.5%, p = ns) and lower MNBI (1811 ± 372 vs. 2123 ± 86 ohms, p = ns). The role of contraction reserve in modifying esophageal reflux burden could not be evaluated because of insufficient numbers with MRS data. ≥50% failed sequences uniformly predicted abnormal AET (p ≤ 0.009), but MNBI was consistently low with failed sequences (1815 ± 151 ohms) and not discriminative (p≥0.2).

Conclusion: Long breaks in esophageal peristaltic integrity seen with fragmented and failed sequences are more relevant to abnormal esophageal acid burden than weak sequences, but all hypomotility processes can contribute to low MNBI. Fragmented sequences can be graded into mild (≤70%) and severe based on abnormal reflux metrics. Failed sequences consistently predict abnormal reflux metrics, in contrast to weak sequences. Our findings suggest that further review of the CC 3.0 diagnostic criteria for IEM and fragmented peristalsis is warranted in the context of reflux disease.

Disclosure: Nothing to disclose

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P1125 COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE AND HIGH-RESOLUTION MANOMETRY IMPROVES DETECTION OF CLINICALLY RELEVANT ESOPHAGOGASTRIC JUNCTION OUTFLOW OBSTRUCTION

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Introduction: Combined multichannel intraluminal impedance and high-resolution manometry improves detection of clinically relevant esophagogastric junction outflow obstruction.

Aims and Methods: A total 169 patients diagnosed as having EGJOO between June 2011 and February 2018 were analyzed. All the patients received a combined MII and high resolution manometry (CMII-HRM, Sandhill system). MII was reported as having abnormal liquid bolus transit (LBT) if < 80% of swallows had complete bolus transit. EGJOO was defined as a median integrated relaxation pressure of > 20 mmHg and when the criteria for achalasia were not met. Patients who progress to achalasia, show significant passage disturbance, or require pneumatic dilatation were defined as having a clinically relevant EGJOO.

Results: Among the patients with EGJOO ($n = 169$), the clinically relevant group ($n = 10$) had higher incidence rates of dysphagia (100% vs 25.2%, $p < 0.001$), compartmentalized pressurization (CP; 90.0% vs 22.0%, $p < 0.001$), and abnormal LBT (100% vs 66.7%, $p = 0.032$) than the non-relevant group ($n = 159$). The combination of dysphagia, CP, and abnormal LBT showed the best predictive power for clinically relevant EGJOO (sensitivity 90%, specificity 92.5%, positive predictive value 42.9%, negative predictive value 99.3%, positive likelihood ratio 11.9, and negative likelihood ratio 0.1). When CMII-HRM was used, an additional 8.3% of clinically relevant EGJOO cases were identified as compared with HRM alone.

Conclusion: Clinically relevant EGJOO can be predicted using CMII-HRM and clinical factors.

Disclosure: Nothing to disclose

P1126 A SINGLE-CENTER EXPERIENCE WITH PERORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA- TWO-YEAR FOLLOW-UP AND BEYOND

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Introduction: Per-Oral Endoscopic Myotomy (POEM) is nowadays a widely accepted treatment method for esophageal achalasia, not only because of its attractiveness but also favorable mid-term efficacy and safety profile, although long-term outcomes are still yet to be proved. Furthermore, serious concerns regarding post-POEM reflux are more than legitimate.

Aims and Methods: The aim of our prospective single-center case series was to assess the long-term clinical outcomes of POEM in terms of efficacy, durability and complications. A total of 266 POEM procedures were performed in 254 consecutive patients with confirmed achalasia referred to our tertiary center from 12/2012 to 4/2018. Follow-up visits at 3, 12, 24, 36 and 48 months were completed in 217, 164, 115, 66 and 44 patients. All patients underwent upper GI endoscopy, high-resolution manometry (HRM) and 24-hour pH-monitoring at 3 months after POEM; endoscopy was then repeated between 24–36 months. The main outcomes were treatment success defined as Eckardt score < 3, recurrence rate, adverse events and post-POEM reflux.

Results: At 3, 12, 24, 36 and 48 months, treatment success was achieved in 97.7% (CI 96–98), 96.0% (95–97), 91.0% (89–93), 85.5% (82–89) and 81.6% (77–87) of patients. A total of 19 patients experienced treatment failure (n = 5) or recurrence (n = 14). The recurrences occurred most often in patients with type I achalasia (8 out of 43, 18.6%). At 3 months, reflux esophagitis was endoscopically confirmed in 86/214 patients (40.1%; 9 patients had LA C/D esophagitis) and abnormal acid exposure was found on pH-metry studies was detected in 74/192 patients (38.5%). At 24–36 months, endoscopy was performed on 71 patients and reflux esophagitis was present in 21 (29.6%) of them. The proton pump inhibitors were administered on average to 37% of patients at the follow-up visits. So far there have not been any complications detected with regard to the post-POEM reflux such as Barrett's esophagus or stenosis. The procedure-related complications were as follows: decompression of capnoperitoneum (145/254, 57.1%), subcutaneous emphysema (90/254, 35.4%), and in less than 5% of patients periprocedural bleeding, mucosal injury or postprocedural fever were each observed. Unfortunately, we experienced one fatal complication during POEM which was due to sudden cardiac death in a patient with silent pulmonary hypertension. Two cases of prolonged hospitalization were caused by fluidothorax/pneumofluidothorax.

Conclusion: POEM successfully amended the spectrum of effective treatment modalities for achalasia with sustained treatment success of 91% at 2 years, which slightly decreases over time to 81.6% at 4 years after the procedure. The rate of post-POEM reflux is detected in as high as 40% of patients. Despite POEM being considered a safe method overall, severe complications may still occur.

Disclosure: Nothing to disclose

P1127 COMPARISON OF BEHAVIORAL THERAPY AND STANDARDIZED DOCTORS' INFORMATION IN REDUCING SYMPTOMS OF SUPRAGASTRIC BELCHING

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Introduction: Supragastric belching (SGB) is a behavioral disorder where air is ingested in to the esophagus and immediately expelled. It can appear as excessive belching and it may reduce quality of life but might not be related to anxiety or depression.

Aims and Methods: The aim of this study was to evaluate the efficacy of behavioral therapy in reducing belching, improving quality of life, and relieving depression and anxiety in a six-month follow-up compared to standardized doctors information. Patients (n = 20, age 26–79, 16 female) with SGB diagnosed in

esophageal 24-hour impedance monitoring were randomized to receive either 5 sessions of behavioral therapy performed by a speech therapist or only standardized doctor's information about the mechanisms of supragastric belching. The frequency and intensity of gastric belching and quality of life (QOL) were evaluated by a visual analog scale (0–10) at onset and after 6 months follow-up. RAND-36 and 15D questionnaires were used to evaluate QOL and BAI and BDI for anxiety and depression. After the initial 6 months follow-up also the controls had the possibility of behavioral therapy with additional evaluation after 6 months.
Results: The frequency and intensity of belching were significantly reduced in the therapy group ($n = 7$, $P = 0.042$, $P = 0.027$) but not in the controls ($n = 6$) at 6 months follow-up. Anxiety and depression were relieved but not significantly. QOL did not change. In all patients after therapy ($n = 10$, including 3 patients from control group) both the frequency ($P = 0.005$) and intensity ($P = 0.005$) of belching were significantly reduced. The study was interrupted by 2 patients and 5 patients are coming to follow-up.
Conclusion: Behavioral therapy seems to be effective in reducing belching in patients with SGB and to be superior to standardized doctor's information.
Disclosure: Nothing to disclose

P1128 AGE AND MALE GENDER ARE ASSOCIATED WITH A DECLINE IN FUNCTIONAL GASTROINTESTINAL SYMPTOMS: 10-YEAR FOLLOW-UP OF THE KALIXANDA STUDY

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Introduction: Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are prevalent conditions in the population. The overall prevalence in the population is stable but presentation of symptoms may fluctuate over time. Overlap of FD/IBS symptoms is common and higher than expected by change. Known factors influencing symptom fluctuation include anxiety at baseline, however to date, age and gender have not been evaluated.
Aims and Methods: Our aim was to explore the role of age and gender in symptom stability in a prospective population based follow-up study. Study participants ($n = 3000$) were randomly selected from the national Swedish population register and surveyed in 1998 by a validated abdominal symptom questionnaire (ASQ). 1000 individuals randomly selected completed an oesophagogastroduodenoscopy in 1999–2001. All eligible from those ($n = 887$) were invited to a follow-up in 2010 with the ASQ. Data were analyzed by testing difference of mean age of subjects with FD and IBS versus controls at baseline and at follow-up with the T test.
Results: In total 703 out of 887 subjects (79.3%) completed the questionnaires. FD was reported by 110 subjects at baseline and by 92 at follow-up. FD without overlap with IBS was reported by 56 subjects at baseline and by 34 subjects at follow-up. IBS was reported by 200 subjects at baseline and by 185 subjects at follow-up (Table). IBS without overlap with FD was reported by 144 subjects at baseline and by 127 subjects at follow-up. The mean age of those with FD was not lower than that of controls at baseline (52.2 vs 53.2 years, $p = 0.45$) but at follow-up it was (60.0 vs 63.7 years, $p = 0.009$). The mean age of those with FD at follow-up was significantly lower in male (57.0 vs 63.7 years, $p = 0.004$) but not in female (61.5 vs 63.7 years, $p = 0.19$). However, in FD cases without overlap with IBS there was no significant difference in mean age at follow-up (62.6 vs 63.7 years, $p = 0.62$). The mean age of those with IBS was not lower than that of controls at baseline (51.8 vs 53.5 years, $p = 0.11$) but at follow-up it was (60.1 vs 64.3 years, $p < 0.001$). In IBS the mean age was significantly lower both in male (57.5 vs 64.3 years, $p < 0.001$) and in female (61.4 vs 64.3 years, $p = 0.020$) at follow-up. In cases with IBS without overlap with FD there was a significant difference in mean age both at baseline (51.1 vs 53.5 years, $p = 0.04$) and at follow-up (60.8 vs 64.3 years, $p = 0.004$). There was no significant difference in mean age at follow-up in female (62.0 vs 64.3 years, $p = 0.11$) but in male there was (58.6 vs 64.3 years, $p = 0.003$).
Conclusion: The mean age of those with FD or IBS was statistically significantly lower at follow-up but not at baseline, except in IBS without FD at baseline, showing that functional GI symptoms decline with age which is associated with male gender.
Disclosure: Nothing to disclose

P1129 DIFFERENT DYSREGULATION OF SYMPATHETIC AND PARASYMPATHETIC AUTONOMIC RESPONSE TO STRESS IN PATIENTS WITH FUNCTIONAL DYSPEPSIA

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Introduction: Functional dyspepsia (FD) is a common functional gastrointestinal disorder (FGID). The pathophysiological mechanisms of FGID are complex. Accumulating evidence indicates that autonomic dysregulation contributes to FGID. The symptoms of FGID are often triggered by stress, however, the mechanisms of autonomic dysregulation in FGID, especially in response to stress are incompletely understood.
Aims and Methods: The aim of this study was to assess potential changes of vagal and sympathetic regulation in patients suffering from FD in response to distinct types of stressors (active mental stress vs. passive physical stress). Studied population included 10 patients diagnosed with FD and 11 age- and sex-matched healthy controls. All patients were diagnosed according to ROME IV criteria for functional gastrointestinal disorders. Blood pressure (BP) and heart rate were continuously recorded using Finometer MIDI (FMS, Netherlands) at rest and during two distinct stressors – mental arithmetic test and cold pressor test (cooling of forearm in 1–3°C water bath for 5 min). Evaluated parameters: 1) baroreflex sensitivity (BRS, calculated from spontaneous heart rate variability and BP variability) reflecting vagally-mediated heart rate regulation in response to changes of BP, 2) spectral power in low-frequency band of systolic BP variability (LF-SBP) reflecting sympathetic alpha-adrenergic stimulation of vascular smooth muscles, 3) systolic and diastolic BP, and 4) mean heart rate.
Results: BRS (reflecting vagal function) in patients with FD was substantially (by 50%) reduced compared to controls at rest and in response to both mental arithmetic test and to cold pressor test ($p < 0.01$ for all comparisons). In contrast, LF-SBP (reflecting sympathetic function) was normal at baseline, but significantly increased in FD compared to controls during both mental arithmetic test and cold pressor test ($p < 0.05$, $p < 0.01$, respectively). No differences were found in systolic and diastolic BP and heart rate.
Conclusion: Our data show impaired dynamic sympatho-vagal balance in patients with functional dyspepsia at rest and in response to different types of stressors. The vagal function is reduced at baseline and not influenced by stress, while the sympathetic response is exaggerated by stress. These findings support the hypothesis of altered autonomic regulation during stress as a potential mechanism worsening the symptoms of FD. We suggest that comprehensive evaluation of stress response using noninvasive analysis of distinct autonomic effectors could help to better understand the role of autonomic dysregulation in functional gastrointestinal disorders.
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Disclosure: Nothing to disclose

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Table 1: FD, IBS, male gender and age groups at baseline and at 10-year follow-up

Age group baseline	20–34, n	35–49, n	50–64, n	65–80, n	Total, n
FD/IBS (male)	11 (3)/ 22 (10)	30 (11)/ 67 (27)	51 (16)/ 79 (32)	18 (6)/ 32 (11)	110 (36)/ 200 (80)
no FD/IBS (male)	52 (25)/ 41 (18)	170 (87)/ 133 (71)	260 (136)/ 232 (120)	111 (54)/ 97 (49)	593 (302)/ 503 (258)
Total	63	200	311	129	703
Age group follow-up	30–44, n	45–59, n	60–74, n	75–90, n	Total, n
FD/IBS (male)	15 (7)/ 30 (12)	30 (10)/ 57 (23)	32 (10)/ 69 (18)	15 (3)/ 29 (8)	92 (30)/ 185 (61)
no FD/IBS (male)	48 (22)/ 33 (17)	160 (79)/ 133 (66)	280 (143)/ 243 (135)	123 (64)/ 109 (59)	611 (308)/ 518 (277)
Total	63	190	312	138	703

P1130 MAST CELL ACTIVATION SYNDROME (MCAS) IN PATIENTS WITH RAPID ONSET OF FOOD INDUCED SYMPTOMS OF DYSPEPSIA, IBS, DIARRHOEA, NAUSEA OR VOMITING REACTS FAVOURABLY ON HISTAMINE 1 OR 2 BLOCKERS OR CROMOGLYCATE. AN OBSERVATIONAL STUDY

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Introduction: Many patients with functional dyspepsia or IBS indicate that their symptoms are being provoked by specific food or food components. This may be due to the mast cell activation syndrome. MCAS of the digestive tract is characterized by 2 major criteria: 1. Multifocal or disseminated infiltrates in mucosal biopsies of >20 CD 117 stained mast cells (MC) per high power field (hpf 400x). 2. Presence of symptoms attributable to pathologically increased MC activity. An additional minor criterion is symptomatic response to inhibitors of MC activation or mediator production. The awareness of MCAS is limited. This milder form of MC hyperreactivity must be distinguished from the more severe and systemic mast cell activation *disease* (MCAD) or mastocytosis where often skin and bone marrow are infiltrated with abundant MC. In regular HE stained slides MC are overlooked. Special staining with CD 117 displays the cells in characteristic brown color followed by cell count per hpf. We investigated the efficacy of histamine receptor antagonists and MC stabilizers in patients with distinct food induced MCAS.

Aims and Methods: Fifty-two patients (45 female, age 41.3 ± 23.3 yrs) with one or more rapid onset (<60 min), food induced symptoms of diarrhea (n = 23), functional dyspepsia (n = 15), IBS (n = 14), nausea (n = 12), abdominal pain (n = 11), bloating (n = 6), vomiting (n = 5) and cyclic vomiting syndrome (n = 3) were included. Biopsies of duodenum (n = 47) and colon or ileum (n = 6) showed an increase of CD 117 stained MC (30,0 ± 13.1) per hpf. Many patients had long standing and persistent complaints with an average of 10.5 ± 18.4 yrs. Therapy was initiated for four weeks, first with H1 receptor antagonist and MC stabilizer ketotifen 1–4 mg bid or fexofenadine 120–180 mg bid and subsequently H2 receptor antagonist ranitidine 150 mg bid or cromoglycate nalcrom 100 or 200 mg qid.

Results: Medication was tried and changed until the desired clinical response was achieved with one of the drugs. Ultimately 12 patients responded to ketotifen, 15 to fexofenadine, 2 to ranitidine and 14 to nalcrom. The therapeutic efficacy varied from excellent (no to minimal residual symptoms) in 17 (33%), substantial improvement in 15 (29%), modest amelioration in 10 (19%) or no effect in 10 (19%). Three patients used a combination of 2 or 3 drugs.

Conclusion: This observational study shows that when rapid onset, food induced symptoms are present and an increased number of MC (>20 per hpf) is found in mucosal biopsies trial and error treatment of MCAS with H1 or H2 receptor blockers or cromoglycate may substantially improve or remedy often longstanding and frequently debilitating symptoms of the GI tract.

Disclosure: Nothing to disclose

Reference

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P1131 OBSERVATIONAL STUDY OF FD/IBS OVERLAP SYNDROME CHARACTERISTICS AND EFFICACY OF TREATMENT

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Introduction: Gastrointestinal (GI) symptoms profile and prevalence or associated factors for the overlap between functional dyspepsia (FD) and irritable bowel syndrome (IBS) group still remain unclear.

Aims and Methods: The aim of study was evaluation of the clinical and demographic features of FD, IBS, and FD-IBS overlap and efficacy of STW 5 as a standard treatment.

In this observational comparative study a total of 1006 patients (254 in the control group, 226 in the FD, 261 in the IBS, and 265 patients in the overlap group, who met the criteria for both FD and IBS) were included. Diagnostics were based on the Rome IV criteria for functional GI disorders. A total of 752 patients from all groups were treated with 3 × 20 drops/day of STW 5. At 4 and 8 week of treatment the symptom assessment was made. The main outcome criterion was the change in a validated Gastrointestinal Symptom Score (GIS) and Visual Analogue Scale (VAS).

Results: Patients with FD-IBS overlap had more severe symptoms (bloating, nausea, vomiting, hard or lumpy stools, defecation straining, and a feeling of incomplete bowel movement) and higher depression scores compared with non-overlap patients. The factors and symptoms, most frequently associated with overlap syndrome in comparison to FD or IBS groups are summarized.

Unmarried status, nausea, bloating, and a feeling of incomplete emptying were more frequent factors in FD-IBS overlap group vs IBS group. In contrast, young age, depression, bloating, and postprandial distress syndrome were positively associated with FD-IBS overlap group vs FD group.

Postprandial fullness (38.4%), belching (28.5%), and regurgitation (27.1%) were the three most prevalent upper GI symptoms in IBS. Functional dyspepsia (47.5%), belching disorders (34.5%), and functional heartburn (27.2%) were the three most frequent upper FGID in FD patients. During STW 5 treatment GIS and VAS showed significant improvement from 8.6 to 3.7 points. In all groups the tolerability of the STW 5 was good with no adverse events.

Conclusion: Bloating was a more frequent symptom for FD-IBS overlap. Patients with postprandial distress syndrome more frequently had concomitant IBS. Mixed IBS is a more frequent factor for FD-IBS overlap. This study confirmed the efficacy of STW 5 in FD, IBS and FD-IBS patients during 8-weeks treatment period. The combination of extracts with specific gastrointestinal mode of action appears to be advantageous for a heterogeneous condition such as functional dyspepsia, irritable bowel syndrome and overlap syndrome.

Disclosure: Nothing to disclose

P1132 SUICIDAL IDEATION IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Suicide ideation, one symptom of depression, was associated with irritable bowel syndrome (IBS), but not with other functional gastrointestinal disorders (FGIDs).

Aims and Methods: The aim of the present study is to search if suicide ideation is associated with FGIDs.

1469 FGIDs patients (71% females) were included in this observational study. They fill the Rome III questionnaire, Beck depression inventory, and state and trait anxiety questionnaires. Data were analyzed using ANOVA with Bonferroni correction and logistic regression analysis.

Results: Suicidal ideation was reported by a minority of patients (15 %), with low intensity (''I have thoughts of killing myself, but I would not carry them out'') in 190 patients (13%), Moderate intensity (''I would like to kill myself'') in 11 patients (1%) and High intensity (''I would kill myself if I had the chance'') in 22 patients (1%) (Table 1).

It was not associated with significant difference of sex ratio (P = 0.520) (Table 2), of age (P = 0.225) or of BMI (P = 0.300).

The presence of suicidal ideation is associated with increase of the three psychological scales: depression (P < 0.001; OR = 1.086; 95%CI = [1.063–1.110]), state anxiety (P = 0.006; OR = 1.025; 95%CI = [1.007–1.043]) and trait anxiety (P = 0.021; OR = 1.030; 95%CI = [1.005–1.057]).

In addition, patients with suicidal ideation report a higher frequency of two IBS subtypes: IBS-Diarrhea (P = 0.016; OR = 1.754; 95%CI = [1.109–2.774]) and Mixed-IBS (P = 0.008; OR = 2.104; 95%CI = [1.210–3.660]).

Conclusion: This study shows a specific association between suicide ideation and some IBS subtypes, and not with other FGIDs.

Disclosure: Nothing to disclose

P1133 GENE POLYMORPHISM AND FUNCTIONAL DYSPEPSIA SUSCEPTIBILITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Functional dyspepsia (FD) is one of the most common chronic gastrointestinal disorders with undefined mechanisms. The phenomenon that FD patients cluster in families supported the crucial role of genetic factors in the pathogenesis of FD. Several epidemiological studies have been performed to explore the associations between gene polymorphisms and FD susceptibility and gave inconsistent results.

Aims and Methods: We performed a meta-analysis of all available data to systematically clarify the associations between gene polymorphisms and FD risk. We conducted a systematic computerized literature search from PubMed, EMBASE, the Cochrane Library prior to April 2018 using the following keywords: ''functional dyspepsia'' or ''dyspepsia'', and ''polymorphism'', ''mutation'', or ''variant''. Inclusion criteria were as follows: (1) case-control studies or cohort studies evaluating the relationship between any gene polymorphism and FD; (2) sufficient data on genotypic frequencies between all participants for estimating an odds ratio (OR) with a 95% confidence interval (CI); and (3) studies with related clinical characteristics limited to those using human subjects and containing demographic information of subjects. Two investigators extracted available data independently to make sure accuracy. ORs with 95% CI were calculated to assess the intensity of the association of related gene polymorphism and FD. *P* value <0.05 was defined as statistical significance.

Results: Thirty case-control studies were included in present systematic review. Of all, 14 studies referred to *GNB3* 825C>T with a total of 1492 cases and 3206 controls, 5 studies referred to *SCL6A4* 5HTTLPR with a total of 428 cases and 1433 controls, 3 studies referred to *CCK-1R* 779T>C with a total of 397 cases and 558 controls were further included into meta-analysis. Four different genetic models (allelic, dominant, recessive, and homozygote) were applied. *GNB3*

polymorphism was associated with increasing risk of FD based on recessive (TT vs CC+CT, OR = 1.20, 95% CI 1.01–1.43, $P = 0.04$) and homozygote (TT vs. CC, OR = 1.26, 95% CI 1.02–1.55, $P = 0.03$) models. Furthermore, subgroup analysis identified TT and T-allele (TT+CT) genotypes both were associated with increased susceptibility to epigastric pain syndrome (EPS) compared with the CC and C-allele genotype. No association was observed in any of four allelic genetic model of *SCL6A4* with FD susceptibility. However, L-allele (LL+SL) genotype of *SCL6A4* was found to be significantly associated with an increased risk of EPS (OR = 1.33, 95% CI 1.04–1.70, $P = 0.03$) and postprandial distress syndrome (PDS; OR = 1.25, 95% CI 1.03–1.52, $P = 0.04$) compared to SS genotype respectively. Finally, recessive model (CC vs. TT+CT, OR = 0.44, 95% CI 0.26–0.73, $P = 0.002$) and homozygote model (CC vs. TT, OR = 0.43, 95% CI 0.25–0.74, $P = 0.002$) demonstrated CC genotype of *CCK-1R* is associated with decreasing risk of FD.

Conclusion: The available evidence of our meta-analysis has shown that there are associations between *GNB3*, *SCL6A4*, and *CCK-1R* polymorphisms and FD susceptibility.

Disclosure: Nothing to disclose

P1134 PSYCHOLOGICAL FACTORS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS: RELATION TO DYSPEPTIC SYMPTOMS AND GASTRIC DYSMOTILITY AS MEASURED WITH ULTRASOUND

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Introduction: Altered gut-brain axis signalling may play an important pathophysiological role in functional gastrointestinal disorders (FGID). We aimed to investigate relations between psychological factors (anxiety, depression and neuroticism) and dyspeptic symptoms and gastric dysmotility in a cohort of patients with irritable bowel syndrome (IBS; n = 85), functional dyspepsia (FD; n = 94), or a combination (IBS/FD; n = 65).

Aims and Methods: Patients were recruited consecutively and examined with ultrasound of the proximal and distal stomach after drinking 500 mL low caloric meat soup (Toro klar kjøttsuppe, Bergen, Norway), and scored their dyspeptic symptoms on a visual analogue scale (0–100 mm) before and after the meal. Psychological symptoms were assessed by HADS (anxiety and depression; n = 46), VSI (gastrointestinal specific anxiety, n = 58), and EPQ-N (neuroticism; n = 203). Correlations were calculated by linear regression, and differences between means were evaluated by Student's t-test.

Results: Mean neuroticism scores for patients with FD and IBS were 3.4 and 3.7, respectively ($p > 0.05$). When analysing all patients with FD and/or IBS (n = 248), we found only a weak correlation between diameter of the fundus 10 minutes after soup intake and neuroticism score by linear regression ($r = -0.156$, $p = 0.047$). There were no other significant correlations between EPQ-N and ultrasonographic measurements of the stomach. We found weak correlations between the following dyspeptic symptoms in a fasting state and EPQ-N: epigastric pain ($r = 0.159$, $p = 0.024$), bloating ($r = 0.215$, $p = 0.002$), and upper abdominal discomfort ($r = 0.171$, $p = 0.015$), but not to postprandial symptoms. Gastrointestinal specific anxiety (VSI) had weak, positive correlations to epigastric pain ($r = 0.308$, $p = 0.008$), bloating ($r = 0.255$, $p = 0.030$) and upper abdominal discomfort ($r = 0.239$, $p = 0.044$) in fasting state. We found no correlations between VSI and postprandial symptoms or ultrasonographic measurements of the stomach.

We found a significant correlation between HAD-D and fasting nausea in FD patients ($r = 0.544$, $p = 0.004$, n = 25). In patients with IBS, we found a correlation between change in nausea after the meal and HAD-D ($r = 0.562$, $p = 0.045$, n = 12). HAD-A was not correlated with any dyspeptic symptoms.

Conclusion: Neuroticism scores in patients with FD and IBS were lower than expected, and EPQ-N-scores were not strongly correlated to gastric dysmotility or upper GI symptoms. VSI had weak correlations to fasting upper GI symptoms, but not postprandial symptoms. The strongest correlations were between HAD-D and nausea scores, suggesting a link between depression and nausea.

Disclosure: Nothing to disclose

P1135 IMPACT OF ITOPRIDE AND DOMPERIDONE ON THE SENSITIVITY OF GASTRIC DISTENTION AND GASTRIC ACCOMMODATION IN HEALTHY VOLUNTEERS

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Introduction: Itopride is a prokinetic with dopamine D_2-antagonistic and cholinesterase inhibitor properties, evaluated for the treatment of functional dyspepsia. The effects of itopride on the perception of gastric distention and postprandial fundus relaxation, two major pathophysiological mechanisms in functional dyspepsia besides delayed gastric emptying, are unknown.

Aims and Methods: The aim of this study was to evaluate the impact of itopride on the sensitivity to gastric distention and on meal-induced gastric accommodation in healthy volunteers and compare to D_2-antagonist domperidone. Fifteen healthy volunteers (6 male, mean age 28.3 ± 5.8) were studied on four separate occasions, after pre-treatment for two days t.i.d. with placebo (P), itopride 50mg (I50), itopride 100mg (I100) or domperidone 10mg (D10) in a placebo-controlled, double-blind cross-over design. A gastric barostat study was performed to assess gastric compliance, sensitivity to distention and accommodation. Symptoms were evaluated by visual analogue scales (VAS). Results are given as mean ± SEM and compared by Student's t-test and ANOVA.

Results: D10, I50 or I100 did not influence pre- and postprandial gastric compliance and sensitivity to gastric distension compared to placebo before and after meal. Consequently, the pressures needed to induce first perception or discomfort and corresponding intra-balloon volumes did not differ significantly between placebo and drugs. No significant differences in accommodation were observed after I100 (preprandial 261 ± 32 ml, postprandial 429 ± 28 ml, accommodation 167 ± 32 ml) compared to placebo. Preprandial intragastric volumes were similar with D10, I50 or P (respectively 244 ± 21, 225 ± 23, and 261 ± 36 ml, NS). However, postprandial gastric volumes after I50 and D10 were significantly lower compared to placebo (respectively 303 ± 34 and 334 ± 37 vs. 448 ± 50 ml, both $p < 0.05$) and gastric accommodation was significantly reduced after D10 (90 ± 26 ml) and I50 (78 ± 25 ml) compared to placebo (186 ± 37 ml, both $p < 0.01$). VAS scores during balloon distentions and before and after meal ingestion did not differ between placebo and any of the treatment arms.

Conclusion: In healthy subjects, itopride and domperidone do not alter gastric compliance or sensitivity to distension. Itopride 50 mg and Domperidone 10 mg t.i.d. decrease gastric accommodation to a meal. No consistent effect on distention-induced symptoms was observed.

Disclosure: Nothing to disclose

P1136 NOT ONLY DUODENAL BUT ALSO JEJUNAL MUCOSAL INTEGRITY ARE IMPAIRED IN PATIENTS WITH FUNCTIONAL DYSPEPSIA. A STUDY USING SMALL BOWEL HRM/IMPEDANCE

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Introduction: Impaired duodenal mucosal integrity has been reported as a pathophysiological mechanism in functional dyspepsia (FD). Little is known about jejunal mucosal integrity in FD. Low baseline impedance (BI) is used as a surrogate marker of impaired esophageal mucosal integrity. We have recently reported that measurement of BI in the duodenum and proximal jejunum is best immediately after the passage of Phase III of the MMC.

Aims and Methods: The aim of this study was to assess duodeno-jejunal mucosal integrity (BI) in patients with FD compared to healthy controls (HC). Fifteen HC (7 females; mean age 36.7 ± 11.5 y) and 9 patients (9 females; mean age 35.4 ± 8.4 y) with FD (Rome IV criteria; 7 postprandial distress syndrome (PDS), 2 PDS + IBS-C) underwent ambulatory duodeno-jejunal HRM/impedance (HRM/Z). The ambulatory HRM/Z system (MMS, Netherlands) included a catheter (UniSensor, Switzerland) with 20 pressure sensors (2 cm apart) and 9 impedance channels. HRM data was analysed to identify MMC phase IIIs (pIIIs). BI in the duodenum (D1, D2, D3, D4) and the proximal jejunum (J1) were determined by measuring impedance immediately after the passage of nocturnal MMC pIIIs (when intestinal fluids are minimal).

Results: A total of 84 nocturnal MMC pIIIs were identified, (72 in healthy subjects, 25 in patients with FD). The BI (mean ± SD) in the D1 was 242.4 ± 44.7Ω in HC and 167.9 ± 49.8 Ω in FD ($p = 0.028$), in D2: 248.5 ± 35.1 Ω and 176.9 ± 28.6 Ω ($p < 0.001$), in D3: 281.3(±37.2) and 206.5 ± 52.7 Ω ($p < 0.001$), in D4: 349.3 ± 44.3 and 255.7 ± 49.5 Ω ($p < 0.001$), and in J1: 383.9 ± 35.6 and 277.4 ± 41.0 Ω ($p < 0.001$), respectively.

Conclusion: This study has confirmed that duodenal mucosal integrity is impaired in patients with FD. Furthermore, we have shown, for the first time using prolonged impedance recordings and BI, a significantly lowered BI in the proximal jejunum in patients with FD. Whether this is a finding exclusively related to FD or it is related to concomitant intestinal functional disorders (IBS) is a matter of current investigation.

Disclosure: Nothing to disclose

P1137 ALL-AGES INCIDENCE AND PREVALENCE OF EOSINOPHILIC ESOPHAGITIS INCREASE CONTINIOUSLY IN CENTRAL SPAIN. A 12-YEAR POPULATION-BASED STUDY

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Introduction: Eosinophilic esophagitis (EoE) is the most common cause of esophageal dysfunction symptoms in children and young adults. Since its first descriptions, the incidence has been increasing slightly while prevalence has

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Table 1: Incidence and prevalence of EoE

Year	New EoE cases (Adults/Children)	Overall Incidence/ 100,000 (Adults/Children)	Male Incidence/ 100,000 (Adults/Children)	Female Incidence/ 100,000 (Adults/Children)	**Overall Prevalence/100,000 (Adults/Children)**	Male Prevalence/ 100,000 (Adults/Children)	Female Prevalence/100,000 (Adults/Children)
2010	**6/2**	**6.50/10.69**	12.82/20.82	0/0	**34.65/16.04**	68.36/31.24	2.20/0
2011	**7/0**	**7.56/0**	12.83/0	2.18/0	**43.21/16.03**	81.23/31.07	4.37/0
2012	**8/4**	**8.62/21.49**	14.92/41.74	2.18/0	**51.73/37.60**	95.92/73.05	6.54/0
2013	**8/3**	**8.76/16.43**	13.06/21.27	4.41/11.30	**61.34/54.77**	110.99/95.69	11.03/11.30
2014	**11/1**	**12.16/5.59**	22.01/0	2.22/11.49	**74.09/61.50**	134.23/97.99	13.34/22.99
2015	**12/5**	**13.47/28.38**	22.44/44.14	4.49/11.69	**88.66/90.82**	159.32/143.46	17.96/35.07
2016	**7/1**	**7.98/5.78**	13.71/11.30	2.27/0	**96.86/98.28**	173.60/158.19	20.47/35.51
2017	**12/2**	**13.85/11.78**	23.23/11.47	4.59/ 12.1	**111.94/111.87**	199.74/172	25.23/48.41
Overall	**98/19**	**9.1/10.6**	16/16.1	2.1/4.7	**-**	–	–

increased rapidly. However, figures vary widely and updated population-based data for Europe are scarce.

Aims and Methods: To estimate the incidence and prevalence of EoE in both children and adult patients in a central region of Spain and analyzed the changes along the 2006–2017 period. Reference population and annual variations data for the catchment area (Hospital General de Tomelloso & Hospital Virgen de Altagracia) were obtained from the National Institute for Statistics. Data of all patients diagnosed with EoE (evidence-based diagnosis criteria 2017) and living in these areas in the study period were prospectively collected. Socio-demographic variables, symptoms, endoscopic findings, personal and familial atopic background and season of diagnosis were registered. Incidence, prevalence, diagnosis delay and length of symptoms before a first consultation were determined.

Results: Between January 2006 and December 2017, 117 patients were diagnosed to EoE overall in the area (reference population of 103,636.89 inhabitants in 2017), including 98 adults & 19 children. Mean age was 29.8 years (SD 10.4, rank 5–82) and 87.2% were male. Half of patients were aged between 20 and 40. In adult population, the overall prevalence of EoE was 111.94 per 100,000 inhabitants in 2017 (being 199.7 per 100,000 in males and 25.2 per 100,000 in females). In children, an overall prevalence of 111.9 per 100,000 inhabitants was found (being 172 and 48.4 cases per 100,000 for boys and girls, respectively). The average annual incidence rate was 10 new cases per 100,000 inhabitants, in both adults and children (Table 1). No seasonal variations in the diagnosis was found (45.3% during pollen season *vs* 54.7% in no pollen season; $p = 0.191$). A median of 6.2 months from first consultation to final diagnosis was found, with no differences between children and adults ($p = 0.185$). In contrast, duration of symptoms from onset to first consultation was significantly longer in adults than in children (4 *vs* 37.2 months; $p = 0.002$). The increase in the number of new diagnoses of EoE exceeded that of the number of upper endoscopies in the same period.

Conclusion: Incidence and prevalence of EoE continue to increase, with this research providing the highest figures reported to date, and approach to those described for Crohn's disease. The growth of the epidemiology of EoE exceeds the increase in the number of endoscopies in the same study period.

Disclosure: Nothing to disclose

P1138 EOSINOPHILIC ESOPHAGITIS, AN ENIGMA? INCIDENCE AND CHARACTERISTICS IN ADULTS WITH DYSPHAGIA: A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: The incidence of Eosinophilic Esophagitis (EoE) has increased in recent years. Currently, esophageal biopsies are recommended in all patients with symptoms of esophageal dysfunction.

Aims and Methods: The aims of this study were to evaluate this strategy and determine the incidence and characteristics of EoE in an adult population with dysphagia. We conducted a prospective observational study of ≥18-year-old consecutive patients referred for esophagogastroduodenoscopy (EGD) due to dysphagia, between January 2016 and December 2017. Two biopsies were performed on the proximal, middle and distal thirds of the esophagus. Patients with another etiology for dysphagia on EGD were excluded. Patients with EoE (≥1 biopsy with ≥15 eosinophils/hpf) started a proton pump inhibitor (PPI) and repeated endoscopy after 8 weeks of therapy. The accuracy of the *UNC Clinical Predictor*[1] in EoE prediction was evaluated.

Results: 113 patients were included, 54.9% ($n = 62$) female, mean age = 52.4 ± 17.5 years. The incidence of EoE was 15.9% ($n = 18$). Patients diagnosed with EoE presented lower age, longer duration of dysphagia, less heartburn, more frequent history of food impaction and atopy (asthma, rhinitis, conjunctivitis and/or food allergy), higher blood concentrations of eosinophils and IgE, more rings and furrows in EGD and more presence of microabscesses, spongiosis and papillary elongation in histology ($p < 0.05$). The area under the ROC curve of the *UNC Clinical Predictor* for EoE prediction was 0.98 (95%CI 0.96–1.00; $p < 0.001$). Considering EoE patients, 55.6% ($n = 10$) presented histological response (<15 eosinophils/hpf in all biopsies) to PPI therapy. No different characteristics were found between patients with and without response to PPI.

Conclusion: The incidence of EoE in adults with dysphagia was 15.9%, a proportion in accordance with recent literature and that demonstrates the importance of esophageal biopsies in this group of patients. Demographic, clinical, endoscopic and histological characteristics were associated with EoE diagnosis but did not predict response to PPI.

Disclosure: Nothing to disclose

Reference

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P1139 MARKERS OF ESOPHAGEAL EPITHELIAL-MESENCHYMAL TRANSITION ARE SIGNIFICANTLY REDUCED IN ACTIVE EOSINOPHILIC ESOPHAGITIS FOLLOWING 16 WEEKS OF TREATMENT WITH RPC4046, AN ANTI-INTERLEUKIN-13 MONOCLONAL ANTIBODY

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Introduction: HEROES was a 16-week double-blind, placebo-controlled phase 2 multicenter trial that evaluated the efficacy and safety of RPC4046 in adults with active eosinophilic esophagitis (EoE). Fibrostenosis of the esophagus is a known complication of EoE and may be mediated in part by epithelial-mesenchymal transition (EMT). We sought to determine whether treatment with RPC4046 modulates EMT.

Aims and Methods: Esophageal biopsy sections were taken at baseline and week 16 from 69 of the 99 patients randomly assigned to weekly subcutaneous (SC) RPC4046 360 mg ($n = 26$), 180 mg ($n = 19$), or placebo ($n = 24$). Slides were stained by duplex immunofluorescence for e-cadherin and vimentin (Cell Signaling Technologies), counterstained nuclei with DAPI, and scanned at 20x on a Vectra® (PerkinElmer) multispectral digital microscopy system. Using inForm® software, a machine learning algorithm mapped the epithelial compartment in each slide. Nuclear, cytoplasmic, and membrane areas of each epithelial cell were defined and fluorescence intensity of each marker on a per-cell basis was recorded. For this EMT substudy, the primary endpoint was change from baseline in percentage of vimentin-positive epithelial cells and secondary endpoints were change in total e-cadherin expression per cell and change in vimentin:e-cadherin ratio per cell.

Results: The change from baseline in mean percentage of vimentin-positive cells was -4.24%, -2.75%, and -0.94% in the RPC4046 360 mg, 180 mg, and placebo groups, respectively ($p < 0.05$ for 360 mg vs. placebo). The change in mean e-cadherin expression per cell was 101.6, 102.4, and 18.3 in the 360 mg, 180 mg, and placebo groups ($p < 0.05$ for each active dose group vs. placebo). The change in vimentin:e-cadherin ratio was significantly different from zero in both dose groups (360 mg, -0.30; 180 mg, -0.18; $p < 0.05$ for each active dose group vs. zero). Similar effects for all markers were observed in each esophageal sampled region (proximal, mid, distal).

Conclusion: RPC4046 treatment for 16 weeks significantly improved EMT markers in esophageal tissue in patients with active EoE. A greater effect generally was observed with 360 mg than with 180 mg. These results, together with the overall clinical data presented separately, support the hypothesis that prevention of IL-13 binding to receptor subtypes IL-13Rα1 and IL-13Rα2 favorably impacts inflammatory and remodeling pathways and may reduce development of esophageal fibrostenotic complications that occur in EoE. Larger studies with longer term treatment are required to determine the impact of these results on the course of EoE.

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P1140 COMPREHENSIVE IMPEDANCE-PH ANALYSIS OF GASTROESOPHAGEAL REFLUX IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease characterized by symptoms related to esophageal dysfunction and eosinophil-predominant inflammation. There is some overlap between EoE and GERD, with similar esophageal motility abnormalities [1], particularly in those EoE patients responsive to proton pump inhibitor (PPI) therapy [2]. Normal esophageal acid exposure time (EAET) has been found in two thirds of 51 EoE cases at pH-only monitoring, and EAET was not a predictor of clinical and histological response to PPI [3]. However, the limits of pH-only monitoring have long been recognized. A comprehensive reflux assessment, based on impedance-pH monitoring and including analysis of post-reflux swallow-induced peristaltic wave (PSPW) index and of mean nocturnal baseline impedance (MNBI), improves our ability to diagnose GERD [5,6] and to predict PPI response [7], and could contribute to clarify the pathogenesis of EoE.
Aims and Methods: We investigated 52 (43 males, mean age 43 years) consecutive incident EoE cases (≥15 eosinophils/HPF in esophageal biopsies) with impedance-pH monitoring, always preceded by high resolution/conventional esophageal manometry. Impedance-pH parameters were compared with those found in 52 (41 males, mean age 39 years) healthy controls (HCs) and 52 (31 males, mean age 45 years) patients with hypersensitive esophagus (HE), the latter group defined by normal endoscopy, normal EAET and positive heartburn-reflux association. Results were examined by analysis of variance and chi-square test with Bonferroni correction, significance set at $P < .05$.
Results: All EoE patients complained of dysphagia, and 24 (46%) reported heartburn. Main impedance-pH parameters are shown in the Table. EAET was comparable among the three groups. On the other hand, the number of total refluxes was significantly higher in EoE and HE than in HCs. PSPW index and MNBI were significantly different among the three groups of subjects, and were significantly lower in EoE than in HE and in both groups of patients than in HCs.
Conclusion: Reflux parameters in EoE and HE are quite similar and significantly different from those found in HCs, suggesting that reflux could play a role in the pathogenesis of EoE. Low values of PSPW index reflect a primary defect of esophageal chemical clearance determining mucosal damage, as shown by low MNBI values, in turn favoring penetration of food antigens and their contact with immune cells; in genetically susceptible individuals this event could be followed by interleukin 5,4 and 13 secretion with subsequent eosinophils recruitment and development of EoE.

Impedance-pH variables	HCs (n = 52)	EoE (n = 52)	HE (n = 52)
EAET (%), mean (SD)	1.0 (1.0)	1.8 (1.9)	1.8 (1.3)
P > .05 for all pairwise comparisons			
Total Refluxes (n), mean (SD)	23 (12)	38 (24)	44 (22)
P < .05 for HC vs. EoE and HE			
Acid Refluxes (n), mean (SD)	16 (11)	30 (21)	30 (18)
P < .05 for HC vs. EoE and HE			
Weakly Acidic Refluxes (n), mean (SD)	6 (6)	8 (9)	14 (13)
P < .05 for HC and EoE vs. HE			
PSPW index (%), mean (SD)	75 (16)	28 (16)	42 (17)
P < .05 for all pairwise comparisons			
MNBI (Ohms), mean (SD)	3045 (843)	937 (552)	2251 (1080)
P < .05 for all pairwise comparisons			

[Impedance-pH findings in EoE, HE and HCs.]
Disclosure: Nothing to disclose

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P1141 THERAPEUTIC MANAGEMENT OF EOSINOPHILIC ESOPHAGITIS- A SURVEY AMONG GASTROENTEROLOGISTS IN GERMANY

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Introduction: Eosinophilic esophagitis (EoE) is an increasingly recognized immun-mediated disease and a common cause for dysphagia and bolus obstruction. The aim of our survey was to evaluate the therapeutic management of EoE among adult gastroenterologists in Germany.
Aims and Methods: Between 11/2017 und 2/2018 a web-based questionnaire was sent to 1393 gastroenterologists (1126 in private practice (bng) and 267 hospital-based (ALGK)), containing a total of 22 questions to general, diagnostic and therapeutic aspects of EoE. Data capture and evaluation was performed using SurveyMonkey.
Results: The responder rate was 28% (bng) and 36% (ALGK). The majority of responder treat and monitor EoE patients by themselves (85%/59%).
In newly diagnosed EoE patients, the initial treatment was mainly either PPI (37%/39%) or topical steroids (34%/40%). Only few initiated elimination diet (4%/6%) or combination therapy (25%/15%). PPI-regimens were diverse: once daily for 4 weeks (20%17%) or 8 weeks (31%/24%), twice daily for 4 weeks (29%/45%) or 8 weeks (20%/25%). Budesonid was the preferred steroide (63%/68%), either nebulized (45%/41%) or as liquid suspension (40%/46%). The most frequently used elimination diet (ED) was 6-Food-ED (54%/46%), followed by allergy test-based ED (17%/15%), 2-Food-ED (14%/23%) or 4-Food-ED (11%/15%). Treatment response was usually monitored (mainly endoscopy-based) after 12 weeks (42%/35%) or 8 weeks (23%/43%). The devices used for endoscopic dilatation (hospital-based) were mainly bougies (61%) followed by ballons (39%). Based on their experience, most responders estimated that 25–50% of patients (47%/49%) or >50% of patients (23%/24%) need long-term treatment of EoE.
Conclusion: The results suggest a significant heterogeneity in the therapeutic management of EoE among gastroenterologists in Germany, both in private practice and in hospitals. This underlines the need of national guidance and for more educational activities.
Disclosure: Nothing to disclose

P1142 EOSINOPHILIC OESOPHAGITIS: THE EXPERIENCE FROM A UK DISTRICT GENERAL HOSPITAL

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Introduction: Eosinophilic Oesophagitis (EO) is a chronic inflammatory condition characterised by eosinophilia of the oesophagus. It can progress to a fibrostenotic disorder, with dysphagia and strictures. EO commonly presents with chronic, intermittent solid food dysphagia. The hallmark of the condition is the presence of >15 eosinophils/high powered field on histology[1].
Treatment includes dietary modification, pharmacological therapy and endoscopic dilatation. We aim to describe the demographics of our DGH patient population and their response to therapy.

Aims and Methods: We retrospectively analysed patient data collected from 2009 -2016 from a single district general hospital in Bury St Edmunds in the UK. All patients presenting with dysphagia with >15 eosinophils/high powered field on histology from random oesophageal biopsies were included.
Results: 86 patients were identified with EO. 52 were male. Average age was 52.1 years.
Response to therapy: 57 of the 86 patients identified attended gastroenterology clinic as follow-up for commencement of treatment.
43% were commenced on an 8 week course of PPI as first-line therapy. 80% of these had symptom resolution following PPI course completion.
35% were offered a 3 month trial of swallowed Fluticasone inhaler, as first-line therapy. 75% had symptom resolution following completion.
10% had symptom control with dietary changes. Additionally, 1 patient required oesophageal dilatation for a stricture which was maintained at 1 year review.
12% of patients had persistent symptoms despite trail of medical therapy.
Follow-up endoscopy findings 10 of the identified 86 patients had repeat OGD between 2009–2016. 5 were performed as follow-up following medical therapy and 5 were performed for alternate reasons listed in table 1.

Reason for OGD	Histological resolution	Dysphagia improved	Time between OGD	Therapy (s)
Follow-up	Yes	Yes	12 weeks	Swallowed fluticasone spray
Follow-up	Yes	Yes	16 weeks	PPI
Follow-up	Yes	Yes	8 weeks	PPI
Follow-up	Yes	Yes	12 weeks	PPI
Follow-up	Yes	No	12 weeks	PPI
Abdo pain	Yes	Yes	3 years	Swallowed fluticasone spray
Abdo pain	Yes	No	5 years	PPI
Dysphagia	No	No	2 years	PPI, Oral steroids
Reflux	Yes	Yes	6 months	PPI
Repeat food bolus	No	No	6 years	Unknown

[Repeat OGD Findings]
In the follow-group, there was 100% histological resolution of eosinophilia, with 80% improvement in symptoms in.those treated with a PPI.
Conclusion: EO is an increasingly recognised condition. European guidelines have recently been published though standadised treatment is yet to be defined[2]. Our data shows PPIs and topical corticosteroids are the most effective therapies, in keeping with known findings. PPIs were the most popular treatment choice.
It is recommended that efficacy of treatment be evaluated by repeat endoscopy. In a DGH, with increasing service pressures this may be challenging. Our asymptomatic patients who had repeat OGDs had histological resolution. One solution, therefore, may be to limit repeat OGDs to those with ongoing symptoms to observe for ongoing present of oesophageal eosinophilia.
In patients not achieving symptom resolution or histologic remission with monotherapy, a trial of combination therapy was shown to be effective and we recommend this should be attempted. Our experience is that combination of PPI and swallowed corticosteroid inhaler therapy was most effective.
Future directions would be evaluation of long-term follow-up of our patients as often they were discharged to GP so long-term resolution of symptoms is unknown.
Disclosure: Nothing to disclose

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P1143 FAECAL CALPROTECTIN AS A BIOMARKER OF GUT INFLAMMATION IS NOT A USEFUL TOOL FOR THE DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, allergen-driven, immune-mediated disease that is increasingly recognized as a leading cause of dysphagia and foregut symptoms in children and adults. The diagnosis of EoE requires an invasive endoscopic evaluation with esophageal biopsies showing at least 15 eos/hpf in at least one hpf. Moreover, since symptoms are not predictive of therapeutic medical response, current guidelines recommend to repeat the upper endoscopy in order to confirm histological disease remission after any kind of treatment (i.e. steroids, diet). Thus, a non-invasive tool to support the need of performing an upper endoscopy in patients with symptoms suggestive of EoE and to monitor EoE after therapeutic interventions and during time is desirable. Calprotectin is a granulocyte cytosolic protein that is considered to be a promising marker of subclinical inflammation. High faecal calprotectin (FC) concentrations have been found in several intestinal diseases, but no data are currently available on patients with EoE.
Aims and Methods: The aim of this prospective pilot study was to evaluate FC levels in incident cases of EoE and to correlate them with clinical score, endoscopy and histological characteristics. Consecutive patients with symptoms suggestive of EoE underwent upper endoscopy to assess the presence of at least 15 eos/hpf on oesophageal biopsies at mid/proximal esophagus and, then, were treated with twice-daily PPI for at least 8 weeks and/or topical steroids. Clinical assessment was carried out in all patients. Endoscopic, according to Endoscopic Reference Score (EREFS), and histologic features were blindly reviewed for each patient. Patients with upper gastro-intestinal symptoms, without evidence of esophageal eosinophilic infiltration, investigated during the same period of time, were used as controls. FC levels were determined by ELISA at the time of index endoscopy (i.e. in presence of active disease).
Results: Seventy patients [58M/12F; mean age 37] reporting dysphagia (94%), bolus impaction (65%) and chest pain (28%) were diagnosed with PPI-REE (n = 32) or EoE (n = 38) and were prospectively recruited. Moreover, a group of 70 [56M/10F; mean age 41] subjects, sex and age matched, were also enrolled. FC levels in incident cases of active PPI-REE/EoE were not significantly different from those in controls (mean 48 ± SD 34 μg/g vs 42 ± 39 μg/g; p = ns). Furthermore, among PPI-REE/EoE, FC concentrations were not significantly different in relation to the level of clinical score, endoscopic severity or histological evaluation (p = ns, p = ns and p = ns, respectively).
Conclusion: This study shows that FC levels in incident cases of PPI-REE/EoE patients do not differ significantly from those in controls. Our data suggest that FC is not a useful tool for the diagnosis and management of patients with eosinophilic esophagitis.
Disclosure: Nothing to disclose

P1144 DO WE HAVE TO EXCLUDE EPIGASTRIC SYMPTOMS TO DIAGNOSE GERD?

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Introduction: Gastroesophageal reflux disease (GERD) could be diagnosed by the typical heartburn symptom. GERDQ is a symptom-based tool for GERD diagnosis, and the epigastric symptoms are excluded to rule out functional dyspepsia. However, it is reported that the rate of pathologic esophageal acid reflux (PEAR) of heartburn patients is quite low in China.
Aims and Methods: The aim of the current study is to assess the epigastric symptoms for GERD diagnosis. Consecutive outpatients aged 18–65 years presented with substernal symptoms including heartburn, regurgitation, dysphagia, substernal pain and epigastric symptoms including epigastric pain, epigastric burning, early satiety and postprandial fullness were enrolled. Patients who had esophageal or gastric surgery, peptic ulcers, upper GI cancer were excluded. All patients underwent upper endoscopy, high-resolution manometry and 24-hour esophageal pH monitoring. Patients with esophagitis would be given esomeprazole 20mg bid for 8 weeks and those who with normal findings for 4 weeks. PEAR was defined as the percentage total time for which a pH value <4 was >4.2% in the distal esophagus. The symptom scores were measured by the frequency score multiplied by the severity scores of the predominant symptom before and at the end of the treatment, and the PPI test was defined as positive if the overall scores of the predominant symptom decreased by >50 % compared with those of the baseline.
Results: A total of 334 patients were included, with predominant symptoms of heartburn (N = 80), regurgitation (N = 66), substernal pain (N = 60), dysphagia (N = 11), epigastric pain (N = 33), epigastric burning (N = 25), early satiety (N = 1) and postprandial fullness (N = 58). Overall, 23.95% of patients (N = 80) had PEAR, with 26.73% (N = 58) in those with predominant substernal symptoms and 18.8% (N = 22) in those with epigastric symptoms. The rates of PEAR were 6%, 28% and 22.41% in patients with epigastric pain, epigastric burning and postprandial fullness, respectively. And the rate of PEAR in patients with epigastric burning (28%, 7/25) is almost the same as those with heartburn (28.75%, 23/80). Moreover, a total of 155 patients (50.82%) had positive PPI test, including 56.34% (N = 111) of those with substernal symptoms and 40.74% (N = 44) of those with epigastric symptoms, of whom the rates were 44.8%, 54.2% and 33.3% in patients with epigastric pain, epigastric burning and postprandial fullness, respectively. There was no significant difference in the positive rate of PPI test between patients with epigastric burning and those with heartburn (54.2% vs 56.2%, p > 0.05). Endoscopy indicated that 65 patients (19.46%) had esophagitis including 20.74% (N = 45) of those with substernal symptoms and 17.1% (N = 20) with epigastric symptoms. If we combined 24h esophageal pH monitoring, PPI test and upper endoscopy, a total of 167 patients (50%) were diagnosed with GERD, 70% of whom (N = 117) had predominant substernal

symptoms and 30% (N = 50) had epigastric symptoms. Among them, 26% of patients presented with heartburn, 23% with regurgitation, 4% with dysphagia, 17% with substernal pain, 8% with epigastric pain, 9% with epigastric burning, 13% with postprandial fullness.
Conclusion: Approximately one-third of GERD patients complain of predominant epigastric symptoms. Excluding epigastric symptoms during symptom-based evaluation of GERD in primary care may miss and delay the diagnosis of real GERD. It is suggested that epigastric symptoms should not be neglected for GERD diagnosis.
Disclosure: Nothing to disclose

P1145 NOVEL SYSTEM FOR IDENTIFICATION OF LOWER ESOPHAGEAL SPHINCTER WITH IMPEDANCE VARIATION STEP-UP METHOD: A FEASIBILITY STUDY

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Introduction: Esophageal manometry is the gold standard for lower esophageal sphincter (LES) localization and for accurate positioning of catheter based pH and multichannel intraluminal impedance pH monitoring (MII-pH). pH variation step-up method is not as accurate as esophageal manometry for LES localization, and needs patients to be OFF therapy. Gastric impedance has very low values compared to esophageal impedance and is not influenced by acid suppression.
Aims and Methods: Our aim was to evaluate feasibility of impedance variation with the step-up method for LES localization. 75 patients (31 male, mean age 48 years, range 38–57) who underwent 24-hr MII-pH monitoring were prospectively enrolled. A catheter with six impedance channel and 1 pH channel was used. Patients with known Barrett's oesophagus were excluded. High-resolution manometry (HRM) was performed before MII-pH monitoring in order to locate the upper and lower border of the LES and to evaluate esophagogastric junction (EGJ) type. A second operator, blinded to HRM finding, performed the MII-pH study: the catheter was introduced into the stomach (presence of stable impedance values <500 ohm in the second distal impedance channel located at the level of the pH sensor) and withdrawn gradually (1 cm every 15 seconds; each cm was marked with the "symptom" button) until a sharp impedance rise was seen (increase of $>50\%$ with respect to gastric baseline); in 62 patients step-up was repeated twice. Abnormal pH-MII study was defined as acid exposure time (AET) $>5\%$ and/or positive SI/SAP. A third operator blinded to both HRM and impedance results, reviewed the step-up impedance of all patients. Bland-Altman analysis with Lin concordance and correlation coefficient were used to compare MII-pH and HRM. Subgroups analysis were performed for the following parameters: ON and OFF PPI test and presence and absence of EGJ type ≥ 2. Interobserver agreement and concordance between the two step up impedance performances were evaluated using Spearman rho correlation coefficient.
Results: Descriptive data are shown in table 1. 12/75 patients were on PPI. Median impedance rising point was on average 0.8 cm caudal (95% limits of agreement, LOA: -2.6 cm to 4.2 cm) to manometric upper border of LES and 1.8 cm cranial (95% LOA: -5.1 cm to 1.5 cm) to manometric lower border of LES (Lin concordance correlation coefficients 0.81 and 0.72 respectively). Agreement between the two step-up impedance performances was excellent (mean 44.9 and 45 cm, rho 0.97). Interobserver agreement was excellent (mean 44.9 and 44.8 cm, rho 0.94). Impedance variation performances were similar between patients OFF and ON PPI and between presence/absence of EGJ type ≥ 2.
Conclusion: In this ongoing study we observed a good correlation between impedance rise and manometric localization of the upper border of the LES. ON-PPI examination and presence of EGJ type ≥ 2 do not alter performance reliability. Intra and interobserver agreement were excellent. Impedance variation with the step-up method is a promising method for LES identification and an alternative to HRM, where it is not available, also for patients ON-PPI.

Manometric upper border of LES, cm	44.1; 42–46
Manometric lower border of LES, cm	46.8; 44–48
Impedance rise LES, cm	44.9; 43–47
Gastric impedance, ohm	327; 230–400
Impedance at variation point, ohm	2149; 1350–2885
MNBI, ohm	1547; 870–2100
Pathological MII-pH, patients	29*

*[Manometric and MII-pH descriptive data in 75 patients. Data expressed as mean;IQR.*11/29 reflux hypersensitivity (i.e. normal AET and abnormal SI/SAP)]*
Disclosure: Nothing to disclose

P1146 PSPW AND MNBI INCREASE THE DIAGNOSTIC YELD OF IMPEDANCE-PH MONITORING AND ARE RELATED TO PPI RESPONSE IN GERD PATIENTS WITH ENT SYMPTOMS

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Introduction: Patients with ENT symptoms are often poor responders to PPIs and present upper endoscopy and 24h mutichannel intraluminal impedance-pH (MII-pH) within the normal range. It has been shown that mean nocturnal baseline impedance (MNBI) and post-reflux swallow-induced peristaltic wave (PSPW) indexes increase the diagnostic yield of MII-pH monitoring in GERD patients. These new variables have been assessed primarily in patients with typical GERD symptoms and few data on patients with ENT symptoms are available. Moreover, their relationship with PPI response has not been fully elucidated in these patients.
Aims and Methods: To explore whether MNBI and PSPW improve the diagnostic yield of impedance pH monitoring in GERD patients with ENT symptoms and their relationship with PPI response in these patients.
Of consecutive GERD patients presenting with ENT symptoms, 121 with absence of hiatal hernia and/or erosive esophagitis at upper endoscopy, performed within 3 months before the study, underwent MII-pH after a 3-weeks wash out from PPIs. The response to previous PPI treatment was evaluated and considered as non-satisfactory if symptom improvement was $<50\%$ on a visual analogue scale. MNBI at 3cm above the lower esophageal sphincter, PSPW, symptom association probability (SAP) and acid exposure time (AET) were calculated according to standardized criteria and considered for the data analysis.
Results: Among all 121 patients, 63 were responders and 58 non-responders to PPIs. The mean reflux number was similar between responders and non-responders. 39/63 (62%) responder and 24/58 (41%) non-responder patients presented positive AET and/or SAP ($p < 0.05$). A positive PSPW and/or MNBI was observed in 41 responders (65%) and 27 non-responders (47%) ($p < 0.05$). 13/24 responder patients with both negative AET and SAP presented a positive PSPW and/or MNBI. 8/34 non-responder patients with both negative AET and SAP (functional heartburn patients), presented a positive PSPW and/or MNBI. Patients with positive AET and/or SAP and patients with positive PSPW and/or MNBI presented a higher probability of PPI response. Results are summarized in Table 1.
Conclusion: The present data show that MNBI and PSPW are promising variables in patients with ENT symptoms, since increase the diagnostic yield of MII-pH. The presence of pathologic MNBI and/or PSPW is able to discriminate ENT patients with a satisfactory response to PPIs.

	Responders (N. 63)	Non responders (N. 58)	Relative Risk for PPI response (95% confidence interval)
Mean reflux number (mean ± 95% confidence interval)	46 ± 29	49 ± 37	
AET+	13 (%)	10 (%)	0.8 (0.5–1.2), p:ns
SAP+	16 (%)	8 (%)	0.6 (0.4–1.0), p:ns
AET+ and/or SAP+	39 (%)*	24 (%)	1.5 (1.1–2.2), $p<0.05$
PSPW+ and/or MNBI+	41 (65%)*	24 (47%)	1.6 (1.1–2.4), $p<0.05$
AET+ and/or SAP+ and PSPW+ and/or MNBI+	52 (83%)*	37 (64%)	1.7 (1.0–2.8), $p<0.05$

[Table]
Disclosure: Nothing to disclose

P1147 CORRELATION BETWEEN PERISTALTIC FUNCTION, ASSESSED BY HIGH RESOLUTION MANOMETRY, AND MUCOSAL INTEGRITY IN GERD PATIENTS

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Introduction: It has been shown that mean nocturnal baseline impedance (MNBI) increases the diagnostic yield of 24h mutichannel intraluminal impedance-pH (MII-pH) monitoring in patients with GERD. The MNBI is directly correlated with mucosal esophageal integrity and intra-luminal clearance. However, the relationship between of esophageal motility and MNBI value needs to be fully elucidated.
Aims and Methods: To explore the relationship between peristaltic vigor and MNBI in GERD patients.
Consecutive GERD patients, with recurrent typical and absence of hiatal hernia and/or erosive esophagitis at upper endoscopy underwent high resolution manometry (HRM) followed by 24h MII-pH. 87 patients with proven GERD (positive AET and/or SAP) were finally enrolled. HRM was performed with patients in a

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	Pts with at least 1/10 peristaltic break (N: 28)	Pts without peristaltic breaks (N: 47)	Pts with at least 1/10 weak contraction (N: 30)	Pts without weak contractions (N: 45)	Pts with at least 1/10 failed contraction (N: 17)	Pts without failed contractions (N: 58)
MNBI 3cm	1478 ± 283Ω	1885 ± 651Ω	1169 ± 412Ω*	2250 ± 783Ω	1142 ± 323Ω**	1828 ± 642Ω
MNBI 19cm	1887 ± 722Ω	2210 ± 887Ω	1709 ± 595Ω	2310 ± 914Ω	2070 ± 493Ω	2090 ± 882Ω

*p < 0.01 vs Pts without weak contraction **p < 0.01 vs Pts without failed contraction.

semi-recumbent position, using a catheter incorporating 24 solid state pressure sensors. 10 saline (5 ml) swallows at 30-sec intervals were analyzed in each patient. Distal contractile integral (DCI) was calculated for each swallow. Each contraction was defined as failed (DCI < 100 mmHg*s*cm) or weak (DCI > 100 mmHg*s*cm and < 450 mmHg*s*cm). Presence of large (> 5cm) breaks of esophageal peristalsis was assessed. MNBI was calculated at 3cm and 19cm above the lower esophageal sphincter according to standardized criteria. Data are shown as mean ± confidence interval.

Results: Overall mean DCI value was 1426 ± 623 mmHg*s*cm. MNBI at 3cm and 19cm values were 1693 ± 575Ω and 2006 ± 893Ω. A positive linear correlation was found between individual mean DCI and MNBI 3cm values (R: 0.8). There was no linear correlation between mean DCI and MNBI at 19cm (R: 0.4). There was no difference between MNBI at 3cm and 19cm in patients with and without presence of at least 1/10 large peristaltic break. Patients with at least 1/10 weak or failed contraction presented significant lower MNBI values at 3cm compared to patients without presence of weak or failed contraction. MNBI at 19cm did not differ in these two groups of patients. Results are in Table 1.

Conclusion: MNBI at distal esophagus is directly correlated with DCI values in GERD patients. Presence of large breaks does not affect the MNBI value. Presence of weak or failed contraction is associated to lower MNBI values at distal esophagus. These results confirm the potential role of esophageal peristaltic dysfunction on epithelial integrity. Larger studies are needed.

Disclosure: Nothing to disclose

P1148 ESOPHAGEAL HIGH-RESOLUTION MANOMETRY CAN UNRAVEL THE MECHANISMS BY WHICH DIFFERENT BARIATRIC TECHNIQUES PRODUCE DIFFERENT REFLUX EXPOSURE

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Introduction: Obesity is a global epidemic and consequently bariatric surgery is increasingly performed. Since there are numerous surgical techniques, the effects of these on the esophageal function are still poorly understood. Furthermore, some bariatric techniques proved to be very effective as antireflux procedures, such as Roux-en-y gastric bypass (RYGB), whereas "de novo" gastroesophageal reflux disease (GERD) and dysmotilities were reported after some bariatric procedures, such as Sleeve Gastrectomy (SG).

Aims and Methods: We aimed at assessing the effect of the most commonly performed bariatric techniques on esophagogastric junction (EGJ) function, esophageal peristalsis and reflux exposure using high-resolution manometry (HRM) and impedance-pH monitoring (MII-pH).

All obese (body mass index, BMI, > 35) patients underwent symptomatic questionnaires (GerdQ), endoscopy, HRM and MII-pH before and one year after surgery. We enrolled only obese without dysmotility or any evidence of GERD, in order to verify the real incidence of de novo GERD. Esophageal motor function and EGJ were classified according to Chicago Classification V. 3.0. EGJ contractile integral (EGJ-CI) was also calculated. Intragastric pressure (IGP) and gastroesophageal pressure gradient (GEPG) were assessed. Total acid exposure time (AET %), total number of refluxes and symptom association probability (SAP) were assessed. A group of healthy-volunteers (HVs) served as control.

Results: One hundred and twelve obese subjects (39 ± 12 years-old, mean weight 135 (97–202) Kg, mean BMI 42 (37–69) Kg/m^2 and 15 HVs (normal weight) were studied. Thirteen underwent endoscopic balloon placement (EBP), 12 gastric banding (GB), 26 sleeve gastrectomy (SG), 18 roux-en-y gastric bypass (RYGB), 15 mini gastric bypass (MGB), 16 biliointestinal bypass (BIBP), and 12 biliopancreatic diversion (BPD). All patients showed a significant decrease of weight and BMI one year after surgery. IGP and GEPG significantly decreased after RYGP, BPD and BPBP, whereas they significantly increased after GB and SG. EGJ morphology changed only after GB, with 6 patients showing Type III morphology. EGJ-CI, IRP and DCI increased significantly ($p < 0.001$) only after GB. Hypercontractile and premature contractions waves were present in 40% of patients after GB, whereas ineffective motility (36%) waves were present after SG. "De Novo" GERD symptoms were observed in 1 SG and 2 GB. Postoperative greater AET ($p < 0.05$) and increased total number of reflux ($p < 0.001$) were present after GB and SG. RYGB and MGB showed a significant decrease in AET ($p < 0.05$) and total number of reflux ($p < 0.001$), whereas BIBP showed a non-significant reduction in AET and reflux events but similar to HVs patterns (Table 1).

Conclusion: HRM verified that different bariatric techniques produced different modification of IGP and GEPG, leading to different reflux exposure. Only GB and SG can negatively impact on esophageal function and reflux exposure, and they should be avoided in obese patients with pre-existing GERD.

Disclosure: Nothing to disclose

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Table 1: HRM and reflux features before and after bariatric surgery

Surgical Procedure	HRM EGJ Type	HRM EGJ pressure (mmHg)	HRM EGJ-CI (mmHg*cm)	HRM IRP	HRM IGP (mmHg)	HRM GEPG (mmHg)	MII-pH Total Reflux (n)
HV	Type I	32 (28–39)	4 (2–6)	6 (5–7)	6 (5–7)	5(3–7)	26 (18–40)
OBESE PRE-BIB	Type I	19 (17–22)	24 (20–28)	4.7 (2–8)	15.2 (13–18)	11 (9–14)	34 (25–51)
OBESE POST-BIB	Type I	19.2 (17.4–22.5)	24 (20–28.5)	5 (2–8)	14 (12–16)	10 (8–12)	30 (22–48)
OBESE PRE-LAGB	Type I 6 Type I 6 Type III*	24.1 (20.6–29)	26 (22–38)	5.4 (3–8)	14.5 (12–17.6)	10.4 (8–13.4)	30 (20–49)
OBESE POST-LAGB		40.1 (20.6–70)*	42 (28–82)*	17 (10–22)*	22 (19–29)*	13 (11- 16)*	64 (42–82)*
OBESE PRE- SG	Type I 25 Type I 1 Type II	21.3 (18.5–33)	24 (19–42)	6.5 (5.5–7.2)	14.8 (12.6–18.2)	10.1 (8.3–14)	33 (20–39)
OBESE POST-SG		22 (19–33)	23 (19–30)	6.3 (3.92–10.9)	18.8 (10.2–21.2)*	13.1 (10.7–15.1)*	53 (30–57)*
OBESE PRE-MGBP	Type I Type I	22.6 (20.8–27)	23 (18–37)	6.8(3.2–11-1)	15.5 (13.1–17.2)	10.3 (8.6–14.5)	41 (20–66)
OBESE POST-MGBP		23 (21.2–26.2)	23 (19–38)	6.5 (3.2–11)	9.5 (7.5–10.3)*	6.4 (4–8.1)*	7 (3–14)*
OBESE PRE-RYGB	Type I Type I	21.1 (19.8–25)	22 (18–31)	5.4 (2.1–9)	16 (14–19)	11.6 (9–13)	44 (23–68)
OBESE POST-RYGB		23.4 (20–25)	23(19.4–32)	5.2 (2–9)	9 (7–10)*	6 (4–8)*	3 (0–7)*
OBESE PRE-BPBI	Type I Type I	20.1 (16–25)	19 (18–22)	5.4 (2–10)	15.9 (13.7–17.9)	10.4 (8.9–15)	40 (21–62)
OBESE POST-BPBI		22.3 (18–28)	21 (20–23)	5.3 (2–10)	10.7 (8–12.4)*	8 (6–9.5)*	26 (12–35)*
OBESE PRE-DBP	Type I Type I	19.4 (16–23)	19 (17–24)	5 (2–9)	16.2 (14–19.3)	12 (10.2–17)	35 (20–55)
OBESE POST-DBP		19 (15.9–24)	19 (17–25)	5.1 (2–8.5)	12.3 (10–14)*	10 (7–11)*	32 (17–45)

*P < 0.05

P1149 ESOPHAGEAL DYSMOTILITY AND PREVALENCE OF EXPRESSION CD25 MARKER IN GERD PATIENTS

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Introduction: The modern understanding of gastroesophageal reflux disease (GERD) pathogenesis includes Th1/Th2 immune response imbalance that can be determined as phenotype of macrophages (M1 or M2). Studies using high-resolution manometry (HRM) with 22-channel water-perfused catheter have shown that esophageal motility disorders frequently occur in patients with gastroesophageal reflux disease (GERD).
Aims and Methods: The aim of the present study was to investigate the role of esophageal motility disorders and immune response in diagnosis GERD phenotypes. To determine correlation between esophageal motility disorders, immune response and diagnosis of nonerosive reflux disease (NERD), erosive reflux disease (ERD), Barrett's esophagus (BE). 68 patients with GERD were studied: 28 (14 men, 45.74 ± 2.23 yr) NERD, 22 (15 men, 45.0 ± 3.24 yr) ERD and 18 (13 men, 47.22 ± 2.95 yr) BE. All the patients were performed HRM with 22-channel water-perfused catheter (Solar GI MMS, The Netherlands). We analyzed distal contractile integral (DCI). Monocytes were isolated from the patients' blood samples and cultured to macrophages in standard conditions – RPMI1640 medium, 10% FBS, 37oC, 5% CO2. Pooled analysis of macrophage and monocyte derived macrophages included typical M1/M2 surface macrophage CD markers (CD25, CD80 and CD163, CD206, respectively) performed by flow cytometry (Beckman Coulter FC500). The statistical analysis was done using SPSS Statistics 17.0.
Results: In NERD patients median DCI was 991 [104;3759], in ERD – 570 [41;2462], in BE – 505 [0;1933] mm Hg *c*cm. DCI in NERD patients was significantly higher than in ERD and BE ($\chi2 = 2.81$, $p = 0.03$ and $\chi2 = 3.13$, $p = 0.076$, respectively). DCI in patients with BE tended to be lower than in patients with ERD, although without statistical significance. In NERD patients median expression of surface M1/M2 macrophage CD markers was CD25–37.2 [6.1;69.4], CD80–19.6 [2.8;49.3], CD163–15.7 [2.7;37.2], CD206–10.5 [0.4;21.6], in ERD was CD25–34.7 [13.1;59.6], CD80–22.8 [6.1;43.6], CD163–17.4 [0.6;37.2], CD206–12.6 [0.3;30.6], in BE was CD25–39.2 [16.3;67], CD80–21.9 [8.3;41.6], CD163–14.9 [18;34], CD206–8.9 [0.5;25.9]. We determined negative correlation between NERD and expression of CD25 ($P = -0.402$, $P = 0.001$) and positive correlation between BE and expression CD25 ($P = 0.338$, $P = 0.005$). In GERD patients there were no significant correlation between expression CD25 and DCI.
Conclusion: Analysis of monocyte derived macrophages phenotype showed the prevalence of expression CD25 marker in all groups patients that characterizes M1 pro-inflammatory activated macrophages (Th1). These results suggest that type of immune response may play a major role in the pathogenesis of esophageal inflammation in GERD. We observed that NERD patients have a significantly higher DCI than ERD and BE. Patients with BE had a lower DCI than patients with ERD. This study points to a clear association between esophageal dysmotility and GERD.
Disclosure: Nothing to disclose

P1150 CARDIAC ARRHYTHMIA AND GERD IN CHILDREN

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Introduction: Gastroesophageal reflux disease (GERD) is a digestive disorder that is caused by gastric acid flowing from the stomach into the esophagus. Prevalence of GERD in children ranges from 8.5% to 20% (Amy Wu, *Pharm D*, 2015). Among 1-year-old children the incidence is 1.48 per 1000 person-years, it increased to a maximum at 16–17 years of 2.26 per 1000 person-years for girls and 1.75 per 1000 person-years (A. Ruigómez et al, 2009).
Except typical esophageal complaints such as heartburn, acid regurgitation, dysphagia, pain behind the sternal bone, there are atypical (extraesophageal) symptoms in children with GERD (laryngitis, bronchoobstructive syndrome, sinusitis, chronic cough, heart rhythm disorders). Presence of heart rhythm disorders can be explained that inflammation of the esophageal mucosa affects local receptors that may induce afferent-efferent reflex mechanisms of the cardiac rhythm, which can lead to secondary stimulation of the vagal nerves (M Floria, V Liviu, 2015; Cuomo R, DE Giorgi F, 2016).
Aims and Methods: The aim of investigation is to determine the frequency of heart rhythm disorders in children with GERD.
82 patients with GERD within the age of 10–17 years were investigated. The diagnosis was established according to ICD -10 (K. 21, K. 21.9). Group I included 26 patients, who had GERD with esophagitis and group II included 56 patients who had GERD without esophagitis. Diagnosis was verified by upper endoscopy (with using the Los Angeles Classification of Oesophagitis). Electrocardiogram (ECG) was done for each patient.
Results: Sinus tachicardia was observed in 4 children (15.4%) with GERD with esophagitis (I group). It exceeded ($p < 0.05$) same parameters in children without esophagitis (II group) (2 persons; 3.6%). 3 children (11.5%) from group I and 2 children from group II (7.3%) had sinus bradycardia. There was no statistical difference in the indices of the study groups ($p > 0.05$). 3 children (11.5%) from group I had short PQ interval on ECG. It was higher ($p < 0.05$) than in children from group II (2 persons; 3.6%).
Conclusion: Frequency of disorders of rhythm is higher ($p < 0.05$) in children with GERD with esophagitis (14 persons; 53%) than in children with GERD without esophagitis (8 persons; 14.2%).
Frequency of sinus tachycardia and short PQ interval is higher ($p < 0.05$) in children with GERD with esophagitis than in children with GERD without esophagitis.
Disclosure: Nothing to disclose

P1151 EFFECT OF ADVANCED DIAGNOSIS MODALITIES AND DISEASE PHENOTYPES ON PPI RESPONSE OF GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: In Western countries, response rates for proton pump inhibitors (PPIs) are about 60–70% and higher in heartburn than regurgitation. The differences between response rates in phenotypes have not been adequately investigated. We evaluated PPI response rates of Barrett's esophagus (BE), erosive esophagitis (EE), nonerosive (NERD), esophageal hypersensitivity esophagus (EH) phenotypes and functional heartburn (FH), and success rates according to the different diagnostic techniques.
Aims and Methods: The aim of this trial is to investigate PPIs response rates of erosive, nonerosive (NERD), hypersensitive esophagus and functional pyrosis fenotypes that are diagnosed by only history, diagnosed by history and upper gastrointestinal endoscopy (UGE), diagnosed by history, UGE, esophageal monometry and 24 h intraesophageal pH-impedance. Patients were randomly chosen among the patients from the database of Ege University Reflux outpatient clinic who were on continue PPIs. Among 1233 patients, 510 patients who accepted to response phone survey were included. Exclusion criteria were medications which other than PPIs and influence the study, upper gastrointestinal surgeries, cholecystectomy, major comorbidity, pregnancy. Subjects were evaluated with a validated questionnaire consisted of 28 questions. Pollsters were medical school students who had been educated for face to face and phone interview techniques.
Results: 54 of those patients were diagnosed with only history. 151 patients were evaluated with history and UGE. 305 patients were underwent to UGE, HRM and 24 h intraesophageal MII-pH (off-PPI). Last group was classified into EE (117), NERD (94), EH (16), FH (58) BE (20). Response rate under 50% for either heartburn and/or regurgitation was accepted as unresponsive (Table). Cumulative response rates for heartburn and regurgitation were 85.3% and 82.2% respectively. When the effect of advanced diagnostic modalities on response rates for heartburn and regurgitation among phenotypes were evaluated, the highest rate was in history + UGE group (91.4%, 85.4% respectively).
Conclusion: We found a higher PPIs response rate than Western populations in all GERD patients. Response rate was not different in regurgitation compared to heartburn. When it is investigated according to the groups, response rate was highest in EE and lowest in EH and FH. Interestingly, response rates were similar between EE and NERD. It should be noted that these results were belong to a single/tertiary referral center with difficult to treat cases. Probably due to this reason, response rates of patients who were diagnosed by using all diagnostic modalities are lower than those who were diagnosed with only history and UGE.

	Erosive Esophagitis	NERD	Esophageal Hypersensitivity	Functional Heartburn
Heartburn	88%*	85.1%	68.8%*	72.4%
Regurgitation	87.2%*	84%	62.5%*	74.1%

[PPI responses according to groups ($p < 0.05$)]*
Disclosure: Nothing to disclose

P1152 THE NEW P-CAB X482 WAS SAFE, TOLERABLE AND PROVIDED 24H INTRAGASTRIC CONTROL, AFTER SINGLE ORAL DOSES IN HEALTHY VOLUNTEERS

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Introduction: Erosive GERD (eGERD), a subgroup within the GERD family, is a chronic disorder with prevalence in North America and Europe of more than 10%. Epidemiology data suggest a lower but increasing prevalence in Asia. Available PPIs have a mediocre effect in severe forms of eGERD leaving 20–40% of patients unhealed after 4–8 weeks. A new class of molecules, potassium-competitive acid blockers (P-CABs), represents a different mode of action and the PK profile may allow full acid control both day and night after a single dose. Animal studies of X842, a prodrug of linaprazan, show a slower uptake, lower Cmax and a longer plasma residence time, resulting in a prolonged control of intragastric acidity compared to the main metabolite linaprazan.

Aims and Methods: The first-in-man Phase 1 study of X842 in healthy volunteers comprised a Single Ascending Dose (SAD) part in which four subjects were included in each cohort. The primary objective was to determine the safety and tolerability of X842. The secondary objectives were to determine PK characteristics and PK/PD relationship of X842 and main metabolite. PD was assessed using an intragastric 24h pH-metry and sequential dose levels were tested. All available safety, tolerability, PK and PD data were reviewed prior to proceeding to the next cohort. The initial dose of X842 was 0.08 mg/kg. Standard safety assessments were applied. The Full Analysis Set (FAS) consists of all subjects who had received at least one dose of X842.
Results: X842 was safe and well tolerated. No serious or severe adverse events were reported. A clear dose-linearity was observed both for PK and for PD. Full control of 24h intragastric pH was obtained after a single dose of X842. Seventy-two minutes after administration of 2 mg/kg, the intragastric pH value presented as the mean of the 10 minutes median intervals was 4.5. The subsequent pH data showed 100% control of intragastric acidity. All means of the 10 minute median intervals for all four subjects showed pH >4 throughout the 24 h assessment time.
Conclusion: X842 was safe, well tolerated and provided full 24h intragastric pH control. The results warrant further investigations with X842 in patients with acid-related disorders.

X842 mg/kg	Cmax* ng/ml	AUC0-∞* h × ng/ml	t 1/2 * h
0.08	65.58	493.5	5.3
0.2	130.7	948.8	4.98
0.5	213.2	1493	9.15
1.0	518.8	4928	14.4
2.0	955.5	7994	12.1

*[n=4, *geometric mean]*
Disclosure: Authors are employees of Cinclus Pharma AG

P1153 HUMAN ESOPHAGEAL MUCOSA TOPICAL PROTECTION, IN VITRO EFFECT OF SULFATED POLYSACCHARIDE FROM MARINE ALGAE *GRACILARIA CAUDATE*

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Introduction: Intact esophageal mucosal integrity is important to prevent symptoms during gastroesophageal reflux events. Recently, we performed in vitro experiments in human esophageal mucosa, showing topical protectant effect of solutions containing alginates and cashew gum. *Gracilaria caudate,* a marine algae rich in sulfated polysaccharides, has shown some gastroprotective and antiinflammatory effects.
Aims and Methods: The present study aims to evaluate an in vitro topical protective effect of sulfated polysaccharide from *Gracilaria caudate* in esophageal biopsies obtained from patients with heartburn. We studied biopsies from patients with heartburn without erosions (n = 19), median age 42 years (range: 21–63, 6M:13F), and patients with esophagitis (n = 18), median age 47 years (range: 21–70, 7M:11F). Biopsies were mounted in mini-Ussing chambers to measure basal transepithelial electrical resistance (TER). The effect of mucosal exposure to acid solution (pH 2 + pepsin 1mg/ml, TDC 5mM) on TER was analyzed with and without pre-coating the mucosa with sulfated polysaccharide from *Gracilaria caudata* in different concentrations (0.1, 0.3 and 1%).
Results: Basal esophageal mucosal electrical resistance was significantly lower in biopsies from patients with esophagitis (TER = 114.4 ± 5.4 Ω/cm^2) compared to biopsies from patiets without erosion (TER = 163.2 ± 8.19 Ω/cm^2, $p < 0.01$). Pre-coated with sulfated polysaccharide from *Gracilaria caudate* (1%) significantly prevented acidic solution (pH 2+pepsin+TDC) induced TER drop in heartburn without erosions (unprotected = 27.21 ± 2.4%, protected 4.06 ± 4.08%, $p < 0.01$), but this effect was not observed in biopsies from patients with esophagitis (unprotected = 19.92 ± 1.7%, protected = 20.83 ± 3.50%).
Conclusion: Sulfated polysaccharide from *Gracilaria caudate* has an in vitro topical esophageal mucosal protectant effect in patients with NERD but not in patients with esophagitis. This finding suggests that degree of inflammation might influence topical protection, perhaps interacting with bio-adhesivity of the compound. The positive effect in patients with NERD should be further explored in development of a topical approach heartburn patients without esophagitis. Financial support: CAPES- Brazil, CNPq- Brazil.
Disclosure: Nothing to disclose

P1154 A PHASE 3, RANDOMIZED, DOUBLE-BLIND, MULTICENTRE STUDY TO EVALUATE THE SAFETY AND EFFICACY OF TAK-438 20 MG ONCE DAILY COMPARED TO LANSOPRAZOLE 30 MG ONCE DAILY IN PATIENTS WITH EROSIVE ESOPHAGITIS: RESULTS FROM A CHINESE SUB-COHORT

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Introduction: Acid suppression with proton-pump inhibitors (PPIs) is considered the standard treatment for erosive esophagitis (EE), despite inadequate treatment outcomes. Vonoprazan (TAK-438) belongs to the novel class of potassium-competitive acid blockers, which, unlike PPIs such as lansoprazole, reversibly inhibits the gastric hydrogen potassium enzyme ATPase responsible for gastric acid secretion, independently of pH. We conducted a phase 3, double-blind, multicentre study that demonstrated the non-inferior efficacy of vonoprazan 20 mg versus (vs) lansoprazole 30 mg in healing EE in non-Japanese Asian patients (pts) during 2, 4, and 8 weeks (wks) of treatment. In this sub-analysis we report the efficacy and safety of vonoprazan 20 mg vs lansoprazole 30 mg in healing EE in the Chinese sub-cohort.
Aims and Methods: Pts were aged ≥18 years with endoscopically-confirmed EE (Los Angeles [LA] classification grade A-D); proportion of pts with EE of LA classification grade C or D was planned to be ≥30%. Pts were stratified by baseline LA classification grade A/B vs C/D. Following a 28-day screening phase, pts were randomized 1:1 to receive vonoprazan 20 mg or lansoprazole 30 mg once daily for up to 8 wks. The primary endpoint was the EE endoscopic healing rate during 8 wks of treatment. The secondary efficacy endpoints were EE endoscopic healing rates during 2 and 4 wks of treatment. Assuming an 8-wk healing rate of 94.7% in both treatment arms, it was estimated that 240 pts per group would provide 90% power to establish non-inferiority with a 10% margin using a two-sided 95% confidence interval (CI). Safety endpoints included treatment-emergent adverse events (TEAEs).
Results: In the China sub-cohort a total of 143 pts received vonoprazan and 131 pts received lansoprazole treatment. Generally, baseline characteristics were comparable between arms (Table 1). The 8-wk EE healing rate was 92.0% with vonoprazan and 89.0% with lansoprazole (difference [95% CI]: 3.0% [-4.103, 10.092]); the non-inferiority of vonoprazan vs lansoprazole was therefore demonstrated. The 2-wk EE healing rate with vonoprazan (77.9%) also demonstrated non-inferiority to lansoprazole (72.0%) (difference [95% CI]: 5.9% [-4.572, 16.454]), as did the 4-wk EE healing rate with vonoprazan (83.9%) vs lansoprazole (83.5%) (difference [95% CI]: 0.5% [-8.442, 9.396]). In patients with baseline LA classification grade C/D, 2-, 4- and 8-wk EE healing rates were slightly higher with vonoprazan vs lansoprazole (63.5% vs 56.8%, difference [95% CI]: 6.6% [-12.991, 26.278]; 69.8% vs 68.9%, difference [95% CI]: 0.9% [-17.400, 19.245]; and 83.0% vs 77.8%, difference [95% CI]: 5.2% [-10.562, 21.044], respectively). TEAE rates were similar between the vonoprazan arm (44.8%) and lansoprazole arm (42.0%).
Conclusion: Findings demonstrated the non-inferior efficacy of vonoprazan vs lansoprazole in achieving EE healing at Wk 8 in this Chinese sub-cohort. Safety outcomes were similar between both treatment arms.

	Vonoprazan (n = 143)	Lansoprazole (n = 133)	Total (n = 276)
Age[a], years, mean (SD)	51.8 (13.7)	51.5 (12.5)	51.7 (13.1)
Males, n (%)	105 (73.4)	110 (82.7)	215 (77.9)
Weight, kg, mean (SD)	69.4 (11.0)	71.8 (11.7)	70.5 (11.4)
BMI, kg/m2, mean (SD)	24.6 (2.9)	25.1 (3.3)	24.9 (3.1)
Never smoked, n (%)	93 (65.0)	78 (58.6)	171 (62.0)
No alcohol consumption, n (%)	91 (63.6)	74 (55.6)	165 (59.8)
No caffeine consumption, n (%)	131 (91.6)	129 (97.0)	260 (94.2)
LA classification, n (%)			
Grade A/B	89 (62.2)	85 (63.9)	174 (63.0)
Grade C/D	54 (37.8)	46 (34.6)	100 (36.2)

[Table 1. Patient demographics and baseline characteristics (randomized set) [a]At the date of informed consent.]
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P1155 THE EFFICACY OF HANGESHASHINTO IN PATIENTS WITH PPI REFRACTORY GERD -RANDOMIZED, MULTICENTER EXPLORATORY STUDY

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Introduction: The proton pump inhibitors (PPIs) are used to the upper gastrointestinal disorder, such as heartburn, and belch in the patients with gastroesophageal reflux disease (GERD). However, some patients are incomplete response to PPI therapy in these symptoms. Hangeshashinto (HST), a traditional Japanese (Kampo) medicine, has been widely prescribed to relieve chemotherapy-induced diarrhea and stomatitis[1)] in Japan. One of the mechanisms of HST has been reported to have anti-inflammatory effect via inhibition of prostaglandin E_2 production[2)]. HST is used empirically for dyspepsia and heartburn, but has not been fully elucidated. Taken together, these reports and empirical use suggested that HST can be a promising agent for the upper gastrointestinal disorder patients. We investigated the efficacy of HST in patients with PPI refractory GERD.
Aims and Methods: We conducted the randomized, multicenter exploratory study for the efficacy of HST in gastroesophageal reflux disease (GERD) patient refractory to PPIs. All patients were diagnosed with GERD with a frequency scale for the symptoms of gastroesophageal reflux disease (FSSG) total score ≥ 8 following treatment with PPIs for a more than 4 weeks. Patients were randomly allocated to HST 7.5g/day with a standard-dose of rabeprazole10mg/day (HST group) or a double-dose of rabeprazole 20mg/day (PPI double-dose group).
The gastrointestinal symptoms were evaluated by FSSG and Gastrointestinal Symptom Rating Scale (GSRS). The primary endpoint was to determine the change in total score FSSG after 4 weeks treatment to estimate the difference between the two treatment groups. The secondly endpoint was the changes in GSRS, and also was assessed using the each symptom questionnaires prior to and 4 weeks following treatments. Additionally, the subpopulation analysis based on patient background factors was performed.
Results: Of a total 78 patients were enrolled in this study, 70 subjects of effective analysis (HST group 38, double-dose group 32) were examined. The change in FSSG total score was significantly improved after 4 week treatment in both groups. However, there were no significant differences between two groups. The total score FSSG was significantly decreased after 4 week treatment in both groups (HST group: from 19.5 ± 9.6 to 9.8 ± 7.6, $p < 0.001$, PPI double-dose group: from 16.3 ± 6.2 to 10.1 ± 7.1, $p < 0.001$). HST group was showed improvement of acid related dysmotility (ARD) score after 1 week treatment, meanwhile double-dose group showed a significant improvement effect of ARD three weeks after administration. There were no significant differences in the improvement degrees of GSRS scores between the two groups after 4 week treatment, but the GSRS score was significantly improved compared to pretreatment in both groups. By factor analysis for the change in the improvement degrees of FSSG score, it is found that having an abdominal symptom, a history of allergic and being treated with a combination of HST and standard dose PPI therapy were significant factors for decreasing FSSG score.
Conclusion: There is no difference in treatment of combination therapy (HST and standard dose PPI) and double dose PPI. However, these results suggest that combination therapy may be an effective therapeutic option for the treatment of PPI-refractory GERD patients, though detailed clinical study required to clarify clinical efficacy of the HST.
Disclosure: Nothing to disclose

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P1156 FARNESOID-X-RECEPTOR EXPRESSION HAS A PROTECTIVE FUNCTION AND EMERGES AS POTENTIAL TARGET TO PREVENT PROGRESSION FROM BARRETT ESOPHAGUS TO ADENOCARCINOMA

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Introduction: The main precursor condition of Esophageal Adenocarcinoma (EAC) is Barrett's Esophagus (BE). BE is mainly attributed to inflammation due to chronic reflux of gastric and bile acid. Risk of progression to EAC correlates with obesity and a western-style diet, which further affects the gut microbiome. In previous studies on our L2-IL-1ß (IL-1ß) overexpressing BE mouse model it was shown that treatment with bile acids, especially deoxycholic acid (DCA), accelerated tumorigenesis in the mice (1).
Aims and Methods: We are aiming to clarify the effect of bile acid exposure and the associated nuclear bile acid receptor Farnesoid-X-Receptor (FXR) in coherence with diet and gut microbiome on the development of BE and EAC. Thus, we analyzed cohorts of IL-1ß mice with & without FXR whole body knockout and with & without a high fat diet (HFD) through histology, gene expression and a characterization of the microbiome. Effects of an FXR agonist (obeticholic acid (OCA)) were analyzed on 3D organoid cells before testing on IL-1ß mice fed control (CD) or high fat diet (HFD). In organoids, mice and human patients, analyses including flow cytometry, 16s- sequencing, gene expression- and serum bile acid analyses were performed.
Results: Gene expression analyses demonstrate that FXR, a key regulator in bile acid-metabolic and inflammatory signaling, was upregulated in BE but downregulated in EAC in humans and mice. A germline knockout of FXR in IL-1ß mice accelerated malignant progression of BE with increased DNA damage, stem cell numbers and cellular dedifferentiation, suggesting a protective function of FXR in BE. Importantly, OCA, a selective FXR agonist, had a protective function and eliminated the toxic effect of DCA in organoids. In IL-1ß mice, resembling human western-style diet, high-fat diet (HFD) causes a change in the gut microbiome including distinct bile acid metabolizing bacteria and accelerates malignant progression, which correlates with changes in circulating bile acid levels in the serum. In these mice, OCA increases differentiation in the metaplastic tissue, suggesting it to suppress malignant progression. An ongoing analysis of the microbiome of the human study cohort will lead to a better understanding of the postulated coherences.
Conclusion: In summary we propose that the gut microbiome, which is altered by a HFD is partly metabolizing primary bile acids leading to altered bile acid metabolites in the blood. The nuclear bile acid receptor, FXR, on metaplastic BE cells seems to be an important player to regulate the inflammatory effects of bile acid exposure and the differential potential of progenitor cells at the gastro-esophageal junction, suggesting a protective function that could be activated through OCA treatment. Thus, we provide evidence for a novel mechanism how secondary bile acids accelerate esophageal carcinogenesis and how FXR activation could be used for preventive or therapeutic approaches in BE and EAC patients.
Disclosure: Nothing to disclose

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P1157 APPLICATION OF A SELF-ASSEMBLING PEPTIDE MATRIX PREVENTS ESOPHAGEAL STRICTURE AFTER CIRCUMFERENTIAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN A PIG MODEL

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Introduction: Circumferential endoscopic submucosal dissection (ESD) allows to treat large esophageal superficial neoplasia, however with high occurrence of severe esophageal stricture. In a previous work we demonstrated that the application of a prototype of self-assembling peptide (SAP) matrix on esophageal wounds after a circumferential-ESD delayed the onset of esophageal stricture in a porcine model (1). The aim of this work was to consolidate these results using the commercialized version of this SAP matrix, a short peptide "RADA16" (4 [Arg-Ala-Asp-Ala]), currently used as a hemostatic agent.
Aims and Methods: Eleven pigs underwent a 5 centimetres-long circumferential esophageal ESD under general anesthesia. Five pigs were used as a control group and six were treated with the SAP. In the experimental group, 3.5 ml of the SAP matrix were immediately applied on the ESD wound with a dedicated catheter. At day 14, an endoscopy and an esophagogram were realized. Animals were then euthanized and underwent necropsy with *en bloc* esophagectomy. Pathology with Hematoxylin Eosin Saffron coloration and immunohistochemistry with the use of Collagen I and III, and Alpha smooth muscle actin antibodies were performed.
Results: At D14, two animals in the treated group had an esophageal stricture without any symptom versus all animals in the control group who had a symptomatic stenosis (33 vs. 100%, $p = 0.045$). In the treated group, the mean esophageal diameter at day 14 was 9.5 ± 0.98 millimeters vs. 4 ± 0.6 mm in the control group ($p = 0.004$). Histologically, the neoepithelium was longer in the SAP treated group vs. the control group (3075 µm vs. 1155µm, $p = 0.014$). On immunohistochemistry, the staining of Alfa smooth muscle actin was significantly greater in the SAP treated group vs. the control group.

Conclusion: Apposition of a self-assembling peptide matrix immediately after a circumferential esophageal ESD reduced by 67% the occurrence of a stricture at day 14, by promoting re epithelialisation of the resected area.
The authors would like to thank 3D Matrix Europe for their material support.
Disclosure: Nothing to disclose

Reference

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P1158 INHIBITORY EFFECT OF HYDROGEN SULFIDE ON BARRETT'S ESOPHAGUS METAPLASIA DEVELOPMENT

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Introduction: Barrett's Esophagus (BE) is a premalignant condition occurring as gastroesophageal reflux disease (GERD) complication. GERD symptoms are observed in approximately 20% of the developed countries population. On the other hand, hydrogen sulfide (H_2S) has been shown to prevent gastric mucosa injury induced by NSAIDs, topical irritants or stress. However, the role of H_2S in the pathogenesis of BE has not been elucidated.
Aims and Methods: We investigated if the enzymatic pathway of H_2S biosynthesis is involved in the development of BE and if the treatment with H_2S precursor (L-cysteine) or donors (NaHS or GYY4137) prevents BE progression in vivo and in vitro. An anastomosis between the gastroesophageal junction and the duodenum on its anterior mesenteric border was created to induce mixed duodenogastroesophageal reflux in Wistar rats. Next, animals were treated daily for 8 weeks with water (vehicle), NaHS (0.1–20 mg/kg), GYY4137 (5 mg/kg), L-cysteine (1–50 mg/kg) or D,L-propargylglycine (PAG, 1–30 mg/kg), inhibitor of cystathionine-g-lyase (CTH). Esophageal lesions/metaplasia index (ELMI) was assessed macroscopically and microscopically using H&E and PAS staining. Esophageal blood flow (EBF) was measured by laser flowmetry. Expression of mRNA for proinflammatory iNOS and COX-2 was determined in esophageal mucosa by real-time PCR. H_2S production in esophageal mucosa was assessed using methylene blue method. CTH or CBS gene knock-outs were induced using CRISPR/Cas9 technique in human-derived non-neoplastic Barrett's epithelial cells (BAR-T), esophageal keratinocytes (EPC2) and squamous esophageal epithelial cells (HET-1A).
Results: Chronic reflux led to esophagitis, metaplasia, fall in EBF, and upregulation of iNOS, COX-2 and decreased H_2S production. NaHS and GYY4137 but not L-cysteine significantly decreased ELMI, mucus production, iNOS and COX-2 expression and increased EBF. PAG (15 or 30 mg/kg/day) increased ELMI, mucus generation, mRNA expression of iNOS, COX-2 and decreased EBF. CTH or CBS gene knock-out did not affect BAR-T, HET-1A and EPC2 viability.
Conclusion: We conclude that decreased H_2S production in esophageal mucosa exposed to GERD could be involved in the development of BE metaplasia. CTH/CBS genes are not essential for the maintenance of BAR-T, EPC2 or HET-1A viability. Treatment with NaHS or GYY4137 prevents BE development by the compensation of decreased H_2S production. This effect involves vasodilatory and anti-inflammatory properties of H_2S. [Funding source: National Science Centre, Poland (UMO-2016/23/D/NZ4/01913)].
Disclosure: Nothing to disclose

P1159 IMPROVING BARRETT'S SURVEILLANCE PRACTICE THROUGH THE USE OF PRAGUE CLASSIFICATION OR LENGTH OF BARRETT'S OESOPHAGUS – A RETROSPECTIVE STUDY IN A DISTRICT GENERAL HOSPITAL

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Introduction: Barrett's Oesophagus (BO) surveillance is recommended in the presence of columnar epithelium visible at or more than 1cm above the gastroesophageal junction (GOJ), with histological confirmation of intestinal metaplasia.[1] The risk of developing oesophageal adenocarcinoma in patients with BO supports the rationale for repeat endoscopic surveillance, with quadrantic biopsies taken for every 2 cm of BO as per the British Society of Gastroenterology (BSG) guidelines.[2] The Prague Classification was introduced in 2004 by the International Working Group as a standardized method of measuring and recording BO.[3] It has now become widely accepted as the universal standard.[1,4]
Aims and Methods: In this retrospective study we aim to assess whether implementation of compulsory basic data input of Prague Classification or length of BO improves adherence to the BSG guidelines for Barrett's surveillance. Data was collected from endoscopy reports from May to Sept 2014 (5 months). The list of patients were obtained from the Barrett's surveillance programme on the endoscopy reporting system "Unisoft". Prague classification or the length of Barrett's was implemented as compulsory basic data input for endoscopy reporting of BO in 2016 and a re-audit was conducted with data collected from Nov 2017 to May 2018 (5 months). Exclusion criteria were incorrect Prague classification used or no length of Barrett's documented. The two cohorts were not overlapping as the 2014 cohort would have been followed up for repeat endoscopy by 2016, whereas the second cohort commenced from Nov 2017. The length of BO, Prague classification and number of biopsies taken were obtained from each report. The endoscopy was deemed non-adherent to the guidelines if no reason was provided as to why quadrantic biopsies were not taken. The data was entered onto a Microsoft Excel 2010 spreadsheet and the Chi square test of Independence was applied.
Results: 174 reports were retrieved from 2014 of which 26 were excluded from the study. Of the 148 reports, 45% (66) adhered to the BSG guidelines. In the re-audit, 212 reports were collected, with 73 excluded. Of the 139 reports collected from 2017, 76% (106) adhered to the BSG guidelines. Thus, the implementation of compulsory basic data input of Prague classification, or length of Barrett's was found to correlate significantly with the correct number of biopsies taken ($p < 0.001$). Prague classification was documented in 68% (95) of the 2016 cohort and in none of the 2014 cohort. Potential confounding factors were the endoscopists' increased awareness of Barrett's surveillance after the first audit cycle which could not be measured.
Conclusion: This study found that the implementation of compulsory basic data input of Prague classification or length of Barrett's in reporting, significantly improves Barrett's surveillance[5, 6]. It is postulated that compulsory data input of Prague classification or length of BO, helps to assist the endoscopist's thought process of adhering to the guidelines. Therefore, adjustments to software used to document findings of Barrett's surveillance may help to improve adherence to the BSG guidelines and as a result the quality of surveillance.
Disclosure: Nothing to disclose

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P1160 MUCOSA-ASSOCIATED MICROBIOTA DIVERSITY SIGNIFICANTLY DIFFERS IN BARRETT'S ESOPHAGUS AND PROGRESSION TO ESOPHAGEAL ADENOCARCINOMA

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Introduction: Alterations in the human gut microbiome have been linked to health and disease including metabolic syndrome, autoimmunity, and IBD. In addition, microbes and their metabolic byproducts have been linked to gut neoplasia. We hypothesized that alterations in mucosa-adherent Barrett's microbiota could be a link to risk factors for neoplasia
Aims and Methods: We sought to detect significant differences in Barrett's esophagus (BE) with and without neoplasia and paired squamous mucosa associated microbiota. Taxa were considered one-by-one using a generalized linear model based on the negative binomial distribution and the log link function as designed by the functions of the R Bioconductor package edgeR. We identified 53 patients who were enrolled in an IRB-approved protocol for research biopsies (Normal controls-10, Intestinal metaplasia (IM) -10, Low-grade dysplasia (LGD) -10, High-grade dysplasia (HGD) -10, Esophageal adenocarcinoma (EAC)-12). Biopsies of the Barrett's, EAC and normal esophagus (3 cm cephalad) were obtained for mucosa-associated bacteria along with gastric secretions for 16S rRNA V4 DNA sequencing.

Results: We analyzed the microbe composition of paired mucosa-associated microbes comparing changes in bacteria in samples representing progression of disease from intestinal metaplasia to LGD to HGD to adenocarcinoma. We found significant increases in phyla Synergistetes, OP8, and Chlamydiae and significant decreases in the archaean Crenarchaeota ($p < 0.05$, FDR corrected). At the genus level, Pyramidobacter, Plesiocystis, Synergistes, and Paenibacillus were the microbes most significantly increased and Siphonobacter, Propionivibrio, and Sphingobacterium among those most significantly decreased. Overall the significant changes either up or down are in genera that represent $<10\%$ of the entire bacterial community.
Conclusion: There are significant changes in specific bacterial genera, both increased and decreased, in esophageal biopsies representing the presumed progression of Barrett's mucosa toward neoplasia. Further study will be needed to establish the biologic plausibility of the effects on the epithelium induced by these microbes that could contribute to protection from or induction of dysplasia.
Disclosure: Nothing to disclose

P1161 COMPUTER-AIDED DIAGNOSIS AND DEEP LEARNING IN THE EVALUATION OF EARLY BARRETT'S CANCER

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Introduction: The endoscopic detection and characterization of early Barrett's cancer can be challenging, especially for endoscopists with limited Barrett experience. The evaluation of Barrett's esophagus with the help of computer-aided diagnosis (CAD) may be a valuable adjunctive tool for endoscopists managing patients with Barretts esophagus. As of date, there is only limited experience in the use of deep learning for computer-aided diagnosis of early Barrett's cancer[1].
Aims and Methods: A CAD system was trained using deep learning and then tested for sensitivity and specificity using 33 endoscopic images of histologically confirmed early Barrett's cancer and 41 images of Barrett's mucosa without dysplasia. All endoscopic images were collected prospectively at the Klinikum Augsburg and included near-focus white light and narrow band Images. Early Barrett's cancer was limited to the mucosa or superficial submucosa (sm1 $\leq$ 500 µm). Histology was the gold standard with which the test results of the CAD system was compared. Training of the system included training patch generation, image augmentation, adjustment of a convolutional neural network, patch probability computation and finally image classification.
Results: After training of the CAD system, sensitivity and specificity was 97% and 88% for white light images and 94% and 80% for narrow band images respectively.
Conclusion: CAD can be trained to classify Barrett's cancer using a deep learning approach with excellent diagnostic performance. A much larger pool of images is needed to improve the ability of the CAD system. However, if developed further, CAD using deep learning could become a useful adjunctive tool for endosocpists in the evaluation of Barrett's esophagus.
Disclosure: Nothing to disclose

Reference

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P1162 THE IMPACT OF THE POLICY-PRACTICE GAP ON COST-EFFECTIVENESS OF BARRETT'S OESOPHAGUS MANAGEMENT

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Introduction: Oesophageal adenocarcinoma (OAC) incidence has increased dramatically over the last four decades. Barrett's oesophagus (BO) is the most important risk factor to develop OAC. Clinical guidelines recommend surveillance and, if there is an indication, endoscopic eradication therapy (EET) of BO patients. However, an important policy-practice gap exists between recommended and observed intervals for BO surveillance.
Aims and Methods: We aimed to determine how current practice of surveillance of BO patients in the Netherlands affects costs and benefits of the surveillance programme, compared to the recommended policy in the Dutch guideline. We used the Microsimulation Screening Analysis (MISCAN) model to simulate a 60-year-old Dutch BO cohort and evaluated 4 different surveillance strategies. In the first strategy, surveillance was simulated according to the Dutch guideline: non-dysplastic BO (NDBO) patients underwent surveillance every 3–5 years, low-grade dysplasia (LGD) patients every 6 months to 1 year, and patients with T1a, HGD, or persistent long-segment LGD received EET. The other three strategies simulated a more intensive surveillance strategy for either NDBO (every 2–3.5 years), LGD patients (every 3–6 months), or both in accordance with intervals observed in practice. For each strategy, we computed number of OAC cases, life-years gained, and costs. Also, we calculated the difference between Dutch guideline strategy and the more intensive strategies.
Results: In the Dutch guideline strategy, the costs for surveillance and treatment were €6.5 million per 1,000 patients, while 35 OAC cases (excluding T1a) were prevented (Table 1). The more intensive surveillance practice for NDBO, resulted in 26% higher costs (+€1.7 million) compared to the Dutch guideline strategy, while only 8 more cases (+23%) were prevented and 42 more (+19%) quality-adjusted life-years (QALY) were gained. The more intensive surveillance for LGD increased costs by a half million and prevented only 2 more OAC cases (+6%) resulted in gaining 4 more QALYs (+2%). In the more intensive surveillance practice for both NDBO and LGD, the costs increased by 37% (+€2.4 million) compared to the Dutch guideline strategy. Only 11 more OAC cases were prevented (+31%) and 51 more QLAYs (+23%) per 1,000 BO patients were gained. As a consequence, the incremental cost-effectiveness ratio of all these non-adherent strategies exceeded €40,000 per QALY compared to the Dutch guideline strategy.
Conclusion: Our findings indicate that the policy-practice gap in BO surveillance intervals leads to up to 50% higher costs for BO surveillance for less than 25% increase in QALY gained. The actual impact of the policy-practice gap in BO management is likely to be even higher, because other deviations from the guideline, such as adherence to the biopsy protocol, were not considered. It is important to develop incentives to eliminate this policy-practice gap so that the burden of BO management on health care resources can be reduced.

Strategy	Dutch guideline	More intensive for NDBO[1]		More intensive for LGD[1]		More intensive for NDBO and LGD[1]	
Prevented OAC cases	35	43	+8	37	+2	46	+11
Endoscopies	6,750	9,403	+2,652	7,355	+605	10,319	+3,506
Initial EET	111	135	+24	128	+17	159	+48
EET touch-ups	63	74	+11	71	+8	87	+24
Esophagectomy	12	14	+2	12	0	15	+3
Net cost (€)[2]	4.6 m	6.3 m	+1.7 m	5.1 m	+0.5 m	7.0 m	+2.4 m
LYG[2]	214	249	+35	218	+4	257	+43
QALY gained[2]	220	262	+42	224	+4	271	+51
ICER (€/QALY)[3]	N.A.	40,006		117,488		47,158	

ICER: incremental cost-effectiveness ratio, BO: Barrett's esophagus, OAC: oesophageal adenocarcinoma, HGD: high-grade dysplasia, LGD: low-grade dysplasia, LYG: life-years gained, m:million, ND: non-dysplastic, QALY: quality-adjusted life-years, EET: endoscopic eradication therapy. ICER: incremental cost-effectiveness ratio, BO: Barrett's oesophagus, OAC: oesophageal adenocarcinoma, HGD: high-grade dysplasia, LGD: low-grade dysplasia, LYG: life-years gained, m:million, ND: non-dysplastic, QALY: quality-adjusted life-years, EET: endoscopic eradication therapy 1. Difference of the results of these strategies and Dutch guideline strategy are presented in the second column. 2. All discounted by the annual rate of 3%. 3. Compared to the Dutch guideline strategy.
[Table 1. Results per 1,000 patients by surveillance strategy]
Disclosure: Nothing to disclose

P1164 THE LONG-TERM OUTCOME OF ENDOSCOPIC THERAPY IN ULTRA-SHORT BARRETT'S ESOPHAGUS WITH HIGH-GRADE DYSPLASIA AND EARLY ESOPHAGEAL CARCINOMA

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Introduction: According to current guidelines, endoscopically visible columnar metaplasia <1 cm does not qualify as Barrett's esophagus (BE). However, Barrett's neoplasia [high-grade dysplasia (HGD) and early esophageal adenocarcinoma (EEA)] is still encountered in many of these patients.
Aims and Methods: Our aim was to evaluate the long-term outcomes and safety of endoscopic eradication of Barrett's neoplasia in patients with ultra-short (US) BE. Data on patients with histology proven HGD\EEA undergoing endoscopic eradication was collected prospectively. Consecutive endoscopic resection (EMR) combined with radio-frequency ablation (RFA) were performed until endoscopic and histologic eradication of dysplasia and metaplasia was achieved.
Results: Between 2004 and 2017, 511 patients underwent endoscopic eradication for HGD\EEA, of which 83(16%) patients had an US ($\leq$1cm) segment of BE. Eighteen patients were found to have high-risk histological features and were referred for surgical consultation. In the remaining 65 patients, 71% had EEA and 29% had HGD. Complete eradication of neoplasia and intestinal metaplasia (IM) was achieved in 92%(60/65) and 74% (48\65) of patients, respectively. After a median follow-up of 9.9 months following the first negative endoscopy control, neoplasia recurred in 10% and IM in 6%. Esophageal dilation was required in 38.5% (median 3 dilations) at a median follow-up of 23 months.
Conclusion: Routine biopsies and surveillance is not recommended in BE less than 1cm in length. However, a significant proportion of our patients were found to have neoplastic BE within an US segment. In these patients, endoscopic therapy consisting of EMR and RFA was found to be highly effective and safe.
Disclosure: Nothing to disclose

P1165 HYBRID ARGON PLASMA COAGULATION IS SAFE AND EFFECTIVE FOR THE ABLATION OF DYSPLASTIC BARRETT'S OESOPHAGUS: INTERIM ANALYSIS OF A PROSPECTIVE STUDY

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Introduction: Endoscopic therapy is recommended for removal of dysplastic Barrett's oesophagus (BO) to prevent progression to oesophageal adenocarcinoma. Hybrid Argon Plasma Coagulation (HAPC) is an upcoming ablative technique, however, only limited data are available. HAPC can be performed using a standard electrosurgical unit that is available in most hospitals. It is therefore more widely available with reduced equipment cost compared to Radio Frequency Ablation.

Aims and Methods: The primary aim of this feasibility study is to assess efficacy of HAPC for ablation of dysplastic BO. The secondary aim was to assess adverse event rates.

This was a prospective single-arm study including patients with histologically confirmed low-grade dysplasia, high-grade dysplasia or T1a adenocarcinoma. Patients with a BO segment >13cm, previous oesophageal ablative therapy and presence of endoscopically visible abnormalities at initial treatment were excluded. Submucosal injection of a sodium chloride 0.9% fluid cushion followed by APC treatment using a flexible HAPC probe and ERBE waterjet™ was performed. HAPC therapy was performed at 8-week intervals until complete endoscopic removal of BO had been achieved upon inspection with high-resolution endoscopy and (virtual) chromoendoscopy. Biopsies were taken after eradication of BO. If BO was detected additional HAPC sessions were performed, to a maximum of 5 sessions. After each session adverse events were assessed by phone call at 24 hours and during follow-up visit in clinic 2 weeks post treatment. Patients underwent follow-up endoscopy after treatment at 3, 6, 12, 18, 24, 30, 42, 48, 54 and 60 months.

Results: In total 8 patients [75% male, mean age 66 +/− 6 years;] were enrolled. Currently, 3 patients have achieved histologically complete eradication after a median of 3 treatments (IQR 2–4 treatments). All patients tolerated the procedure well and BO was successfully eradicated using HAPC. None of the patients required the maximum number of 5 sessions at this stage. Five patients are currently being treated with HAPC sessions and are awaiting complete eradication. Median procedure time of all procedures was 12 minutes (IQR 5–18.5 minutes). No treatment-related complications or post-procedural adverse events have been reported to date.

Conclusion: Our interim analysis shows that HAPC is effective and safe for removal of dysplastic BO in a small patient group. Further data will follow on cost-effectiveness of this treatment that is more widely available to patients than the current standard of care.

Disclosure: Nothing to disclose

P1166 WIDE-FIELD ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE TREATMENT OF BARRETT'S ESOPHAGUS NEOPLASIA (WF-ESD)

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Introduction: The role of ESD on Barrett's esophagus (BE) neoplasia has been studied in some small series with suboptimal results, mainly due to positive lateral margins (LM). We started ESD for neoplastic BE on 2011. Due to early suboptimal results because of positive lateral margins (LM), we decided to perform wide-field ESD of Barrett's neoplasia from 2015. With the new approach resection is performed, as described for wide-field colorectal EMR, with wider (5–10mm) free margins, after careful BE assessment. Our aim was to evaluate the feasibility, safety and efficacy of wide field ESD (WF-ESD) for resection of BE neoplasia comparing it to conventional ESD (C-ESD).

Aims and Methods: Patients, tumors and ESD procedures characteristics were assessed, and a comparison between c-ESD with WF-ESD was performed. In order to reduce stricture risk, oral steroids were used in patients with more than 3/4 resection of all circumferential lumen of the esophagus. The primary outcomes were the rates of *en bloc*, R0 and curative resection rates. The secondary outcomes were the rates of negative LM and adverse events rate such as bleeding, perforation and stricture. This study was approved by the Stockholm Regional Ethical Committee and all patients were discussed in multidisciplinary conference before inclusion.

Results: In total, 72 consecutive ESDs of Barrett's neoplasia were performed in 57 patients in our center between 01.2011–12.2014 and 01.2015–03.2018. The mean age was 67.1 ± 9.9 vs 67.6 ± 10.1 and the male/female ratio was 13/6 vs 33/6, in c-ESD and WF-ESD, respectively ($p > 0.05$). The resected specimen size was 43.7 ± 26.0 vs 51.1 ± 24.4 and lesion size was 18.4 ± 19.1 vs 23.3 ± 17.7 in c-ESD and WF-ESD, respectively ($p > 0.05$). Considering primary outcomes, en-block resection rate was 91.3 vs 100% (21/23 vs 49/49), R0 resection rate was 69.6 vs 85.7% (16/23 vs 42/49), curative resection rate was 56.5 vs 73.5% (13/23 vs 36/49) in c-ESD and WF-ESD, respectively. Considering secondary outcomes, positive LM rate was 26.1 vs 4.1% (6/23 vs 2/49), adverse event rate including perforation and bleeding was 4.3 vs 8.3% (1/23 vs 4/48) and stricture rate was 26.1 vs 6.1% (6/23 vs 3/49) in c-ESD and WF-ESD with $p < 0.05$ for LM and stricture rate. All complications were managed endoscopically.

Conclusion: Wide-field ESD is associated with improved efficacy and good safety profile, with marked decrease in positive lateral margins. Moderate increase in curative resection is related with more advanced lesions treated with ESD in the second cohort as a consequence of technique's efficacy and safety, and considering high morbidity of the alternative treatment (surgery) in that setting.

Disclosure: Nothing to disclose

P1167 CLINICOPATHOLOGICAL FEATURES OF GASTRIC ADENOCARCINOMA OF THE FUNDIC GLAND TYPE ACCORDING TO COLOR AND MORPHOLOGICAL CLASSIFICATION

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Introduction: Gastric adenocarcinoma of fundic gland type (GAFG) is newly added as a special type cancer in Japanese classification of gastric carcinoma, the 15th Edition (1). GAFG is an uncommon variant of gastric adenocarcinoma which has a distinct clinicopathological, immunohistochemical, and endoscopic features (2–4). GAFG is defined by positive immunohistochemical staining for pepsinogen-I (a marker of chief cells) and/or H+K+-ATPase (a marker of parietal cells) and is not associated with *H. pylori* infection. Histopathologically, GAFG is classified into pure GAFG and gastric adenocarcinoma of fundic gland mucosal type (GAFGM) which exhibited differentiation toward gastric foveolar epithelium in addition to fundic gland differentiation and is suspected as an aggressive type of pure GAFG. Endoscopically, the most common features with white light image (WLI) were submucosal tumor shape, whitish color, dilated vessels with branching architecture and background mucosa without atrophic change (3). The most frequent features with magnifying endoscopy with NBI (ME-NBI) were indistinct line of demarcation between lesion and surrounding mucosa, dilatation of crypt opening, dilatation of intervening part between the crypts and microvessels without distinct irregularity (4). However, the color and morphological classification of GAFG has not been established, and the clinicopathological features of GAFG according to the classification have not been well investigated.

Aims and Methods: The aim of this study was to establish the color and morphological classification of GAFG and elucidate the clinicopathological features of GAFG according to the classification. A total of 40 patients with 46 GAFGs were retrospectively evaluated from January 2008 to December 2017. All GAFGs were classified into 4 types according to color and morphology, as follows: Type 1. whitish protruded type (n = 23), Type 2. whitish flat/depressed type (n = 12), Type3. reddish protruded type (n = 7), Type 4. reddish flat/depressed type (n = 4). We then compared them via a clinicopathological evaluation and endoscopic features which we have reported (3,4).

Results: All GAFGs were classified into 37 pure GAFGs and 9 GAFGMs, Type 1. (n = 23, 21: 2), Type 2. (n = 12, 11: 1), Type3. (n = 7, 3: 4), Type 4. (n = 4, 2: 2). The frequency of GAFGM was significantly higher in Type 3 (4/7) and Type 4 (2/4) than in Type 1 (2/23) and Type 2 (1/12) ($p < 0.01$). There were no significant differences between the 4 types in the following findings: location of lesion, method of treatment, depth of invasion, lymph node metastasis, proliferative activity, p53 protein overexpression, and H. pylori infection. The average of tumor size (8.7 vs. 7.3 vs. 10 vs. 23.8mm, $p < 0.05$) was significantly greater and the rates of lymphatic invasion (0/23 vs. 1/12 vs. 0/7 vs. 2/4, $p < 0.05$) was significantly higher in Type 4 than in other Types. Endoscopically, the frequency of dilated vessels with branching architecture in WLI (17/23 vs. 9/12 vs. 1/7 vs. 1/4, $p < 0.05$) and indistinct line of demarcation between lesion and surrounding mucosa in ME-NBI (16/17 vs. 9/11 vs. 2/6 vs. 2/3, $p < 0.05$) were significantly higher in Type 1 and 2 than in Type 3 and 4. Furthermore, the background mucosa with atrophic change was more often seen in Type 4 (2/4, $p = 0.05$).

Conclusion: The reddish GAFGs (Type 3 and 4) has higher frequency of GAFGM than the whitish GAFG (Type1 and 2), and present atypical endoscopic features. Additionally, Type 4 may have a high malignant potential, and background mucosa with atrophic change may be related to the tumor progression.

Disclosure: Nothing to disclose

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P1168 GASTRIC CANCER MORTALITY BY AGE, GENDER, AND BODY MASS INDEX

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Introduction: There is rare report for the effect of body mass index (BMI) on gastric cancer mortality. We evaluated gastric cancer mortality by age, sex, and BMI.
Aims and Methods: Patients with gastric cancer diagnosed from 2005 to 2013 in a single tertiary center were enrolled and followed up until December 2017. To evaluate gender-specific gastric cancer mortality by age and BMI, they were categorized. Age groups: <50yr, 50–60, 60–70, and ≥70yr. BMI groups by Asian-Pacific guideline; <18.5, 18.5–23, 23–25, 25–30, and ≥30 kg/m^2. Cox regression analysis using hazard ratios (HRs) and 95% confidence intervals (CIs) was performed to assess gender-specific mortality by age and BMI.
Results: A total of 6005 gastric cancer patients (4007 men and 1998 women) underwent ESD (n = 1056, 17.6%), gastrectomy with or without chemotherapy (n = 4529, 75.4%), or palliative chemotherapy only (n = 420, 7.0%). In adjusted analysis, mortality was higher in advanced stage (HR, 3.39; 95% CI, 3.16–3.67) and increased by aging (HR, 1.69; 95% CI, 1.57–1.82). Mortality was higher in low BMI (HR, 0.78; 95% CI, 0.72–0.84) and male sex (HR, 1.59; 95% CI, 1.36–1.85).
Conclusion: Gastric cancer mortality increased by aging and was higher in low BMI and male sex.
Disclosure: Nothing to disclose
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P1169 ENDOSCOPIC PREDICTION OF TUMOR INVASION DEPTH IN EARLY GASTRIC SIGNET RING CELL CARCINOMA

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Introduction: Signet ring cell carcinoma (SRC) is a poorly differentiated cancer of the stomach. Recent studies imply that early gastric SRCs can be well managed by endoscopic resection. Unfortunately, unlike differentiated cancers, the endoscopic features of early gastric SRCs have not been well studied. We not only evaluated the endoscopic features of early gastric SRC, but also the risk factors regarding submucosal (SM) invasion through this study.
Aims and Methods: The medical records of patients from 7 tertiary hospitals (Daejeon and Chungcheong province), who underwen surgery or endoscopic resection from January 2011 to December 2016, were reviewed to examine endoscopic findings and clinical data. The patients were divided into two groups (derivation group and validation group), in order to develop an endoscopic scoring system for SM invasion. Two endoscopists analyzed the endoscopic images separately.
Results: In total, 331 patients (129 patients, derivation group; 202 patients, validation group) were enrolled in the this study. In the derivation group, the risk factors for SM invasion, namely fold convergence, nodular mucosal change, and deep depression were risk factors of SM invasion determined by logistic regression analysis (OR = 3.4, 5.9, 6.0, p < 0.05). A depth-prediction score was created by assigning 1 point for fold convergence and 2 points for other factors. When validation lesions of 0.5 points or more were diagnosed as SM invasion, the sensitivity and the specificity were 76.8%-78.6% and, 61.6%-74.7%, respectively.
Conclusion: Fold convergence, nodular mucosal change, and deep depression are the risk factors for SM invasion in early gastric SRCs. Our depth prediction scoring system may be useful for differentiating SM cancers.
Disclosure: Nothing to disclose

P1170 CLINICAL SUBMUCOSAL INVASIVE GASTRIC CANCER: IS SURGERY THE ONLY OPTION?

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Introduction: The current standard treatment modality for clinical submucosal invasive (cT1b) gastric cancer is surgery. However, there are discrepancies in T staging between pre- and post-operative findings and especially in some cases of overestimation, patients may lose the opportunity to preserve the stomach.
Aims and Methods: The aim of this study is to analyze surgical outcomes of cT1b gastric cancer and to determine the favoring factors for endoscopic submucosal dissection (ESD).
From January 2010 to December 2014, we retrospectively reviewed 466 patients who underwent curative gastrectomy for cT1b gastric cancer with differentiated type histology and 3cm or less in diameter. According to final surgical pathologic results, two groups were classified: the group of patients whose pathologic results were qualified for ESD (ESD qualified group, n = 205) and the group of patients whose pathologic results were not suitable for ESD (ESD disqualified group, n = 261). The preoperative clinical characteristics were compared between two groups.
Results: Forty-four percent of the patients (205/466) who underwent gastrectomy for cT1b gastric cancer was qualified for the ESD; their size of endoscopic lesion tended to be smaller than 2cm (1cm < size≤2cm, odd ratio[OR] = 0.499, 95% confidence interval[CI] = 0.313–0.796, P = 0.003; size≤1cm, OR = 0.267, 95% CI = 0.144–0.495, P = 0.000) and located to the distal part of stomach (middle third, OR = 0.531, 95% CI = 0.279–1.010, P = 0.054; lower third, OR = 0.362, 95% CI = 0.206–0.637, P = 0.000). In addition, ESD qualified group showed significantly higher proportion of well-differentiated adenocarcinoma (OR = 0.565, 95% CI = 0.379–0.843, P = 0.005) in endoscopic biopsy. (Table 1)

	Odd ratio [OR]	95% Confidence interval [CI]	P-value
Endoscopic lesion size			
2cm < size ≤ 3cm	1		
1cm < size ≤ 2cm	0.499	0.313–0.796	0.003
size ≤ 1cm	0.267	0.144–0.495	0.000
Endoscopic location			
Upper third	1		
Middle third	0.531	0.279–1.010	0.054
Lower third	0.362	0.206–0.637	0.000
Pathology of endoscopic biopsy			
Moderate-differentiated adenocarcinonma	1		
Well-differentiated adenocarcinonma	0.565	0.379–0.843	0.005

[Table 1. Logistic regression analysis of favoring factors for endoscopic submucosal dissection]

Conclusion: Forty-four percent of the patients with cT1b gastric cancer who underwent gastrectomy had a chance to preserve the stomach by ESD. Factors such as smaller endoscopic size (≤ 2cm), distal tumor location (middle or lower third) and well-differentiated adenocarcinoma were the important clinical indicators for ESD in cT1b gastric cancer.
Disclosure: Nothing to disclose

P1171 THE CLINICAL CHARACTERISTICS AND THERAPEUTIC OUTCOMES OF NON AMPULLARY DUODENAL NEUROENDOCRINE TUMOR(NADNET): MULTICENTER, RETROSPECTIVE STUDY

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Introduction: Duodenal neuroendocrine tumors (DNETs) are rare tumors and found occasionally during upper endoscopic examination. The incidence of DNETs are increasing. However, the data regarding the treatment outcome are not sufficient.
Aims and Methods: The aim of this study was to evaluate the treatment outcomes of non ampullary DNETs which were resected endoscopically or surgically.
We searched medical records of patients diagnosed as non ampullary DNET from 2004 to 2017 in seven university hospitals. We analyzed clinical characteristics and compared therapeutic outcomes according to endoscopic lesion size and treatment methods retrospectively.
Results: We enrolled 50 non ampullary DNET patients who received endoscopic treatment and 11 patients who received surgical treatment. In endoscopically treated patients, the mean lesion size was 8.2 mm and surgical treatment group was 13.9 mm. En bloc resection, endoscopic complete resection and pathologic complete resection (CR) rate was 88%, 92 % and 50% respectively in endoscopic treatment group. Endoscopic treatment group was divided into 3 group (1–5mm, 6–10mm,≥11 mm). The pathologic CR rate was significantly low in the lesion size ≥ 11 mm (0%, p < 0.05). The lymphovascular invasion was significantly high

(33%, $p < 0.05$) in lesion size ≥11 mm in endoscopic treatment group. The pathologic CR of surgical treatment group was higher (90.9%) than endoscopic treatment group (50%) ($P < 0.05$).
Conclusion: In endoscopic treatment group, the group of lesion size ≥ 11mm had low pathologic CR rate and elevated risk of lymphovascular invasion. Surgical treatment was more effective than endoscopic treatment in lesion size ≥ 11mm.
Disclosure: Nothing to disclose

P1172 CLINICAL RISK FACTORS OF NON-CURATIVE RESECTION BY ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE PATIENTS WITH EXPANDED INDICATION OF INTESTINAL-TYPE EARLY GASTRIC CANCER (CT1), AN ANCILLARY ANALYSIS OF MULTI-INSTITUTIONAL, SINGLE-ARM, CONFIRMATORY TRIAL (JCOG0607)

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Introduction: The multi-institutional, single-arm, confirmatory trial (JCOG0607) showed excellent efficacy and safety of endoscopic submucosal dissection (ESD) for the expanded indication of intestinal-type early gastric cancer (GC)[1]. However, the proportion of non-curative resection (NCR) was as high as 32% of all resected lesions (152/469) for which additional surgeries were required. In order to reduce the proportion of NCR, it is important to improve the diagnostic accuracy of clinical factors of intestinal-type early GC. The aim of this ancillary analysis is to evaluate the clinical factors associated with NCR of ESD for intestinal-type early GC using the data from JCOG0607.
Aims and Methods: The major inclusion criteria of JCOG0607 were as follows: 1) histologically proven intestinal-type adenocarcinoma; 2) cT1aN0M0; 3) lesion without clinical finding of ulcer (cUL (-)) and >2 cm in size, or cUL (+) and ≤ 3 cm in size; 4) age 20–75. The NCR was defined as not meeting any of the following 4 criteria of complete curative resection (CCR): 1) pT1a without ulcer, pT1a with ulcer and ≤ 3 cm in size, or minute invasion to the submucosal layer (SM) (<500 μm) and ≤ 3 cm, 2) intestinal-type dominant with no presence of diffuse-type cancer cells in SM, 3) no lymphovascular infiltration, 4) negative vertical and lateral margin confirmed in the en block resected specimen. Excluding the 4 patients with multiple-fragments resection from the 470 patients enrolled in JCOG0607, we investigated clinical factors associated with NCR in each cUL (-) and cUL (+) groups using log-linear model.
Results: The subjects of this analysis were 260 patients with cUL (-) GC and 206 patients with cUL (+) GC. The incidences of NCR were 33.8% (88/260) in cUL (-) group and 29.6% (61/206) in cUL (+) group. In both groups, the most frequent reason that was not met the criteria of CCR was minute invasion to SM (<500 μm). For cUL (-) GC, a multivariable analysis demonstrated that clinical moderately-differentiated predominant histology (vs papillary or well-differentiated) and lower tumor location (vs upper) were independent factors significantly associated with NCR (histology, risk ratio (RR) 1.93, 95% CI 1.34–2.77; location, RR 0.57, 95% CI 0.34–0.97). Meanwhile, for cUL (+) GC, female (vs male) and >2 cm clinical tumor size (vs ≤ 2 cm) were independent factors associated with NCR (sex, RR 1.62, 95% CI 1.07–2.44; size, RR 1.78, 95% CI 1.22–2.58).
Conclusion: ESD should be applied carefully for the lesions with moderately differentiated adenocarcinoma and/or located in upper of the stomach body in case of cUL (-), and GC >2cm in size in case of cUL (+).
Disclosure: Nothing to disclose

Reference

1. Hasuike N, et al. *Gastric Cancer*. 2018; 21(1): 114–23.

P1173 USEFULNESS OF LINKED COLOR IMAGING FOR RECOGNITION OF EARLY GASTRIC CANCER AND ADENOMA —COMPARISON WITH WHITE LIGHT&INDIGO CARMINE&BLUE LASER IMAGING

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Introduction: Linked Color Imaging (LCI) is a novel color enhancement feature available by using LASEREO endoscopy systems (FUJIFILM Co., Tokyo, Japan), which can enhances the slight difference in mucosal color. Recently we reported that color enhancement of the diffuse redness in gastric mucosa by LCI mode was significantly useful for the diagnosis of active *H. pylori* infection. We expected that LCI facilitate the endoscopic recognition of early gastric cancer and gastric adenoma by enhancing its color difference between normal and atypical mucosa. Furthermore, light source of LCI consist of normal white light and short-wavelength narrowband light, which is used to obtain more detailed mucosal surface and microvessel patterns. Therefore, we expected LCI to facilitate the endoscopic recognition of early gastric cancer and adenoma by emphasizing its color difference as well as slight uneveness on the mucosal surface.
Aims and Methods: The aim of this study was to evaluate the usefulness of LCI for recognition of early gastric cancer and adenoma compared to conventional white light imaging mode (WLI), WLI with indigo carmine contrast (IC) and blue laser imaging bright mode (BLI-brt). We used LASEREO system with EG-L590ZW or EG-L600ZW endoscope (FUJIFILM Co., Tokyo, Japan). We retrospectively analyzed 84 lesions in 76 patients who were examined by all four imaging (WLI, IC, BLI-brt and LCI) before endoscopic submucosal dissection at Asahi University Hospital from June 2014 to March 2018. Both subjective and objective evaluation methods were adopted to quantify the recognition of early gastric cancer and adenoma. Subjective evaluation was performed by three endoscopists. Each lesion was assigned the recognition score (RS) from 3 (excellent visibility) to 0 (no visibility). Objective evaluation was performed with the L*a*b* color space-based color difference scores (CDS) between inside and outside of the lesion (40 × 40 pixels), which was calculated by using CIE76 formula (defined by commission internationale de l'éclairage, Vienna, Austria).
Results: The overall mean RS of LCI was significantly higher ($p < 0.01$) than that of WLI/IC/BLI-brt (2.41 ± 0.71 vs. $1.77 \pm 0.74/2.16 \pm 0.86/1.83 \pm 0.81$). The overall mean CDS of LCI was significantly higher ($p < 0.01$) than that of WLI/IC/BLI-brt (23.94 ± 9.53 vs. $14.38 \pm 7.53/18.54 \pm 8.61/14.73 \pm 7.94$). Subgroup analysis based on tumor type revealed that both RS and CDS of LCI for type 0-IIb or 0-IIc lesions (44 lesions) were significantly higher ($p < 0.05$) than those of WLI/ IC/BLI-brt. On the other hand, regarding type 0-IIa lesions or adenomas (40 lesions), both RS and CDS of LCI, as well as IC, were significantly higher ($p < 0.05$) than those of WLI, however, no significant difference was seen between LCI and IC.
Conclusion: The LCI mode was significantly useful for recognition of flat- or depressed-type early gastric cancer compared to WLI, IC, and BLI-brt.
Disclosure: Nothing to disclose

P1174 PROGNOSTIC VALUE OF NEUTROPHIL-TO-LYMPHOCYTE AND C-REACTIVE PROTEIN-TO-ALBUMIN RATIOS IN GASTRIC ADENOCARCINOMA

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Introduction: The natural history of different neoplasms is influenced by Inflammation, immunity and nutritional status. Asian studies have proven neutrophil-to-lymphocyte and C-reactive protein (CRP)-to-albumin ratios to be related with mortality in patients with gastric adenocarcinoma. This study aimed to investigate this relationship in Western patients.
Aims and Methods: Patients with gastric adenocarcinoma submitted to R0 resection surgery from January/2013 to December/2017 were included. The study consisted of: registration of neutrophil, lymphocyte, CRP and albumin values within 3 months before surgery; calculation of neutrophil-to-lymphocyte and CRP-to-albumin ratios; evaluation of their relationship with gender, age, tumor size, T, N, M, stage (TNM), presence of lymphatic, vascular and perineural invasion; evaluation of the relationship between these ratios and mortality.
Results: One hundred and twenty-seven patients with leukocyte formula (age 67.6 ± 12.4 years old, 52% male) were included, of whom 70 had preoperative CRP and albumin evaluation (age 70.5 ± 11.9 years old, 58.6% male). The average follow-up time was greater than 24 months.
The neutrophil-to-lymphocyte ratio and the number of neutrophils were unrelated to tumor characteristics and did not predict mortality ($AUC = 0.562$, $p = 0.327$ and $AUC = 0.470$, $p = 0.635$, respectively). The number of lymphocytes correlated with tumor size ($p = 0.005$). Based on the ROC curve analysis, it was established 1667 lymphocytes as a cutoff value, with shorter survival times in patients below this cutoff ($p = 0.003$).
CRP and CRP-to-albumin ratio correlated with tumor size ($p = 0.042$ and $p = 0.046$ respectively), with shorter survival times when CRP≥10.2 mg/L or CRP/albumin≥0.28 ($p = 0.002$ and $p = 0.003$, respectively). Albumin values were unrelated to the studied variables and had no value predicting mortality ($AUC = 0.606$, $p = 0.162$).
Conclusion: In this study, the number of lymphocytes and CRP were related to tumor size and survival in patients with gastric adenocarcinoma. There was no additional benefit in using neutrophil-to-lymphocyte and CRP-to-albumin ratios.
Disclosure: Nothing to disclose

P1175 DO AUTOIMMUNE COMORBIDITIES INCREASE THE RISK FOR NEUROENDOCRINE TUMOURS IN PATIENTS WITH AUTOIMMUNE ATROPHIC GASTRITIS? RESULTS FROM AN ITALIAN DUAL-CENTRE STUDY

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Introduction: Autoimmune atrophic gastritis (AAG) is an autoimmune condition that affects patients of all ages causing atrophy of the corpus-fundus mucosa of the stomach, with subsequent vitamin B12 and iron deficiency. AAG may be associated with a number of autoimmune disorders, namely type I diabetes mellitus, vitiligo, Hashimoto's thyroiditis, and Addison's disease. It has been hypothesised that the presence of concomitant autoimmune disorders may be associated with the development of type I neuroendocrine tumours (NET).
Aims and Methods: Aim of the study was to assess the prevalence of autoimmune disorders in relation to the development of NETs in patients with AAG diagnosed in two Italian tertiary referral centres for gastrointestinal disorders (Pavia and Aviano). Over the last twenty years, both centres consecutively enrolled and followed-up all patients diagnosed with AAG (corpus/fundus atrophy with antrum sparing and positivity to anti-parietal cells antibody, according to the Sydney-Houston classification). We therefore analysed the association of autoimmune disorders with the presence of NETs.
Results: Overall, 448 patients suffering from AAG (mean age 63 ± 16 years; F:M ratio 2.3:1) have been evaluated in the two centres. At least one concomitant autoimmune disorder was present in 244/448 patients (54.4%; mean age 60.3 ± 15 years, F:M ratio 2.4:1), whereas at least two autoimmune disorders were present in 51/448 (11.3%; mean age 62.4 ± 14 years, F:M ratio 1.9:1). The most common autoimmune disorders were as follow: 175/448 (39.1%) Hashimoto's thyroiditis, 45/448 (10.0%) connective tissue disorder, 32/448 (7.1%) type I diabetes mellitus, 24/448 (5.3%) vitiligo, 17/448 (3.8%) Grave's disease, 13/448 (2.9%) psoriasis and/or psoriatic arthritis, 11/448 (2.5%) coeliac disease, 10/448 (2.2%) rheumatoid arthritis. Moreover, 64/448 (14.2%) patients were also diagnosed with a neuroendocrine tumour, 39/448 (8.7%) of which at the time of diagnosis. The overall prevalence of NETs did not differ between patients with or without autoimmune comorbidities ($p = 0.685$), nor it was increased in patients with two or more concomitant autoimmune diseases ($p = 0.584$).
Conclusion: Over half of patients with AAG present at least one concomitant autoimmune disorder, namely thyreopaties, connective tissue disorders, type I diabetes mellitus, vitiligo, and rheumatic disorders. The presence of autoimmune comorbidities does not increase the risk of developing NETs. The not negligible proportion of NETs in our AAG cohort warrants a proper endoscopic follow-up.
Disclosure: Nothing to disclose

P1176 THE ROLE OF BIOPSY IN DETERMINING TREATMENT STRATEGY IN EARLY GASTRIC CANCER

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Introduction: A biopsy-based histologic diagnosis is a critical factor for determining treatment strategy in early gastric cancer (EGC). There were some studies about histological discrepancies between initial forcep biopsy and endoscopic resection (ER) pathology. However, there was no study to investigate the role of biopsy to determine treatment including ER and surgery in EGC.
Aims and Methods: The aim was to compare between histologic diagnosis from biopsy sample and final diagnosis from ER and surgical specimens. In addition, we tried to find predictive factors related to discrepancy. 1,043 patients with a biopsy diagnosis of gastric adenocarcinoma were treated by ER or surgery. To compare the histological discrepancy rate, we checked the histologic diagnosis from the biopsy sample and the final diagnosis from the ER and surgical specimen. Clinicopathologic characteristics were also analyzed.
Results: 44% of EGC patents were treated by ER, and 56% of EGC patients were treated by surgery. Among patients who received ER, subjects with histologic discrepancies (Group 1) was 10.3%. Subjects with differentiated EGC (D-EGC) based on biopsy and undifferentiated EGC (UD-EGC) on ER pathology was 84% of Group 1. Among them, curative resection (CR) was 33.3%, and non-curative resection (non-CR) was 66.6%. Subjects with UD-EGC on biopsy and D-EGC on ER pathology was 16% of Group 1, and all of them were diagnosed with CR. In surgery group, subjects with histologic discrepancy were 11.0%. Among histologic discrepancy group (Group 2), subjects with D-EGC on biopsy, and UD-EGC on pathology was 22.1%. All of them were included in beyond expanded indication (EI) for ER. Subjects with UD-EGC on biopsy and D-EGC on pathology was 17.4% of Group 2. Among them, patients who were diagnosed with absolute indication (AI) of ER was 13.3%, EI was 40%, and beyond EI of ER was 46.7% according to final pathology. In patients with D-EGC on biopsy and UD-EGC on final pathology (ER and surgery), age, size, tumor location in the upper-third segment of the stomach, and submucosal 2 invasion were significant predictive factors. Patients with this group were more likely to have elevated gross appearance, but did not reach statistical significance. In patients with UD-EGC on biopsy and D-EGC on final pathology (ER and surgery), elevated gross appearance of tumor was significant predictive factor.
Conclusion: In retrospective view, unfavorable treatment decisions were made in some cases due to histological discrepancies. There were patients who could be treated by ER, but had surgery. In contrary, there were patients whose initial treatment regimen should be surgery not ER. To determine the treatment strategy for EGC more properly, not only biopsy but also endoscopic characteristics should be considered especially for lesions with predictive factors.
Disclosure: Nothing to disclose

P1177 DEPTH DIAGNOSIS PERFORMANCE USING ENDOSCOPIC ULTRASOUND FOR EARLY GASTRIC CANCERS SUSPECTED FOR DEEP SUBMUCOSAL INVASION

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Introduction: Accurate assessment of depth of invasion in early gastric cancer (EGC) has critical importance when selecting appropriate endoscopic treatment for patients [1]. EGC of deep submucosal invasion (more than 500μm: SM2) should be treated by surgery, whereas EGC with only intramucosal cancer (M) or superficial submucosal invasion (within 500μm from the musclaris mucosa: SM1) should be considered for endoscopic resection (ER).
Aims and Methods: In this study, we evaluated the diagnostic accuracy of endoscopic ultrasound (EUS) to differentiate the M-SM1 and SM2 of EGC that had been initially suspected as SM2 by conventional endoscopic diagnosis.
We retrospectively reviewed electronic medical records, endoscopic and histological reports of 250 EGCs with a suspected endoscopic diagnosis of SM2 and subsequently had EUS between April 2008 and July 2017. We further retrospectively reclassified lesions into M-SM1 or SM2 by reviewing conventional endoscopy (CE) and EUS reports individually. A 20 MHz miniature probe was used for EUS examination with water filling method. Endoscopic findings such as location, morphology, size, estimation of depth by CE and EUS, and histological findings such as histological type of differentiation, an ulcer finding, and depth were evaluated. The histological staging was confirmed by the endoscopically or surgically resected specimens. Logistic regression was used to analyze the factors that affected the EUS diagnosis.
Results: Diagnostic sensitivity, specificity and accuracy of EUS in differentiating M-SM1 and SM2 lesions was 75.9%, 71.4% and 74.0% respectively, in comparison to CE which was 69.0%, 45.7% and 59.2% respectively. In the multivariate analysis, factors associated with under-estimation of depth of invasion by EUS was the anterior wall of the stomach ($p = 0.02$), whereas over-estimated lesions included the lesions with ulcer findings ($p = 0.05$).
Conclusion: The diagnostic performance using EUS was superior to that of CE of early gastric cancers suspicious for SM2 invasion. The lesion with ulcer findings or located anterior wall may lead to misdiagnosis in those lesions.
Disclosure: Nothing to disclose

Reference

1. Japanese Gastric Cancer Association. *Gastric Cancer* 2017.

P1178 CHARACTERISTICS, RISK FACTORS AND SURVIVAL OF MISSED GASTRIC CANCER: A MULTICENTRIC COHORT STUDY

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Introduction: Missed gastric cancer (MGC) at upper gastrointestinal endoscopy (UGE) is a poorly documented entity in Western populations.
Aims and Methods:
1. To assess the rate, predictors and survival of MGC.
2. To compare MGC and non-MGC and detect factors associated with negative UGE.
Retrospective-cohort study conducted at 4 tertiary Spanish hospitals. Gastric adenocarcinomas diagnosed between 2008–2015 were included. Patients referred for treatment from other centers ($n = 64$) or without follow-up ($n = 21$) were excluded. MGC was defined as a cancer detected within 36 months after a negative UGE for malignancy. Demographic, clinical, endoscopic, histological and survival data were recorded. Statistics: Unconditional binomial logistic regression and Kaplan-Meier with the log-rank test.

Abstract No: P1178
Table 1: Baseline characteristics. Initial negative endoscopy in MGC patients vs Diagnostic endoscopy in Non-MGC patients

	Initial negative endoscopy in MGC patients (n = 61)	Diagnostic endoscopy in Non-MGC patients (n = 1228)	Univariant (P values)	
Age years, (mean)	69.3	74.3	0.0007	OR = 0.96 (CI 95%: 0.94–0.98), p = 0.001
Male sex	60.6%	61.6%	0.88	
PPI therapy	78.7%	46.3%	< 0.001	OR = 5.72 (CI 95%: 2.9–11.1), p < 0.001
H. pylori infection	73.7%	62.3%	0.082	NS
Family history of gastric cancer	3.9%	7.6%	0.42	
Elective endoscopy	87.3%	86.6%	1	
High-definition	36.1%	40.7%	0.47	
Sedation	26.2%	33%	0.27	
Endoscopist experience (< 5 years)	24.6%	21%	0.5	

Results: 123,395 UGE were performed during the study period, and 1374 GC were diagnosed (1.11%). 1289 patients with GC were finally included in the analysis.
Mean age was 74.1 years (SD: 11.2) and 62% were males. Global MGC rate was 4.73% (61/1289, CI 95%: 3.7–6 %), without significant differences across centers (p = 0.23). Median time between negative UGE and MGC diagnosis was 13.1 months (range: 3.1–35.2). The median number of negative UGEs in MGC group was 1 (range:1–3). Gastritis (51%), intestinal metaplasia (41%), gastric atrophy (31%) and gastric ulcers (29.5%) were the most common findings at negative UGE. These ulcers were benign at histology and were not endoscopically monitored. Compared to confirmed malignant ulcers in Non-MGC group (n = 610), ulcers at negative UGE were smaller (median: 10 vs 30 mm, p = 0.02) and less frequently biopsied (median: 1 vs 3.5, p < 0.001).
At multivariate analysis, negative UGE was independently associated with younger age (OR: 0.96, p = 0.001), PPI therapy (OR: 5.72, p < 0.001), previous Billroth II surgery (OR: 5.2, p = 0.002) and absence of alarm symptoms (OR 0.21, 47.5% vs 78.5%, p < 0.001) (Table 1).
The gastric body (52.4%) and intestinal-type (55.6%) were the most common location and histological subtype of MGC, respectively, without differences with Non-MGC. Compared to Non-MGC, MGC were smaller (31 vs 41 mm, p = 0.04), more frequently flat-depressed (49.2% vs 29%, p = 0.003) and diagnosed at an earlier stage (Stage I-II: 47.4% vs 28.3%, p = 0.023). Overall 2-year survival rate was similar for MGC (34%) and Non-MGC (35.3%) (log-rank p = 0.59).
Conclusion: MGC is frequent and associated with poor 2-year survival.
Our study found independent factors associated with MGC and negative UGE that may be helpful for clinical practice.
High-quality UGE may help to reduce MGC incidence.
Disclosure: Nothing to disclose

P1179 PRETREATMENT PREDICTIVE VALUE OF BLOOD NEUTROPHIL/LYMPHOCYTE RATIO IN R0 GASTRIC CANCER RESECTABILITY

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Introduction: New parameters complementary to clinical TNM classification are needed to orient preoperatively about the possibility of a R0 gastric resection. Blood neutrophil/lymphocyte ratio (N/L) reflects the systemic antitumoral inflammatory response in patients and it has been related with post-operative survival in Asiatic studies. Nevertheless, there are few data concerning pretreatment predictive value of these N/L ratio and radical tumor resection
Aims and Methods: We aimed to analyse the potential predictive value of an elevated blood neutrophil/lymphocyte ratio (N/L) in relation to R0 tumoral resectability.
Observational retrospective study of 257 consecutive gastric cancers, without haematological diseases or neoadjuvant treatment. The optimal cut-off of N/L was: < 5 (ROC curves). Frequency of R0 resection was compared between the group of "normal" N/L ratio: < 5 vs "high" N/L ratio ≥ 5. Multivariate analysis (logistic regression, determining odds ratio (OR) and 95% confidence interval (CI95%) of R0 resectability was performed according to N/L ratio, with the following adjustment variables: preoperatory ASA (1–4), tumoral differentiation grade (well, moderate, poor, undifferentiated) and presurgical TNM stage.
Results: A radical R0 resection was performed in 139 gastric carcinomas (54.1%). A "high" N/L ratio was registered in 46 cases (17.9%). R0 resectability was higher in patients with a N/L ratio < 5: 59.7%, compared to patients with N/L ≥ 5: 28.6% [p < 0.0001; OR = 3.76; CI95% = (1.78–8.04)]. The relation between N/L ratio < 5 and the frequency of R0 resection was maintained in the multivariate analysis: [p = 0.017; OR = 3.46; CI95% = (1.25–9.59)], independently of ASA: [p = 0.004; OR = 2.44; CI95% = (1.33–4.49)], differentiation grade: [p = 0.020; OR = 1.71; CI95% = (1.09–2.67)] and presurgical TNM: [p < 0.0001; OR = 5.60; CI95% = (3.56–8.80)].
Conclusion: 1.- The presence of a "normal" N/L ratio < 5 at the diagnosis of a gastric carcinoma is significantly related with a higher frequency of R0 tumoral resection.
2.- In our series, this higher proportion of R0 resection is independent of presurgical ASA, tumoral differentiation grade and presurgical TNM.
Disclosure: Nothing to disclose

P1180 YOUNG AGE AND RISK OF LYMPH NODE METASTASIS IN DIFFERENTIATED TYPE-EARLY GASTRIC CANCER

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Introduction: Young patients with gastric cancer reportedly have a worse prognosis than older patients owing to delayed diagnosis and more aggressive tumor behavior. However, it is unclear whether this applies to early gastric cancer (EGC), for which endoscopic resection is indicated. We aimed to investigate the association between age and lymph node metastasis (LNM).
Aims and Methods: We identified 4,055 patients diagnosed with EGC of differentiated histology who underwent surgery. The association between age and LNM was examined using logistic regression for each T stage separately with adjustments for multiple covariates. We compared LNM rates for each of the Japanese Endoscopic Resection Guidelines criteria in younger (< 40 years) and older patients (≥40 years).
Results: The median number of lymph nodes examined was the same for T1a and T1b stages (n = 34). The median number of lymph nodes examined was not significantly different within T1a stage (P-value = 0.093), but within T1b stage, the number of lymph nodes examined was significantly different (P-value = 0.019), with the highest number between 50 and 59 years (median = 37), and the lowest number in the 20 to 49 and over 70 age brackets (median = 34). LNM rate and age were not significantly associated within each stage (P-values 0.269, 0.783 for T1a and T1b, respectively). Among patients fulfilling endoscopic resection criteria, the LNM rate in younger patients was lower than in older patients.
Conclusion: In differentiated-type EGC, young age at diagnosis was not associated with LNM rate. Therefore, endoscopic resection criteria for early gastric cancer can be applied to younger patients.
Disclosure: Nothing to disclose

P1181 PPI AND GASTRIC CANCER IN FUNCTIONAL DYSPEPSIA-BRIDGING THE GAP BETWEEN SCIENTIFIC EVIDENCE AND CLINICAL PRACTICE

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Introduction: PPIs are commonly prescribed for a long period of time. Therefore, the long-term safety issue was raised. There are some adverse events including: bone fractures, enteric infections, community-acquired pneumonia and nutritional deficiencies. As PPIs inhibit acid production atrophic gastritis could be worse, a precursor of gastric adeno-carcinoma. Two recent wide health database reports reported a higher risk for gastric cancer (GC) among PPIs long term user (HR 2.44, SIR 3.38) which increased with the duration of PPIs use (1,2). PPIs were proved to be more effective than placebo for the improvement of symptoms and quality of life in Functional Dyspepsia (FD), Epigastric Stress type.
Aims and Methods: We aimed to bridge the gap between evidence and decision making by formulating a decision analysis model focusing on patients with FD

treated by PPI), to address the question whether the improvement in quality of life rationalizes continuity of the PPI treatment despite the risk of GC.
Markov model consisted of an initial decision regarding treatment with PPI, or any other treatment for FD. Patients who initially received PPI or not could developed GC, but the rate in patients who received PPI is greater (HR between 3 to 10). We considered only patients that PPI had a relief with their symptoms and improved quality of life. The primary outputs of the model included life-years (Lys) and quality- adjusted LYs (QALYs). Patients who developed GC were stratified by prognostic stage group to Markov states in the model. The overall mortality rate was derived from the Kaplan-Meier overall survival (OS) curves. The health states of gastric cancer was assigned a health utility score based on quality-of- life data in the CEA Tufts database. The utility value related to the quality of life regarding the dyspepsia without PPI and the improvement using PPI, was tested with sensitivity analysis over a large range of values (patient preferences). A series of sensitivity analyses were performed to evaluate the robustness of the model and address uncertainty in the estimation of model parameters.
Results: The base case model results showed that the use of PPI compared with placebo, resulted in a gain of 2.09 QALY. Univariable sensitivity analyses demonstrated that the most influential variable was: ''Percentage Increasing of Utility with PPI'' followed by the age of the patients and time horizon. For a greater increasing of improvement with PPI more than 0.8%, the use of PPI is better than placebo strategy. For older patients the benefit of PPI is less than for younger patients.
As the comparison between improvement in quality of life and the burden of GC is not equal in all people, we created a calculator which enable to receive a more personalized and accurate decision in such patients with FD.
Conclusion: We found that it is important to discontinue the usage of PPI when there is no improvement in symptoms. However, when there is even small improvement in the quality of the patient's life it is almost always justified to continue the PPI treatment.
Disclosure: Nothing to disclose

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P1182 GENDER- AND SITE-SPECIFIC EFFECT OF METABOLIC COMPONENTS ON DE NOVO GASTRIC CANCER: A NATIONAL POPULATION-BASED STUDY OF 5.49 MILLION KOREANS

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Introduction: Although meta-analysis suggested different effect of body mass index (BMI) on gastric cancer by site, the effect of metabolic components on gastric cancer in general population was rarely reported. We investigated the gender-specific effect of metabolic components and BMI on de novo gastric cancer.
Aims and Methods: This population-based study included subjects who underwent national endoscopic screening and general health examination from March 2011 to December 2011. Data regarding BMI, glucose, high-density lipoprotein (HDL), and age were extracted from the National Health Insurance Service databank and categorized. Adjusted regression analysis was performed to evaluate the risk of de novo gastric cancer using odds ratios (OR) and 95% confidence intervals (CI). Sub-analysis by gender and gastric cancer site was performed.
Results: Gastric cancers were detected in 10,417 subjects in 5.49 million subjects (2.43 million men). In the adjusted analysis, low BMI (<18.5; OR, 1.37; 95% CI, 1.29–1.52), high fasting glucose (≥ 127; OR, 1.28; 95% CI, 1.20–1.36), and low HDL (OR, 1.41; 95% CI, 1.35–1.48) increased gastric cancer. In gender-specific analysis, low BMI increased gastric cancer in men but not in women. High fasting glucose and low HDL had a constant association with gastric cancer in both genders. The effect of most factors on non-cardiac gastric cancer was similar to that on overall gastric cancer. The effect of low HDL (OR, 1.90, 95% CI, 1.34–2.71), high glucose (OR, 1.50; 95% CI, 1.06–2.11), aging, and gender (OR, 3.28; 95% CI, 2.09–5.14) on gastric cancer was more prominent in cardiac cancer than in non-cardiac cancer. Family history, smoking and drinking status was strongly associated with non-cardiac cancer, wherein they had no association with cardiac cancer.
Conclusion: Low BMI, hyperglycaemia, and low HDL independently increased gastric cancer in a large general population. Contributing factors were different by gender and gastric cancer site.
References: This project was funded by the National R&D Program for Cancer Control, Ministry of Health & Welfare, Republic of Korea (1631100) and the National Research Foundation, Republic of Korea (NRF-2015R1D1A1A01059219).
Disclosure: Nothing to disclose

P1183 SARCOPENIA AS AN INDEPENDENT PROGNOSTIC FACTOR FOR SURVIVAL AND PERIOPERATIVE COMPLICATIONS IN PATIENTS WITH GASTRIC CANCER

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Introduction: Patients with cancer often show signs of malnutrition, which might influence morbidity and mortality while undergoing chemotherapy or surgical treatment. The tolerability of perioperative chemotherapy in patients with gastric cancer is often limited.
Aims and Methods: To evaluate the influence of sarcopenia in patients with locally advanced, not metastasized, gastric or gastro-esophageal junction (GEJ) cancer undergoing curative treatment (perioperative chemotherapy and surgery) on morbidity and mortality in order to identify patients in need for nutritional intervention.
Methods: Retrospective study, conducted in two hospitals (Universitätsklinikum Frankfurt and Krankenhaus Nordwest) as part of the University Cancer Center Frankfurt (UCT). A large proportion of the patients were treated in the FLOT trial (NCT01216644). Patients charts were reviewed for the following items: age, sex, tumor type, histology, TNM stage, treatment, Clavien-Dindo-Score, BMI, survival data. Two consecutive CT scans were retrospectively analyzed to determine the degree of sarcopenia. For this, mean total muscle area (TMA) was measured at L3 and set in relation to body height, resulting in the skeletal muscle index, SMI. SMI = TMA [cm^2]/height [m^2]. Sarcopenia was defined as follows: male patients: BMI <25: SMI <43 cm^2/m^2; BMI ≥ 25: SMI < 53 cm^2/m^2; female patients: SMI <41 cm^2/m^2 (regardless of the BMI). Survival was calculated using the Kaplan-Meier method, multivariate analysis was performed using the Cox regression.
Results: 60 patients (72.3%) were male and 23 (27.7%) female. 45 patients (54.2%) had GEJ type 1–3 and 38 (45.8%) gastric tumors, respectively. Sarcopenic patients were significantly older than non-sarcopenic patients (mean age 65.1 years vs. 59.5 years, $p = 0.041$), terminated the chemotherapy significantly earlier (50% vs. 22.6%, $p = 0.037$) and showed higher Clavien-Dindo scores, indicating more severe perioperative complications (score ≥ 3 43.3 vs. 17.0%, $p = 0.009$). Sarcopenic patients had a significantly shorter survival than non-sarcopenic patients (139.6 [95% CI, 101.3–177.9] vs. 206.7 [95% CI, 179.5–233.8] weeks, $p = 0.004$). Cox regression analysis did not reveal factors influencing survival other than sarcopenia.
Conclusion: Sarcopenia is present in a large proportion of patients with locally advanced gastric or GEJ cancer and is an independent prognostic factor for survival. Besides, it significantly influences tolerability of chemotherapy and surgical complications.
Disclosure: TG acts as consultant, served on the speakers bureaus and/or received travel grants from Lilly, MSD, BMS, Celgene, Shire, Bayer and Servier. SEAB has an advisory role with Merck, Roche, Celgene, Lilly, Nordic Pharma, Bristol-Myers Squibb and MSD Sharp & Dohme; is a speaker for Roche, Celgene, Lilly, Nordic Pharma, AIO gGmbH, MCI, promedicis, and Forum für Medizinische Fortbildung; He is CEO/Founder of IKF Klinische Krebsforschung GmbH and has received research grants from Sanofi, Merck, Roche, Celgene, Vifor, Medac, Hospira, Lilly, German Cancer Aid (Krebshilfe), German Research Foundation and the Federal Ministry of Education of Research. All other authors declare no conflict of interests.

P1184 HOXC10 DIRECTLY REGULATED BY MIR129-5P CAN MODULATE WNT SIGNALING PATHWAY IN GASTRIC CANCER: CCND1 IS A CRUCIAL TARGET GENE

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Introduction: HOX genes are highly conserved at the genomic level and have been well-described as important players in regulating numerous processes including differentiation, receptor signaling, motility, apoptosis, angiogenesis, and metastasis.HOXC10 is a member of the HOX gene family and has been found to function as oncogenes in the progression of many cancers, thus it might be useful as a marker for cancer diagnosis or prognosis. We have previously found that HOXC10 is up-regulated in gastric cancer and functions as a candidate tumor promoter, whose high expression indicates poor survival outcome. However, the potential regulatory network of HOXC10 remains less understood.

The WNT signaling pathway is well known for its role in controlling cellular processes such as proliferation, differentiation, and apoptosis. In the nucleus, β-catenin associates with TCF/LEF transcription factors to drive expression of WNT target genes, such as CCND1,CD44, c-MYC and MMP7.
Small, noncoding microRNAs (miRNAs) are important posttranscriptional regulators of gene expression, with each miRNA predicted to regulate hundreds of mRNA target genes. MiR-129 family members were reported to be down-regulated in gastric cancer cells and play important roles in regulating cell proliferation in gastric cancer.
Aims and Methods: The aim of this study is to determine the potential regulatory network of HOXC10 in gastric cancer. As HOXC10 is an important transcription factor, ChIP-seq assay was performed firstly. Bioinformatic analyses, such as Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG) were used to investigate the molecular mechanism affected by the target genes of HOXC10. Additionally, the potential miRNAs targeting HOXC10 were investigated through miRanda, pita, RNAhybrid and targetSCAN. Reverse transcription polymerase chain reaction (RT-PCR) and western blotting were utilized to measure mRNA and protein expression, respectively.
Results: According to ChIP-seq assay, we found a variety of genes involved in the development of gastric cancer. Through KEGG analyses, these target genes may be involved in many cancer-related signaling pathways. We focused on the Wnt signaling-related genes and found down-regulation of HOXC10 significantly influenced mRNA expression including CCND1, CD44, CCND2, MMP7,CREBBP, especially the downregulation of CCND1. Meanwhile, HOXC10 also modulated the phosphorylation of β-catenin but not its total protein levels, which can also influence the expression of CCND1. Positive correlations were found between CCND1and HOXC10 ($r = 0.13$, $P < 0.01$) based on TCGA database. Besides, combined with miRanda, pita, RNAhybrid and targetSCAN analyses, 130 miRNAs were predicted to target HOXC10. We verified that miR-129-5P can significantly decreased mRNA expression of HOXC10, thereby down-regulating CCND1 expression in two ways.
Conclusion: HOXC10 may be an important direct target of miR-129-5P and play a significant role in gastric cancer by regulating various pathways, particularly the Wnt signaling pathway.CCND1 is found to be a crucial target of HOXC10.
Disclosure: Nothing to disclose

P1185 OVEREXPRESSION OF CD44V9 IN GASTRIC CANCER CELLS CONFERS RESISTANCE TO TRASTUZUMAB BY INDUCING ANTIOXIDANT ENZYMES

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Introduction: Cancer stem cells play a role in tumour recurrence, cell proliferation, invasion, and resistance to therapy. CD44 variant 9 (CD44v9), one of the variant isoforms of CD44, is a specific cell surface marker of cancer stem cells. CD44v9 increases expression of the antioxidant glutathione (GSH) via stabilising xCT, a glutamate-cysteine transporter, which provides resistance against reactive oxygen species (ROS). Trastuzumab, a recombinant monoclonal antibody against HER2, has been shown to selectively exert anti-tumour effects in advanced gastric tumours that overexpress HER2. However, trastuzumab-based therapy is not effective in certain patients. The present study was conducted to investigate how CD44v9 regulates the anti-tumour effects of trastuzumab.
Aims and Methods: NCI-N87, a high HER2-expressing gastric cancer cell line, was used for this study. The pRc/CMV expressing plasmid encoding human CD44v9 and standard CD44 (CD44s) was transfected into NCI-N87 cells (NCI-N87-CD44v9 and NCI-N87-CD44s). Cells were incubated for 48 h with different concentrations of trastuzumab and cell viability was evaluated by the MTS assay. Intracellular GSH levels were measured by a luminescence-based assay. Intracellular ROS was detected using an oxidation-sensitive fluorescent probe (DCFH-DA) while mitochondrial ROS was assessed by staining with MitoSOX followed by confocal microscopy. Protein expression was determined by western blot analysis.
Results: Trastuzumab (10, 50 and 200 μg/ml) caused death of NCI-N87 cells (19.7%, 27.3%, and 37.8% cell death, respectively) and NCI-N87-CD44s cells (16.2%, 20.3%, and 27.8% cell death, respectively). However, efficacy of trastuzumab was attenuated in NCI-N87-CD44v9 cells (13%, 16%, and 17.1% cell death at 10, 50, and 200 μg/ml of trastuzumab, respectively). Trastuzumab increased intracellular ROS levels in NCI-N87 cells and NCI-N87-CD44s, but not in NCI-N87-CD44v9. Trastuzumab also increased mitochondrial ROS responses. The intracellular GSH levels were significantly higher in NCI N87-CD44v9 than in NCI-N87 (2.59-fold; $p < 0.01$) and NCI-N87-CD44s (1.38-fold; $p < 0.01$). The expression of MnSOD, a mitochondrial ROS scavenging enzyme, was significantly higher in NCI N87-CD44v9 than in NCI-N87 (2.78-fold; $p = 0.04$). In addition, *MnSOD* siRNA-treated NCI-N87-CD44v9 reacquired sensitivity to trastuzumab ($p < 0.01$).
Conclusion: CD44v9 positive gastric cancer cells attained trastuzumab resistance via attenuation of ROS accumulation, which was caused by an increase in the antioxidants GSH and MnSOD. Targeting cellular antioxidant enzymes could enhance the efficacy of trastuzumab against CD44v9 positive gastric cancer cells.
Disclosure: Nothing to disclose

P1186 PLASMATIC AND MUCOSAL EXPRESSION OF MICRORNAS ALONG THE GASTRIC CARCINOGENESIS CASCADE

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Introduction: Gastric carcinogenesis comprises the sequential progression from normal mucosa, atrophic or metaplastic gastritis, dysplasia to adenocarcinoma. MicroRNAs (miRNAs) are non-coding RNAs capable of epigenetic DNA regulation, whose role in gastric carcinogenesis is not fully established.
Aims and Methods: We aimed to characterize plasma and tissue expressions of different miRNAs for different stages of gastric carcinogenesis.
Single-centre cross-sectional study in patients who underwent upper gastrointestinal endoscopy ($n = 42$), who were classified in 3 groups: 14 with normal mucosa (control group); 13 with extensive atrophic/metaplastic gastritis and 15 early gastric neoplasia. In each patient, peripheral blood samples and endoscopic biopsy samples from the antrum, corpus and superficial lesion (if present) were collected. Seven miRNAs (miR-21, miR-146a, miR-181b, miR-370, miR-375 e miR-490) and an endogenous control (RNU-6B) were extracted and quantified in these samples through relative quantification by real time-PCR.
Results: We found a significant decrease in the mucosal expression of miR-146a e miR-370 between the control and metaplasia groups (86% reduction, $p = 0.018$ and 98% reduction, $p = 0.003$, respectively) and between normal gastric mucosa and superficial lesions (71% reduction, $p = 0.02$ and 66% reduction, $p = 0.027$, respectively). MiRNA-181 showed a tissue expression 44 times greater in the superficial lesion group versus control group ($p < 0.001$) and there were no significant differences between controls and gastric metaplasia. In patients with neoplasia, there were no significant differences in miRNA expression between lesion samples and normal antrum and corpus mucosa. We found no statistically significant differences in the plasmatic miRNA expression of the seven miRNAs between the different groups and no association with their tissue expression.
Conclusion: We found significant changes in tissue expression of several miRNAs across the different stages of gastric carcinogenesis, suggesting a tumor suppressor role for miRNAs such as miR-146a and miR-370 and oncogenic potential for miRNA-181 in gastric carcinogenesis pathways. In individuals with early neoplasia, these changes appear to happen diffusely in the gastric mucosa, which may have implications in these patients' surveillance.
Disclosure: Nothing to disclose

P1187 POLYMORPHISM *-511C/T (RS16944)* OF THE IL1B GENE AND LOW LEVEL OF PGI REPEATEDLY INCREASE GASTRIC CANCER RISK: SIBERIAN PROSPECTIVE CASE-CONTROL STUDY

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Introduction: Data on the association of IL1B gene polymorphism with gastric cancer (GC) risk are quite contradictory. Low serum level of pepsinogen I (PG) and PGI/PGII ratio is detected in atrophic gastritis (AG), including *Helicobacter pylori (H. pylori)* associated and being the main precancerous lesion.
Aims and Methods: We aimed to study the influence of polymorphism -511C/T (rs16944) gene IL1B and low levels of pepsinogens on the GC risk in a prospective case-control study (8 years of prospection).
In the period 2003–2005 within the framework of the international project HAPIEE the population sample of Novosibirsk residents (9360 people aged 45–69 years) was studied and the base of biomaterials was created. Serum and DNA samples were stored at -70^0C. In 2012 this database was compared with the data of the population cancer register. For each GC case in the 1:2 ratio the corresponding age-and sex-control was chosen. As a result, 156 blood serum samples (52-GC; 104-control) were analyzed using a panel of biomarkers (''Gastropanel'', Biohit, Finland) and 167 DNA samples (80-GC; 87-control) were genotyped according to the published method for -511C/T (rs16944) IL1B gene polymorphism. (''Gastropanel'', Biohit, Finland) and 167 DNA samples (80-GC; 87-control) were genotyped according to the published method for -511C/T (rs16944) IL1B gene polymorphism.
Results: In a single-factor analysis, low PGI and PGI/PGII ratio were associated with GC risk: OR 2.9 (95% CI 1.3–6.4, $p = 0.006$) for PGI and OR 3.3 (95% CI 1.5–7.3, $p = 0.002$) for PGI/PGII ratio. In the multivariate regression analysis with the inclusion of quantitative and categorical variables in the model the PGI

level (B = −0.033, p < 0,001, OR = 0.967, 95% CI 0.95–0.98) and PGI PGII ratio (B = −0.548, p = 0.0001, OR = 0.578, 95% CI 0.43–0.77) were significant in the model. Carriers of the T/T genotype of the IL1B had an increased GC risk as compared to carriers of the C/C genotype (B = 2.39; p = 0.047; OR = 10.9; 95% CI 1.03–116.04). In persons with family history of cancers the GC risk was also increased (B = 1.246; p = 0.048; OR = 3.475; 95% CI 1.009–11.97).
Conclusion: The obtained data suggest that the T/T genotype IL1B gene, the low level of PGI and the PGI/PGII ratio are associated with an increased GC risk in Siberian population.
Disclosure: Nothing to disclose

P1188 GENETIC EVENTS AND CLONAL DIFFERENCES IN MULTIPLE OCCURRENCE OF GASTRIC CANCER

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Introduction: Recent molecular analysis by international large-scale collaborative studies of TCGA (The Cancer Genome Atlas) and ICGC (International Cancer Genome Consortium), elucidated the genetic background of gastric cancers into four subgroups e.g., Epstein-Barr Virus (EBV) positive, microsatellite instability (MSI), chromosomal instability (CIN) and genomically stable (GS) gastric cancers. However, the information of genetic analysis of clinically available samples are still limited. In particular, recurrent occurrence of early gastric cancers was often clinically encountered after endoscopic submucosal dissection (ESD), but their molecular events were not elucidated.
Aims and Methods: To explore molecular events in multiple early gastric cancers, tumor tissues from patients who developed synchronous (simultaneous or within one year) and metachronous (one year after initial neoplasm) multiple early gastric cancers were investigated. We performed next generation sequencing on the 83 tumor samples from 31 patients by using "gastric cancer panel" which we created *in house* covering 351,050 base pairs of 58 significantly mutated genes (SMG) (Nature 2014; 513: 202–209). Of these 31 patients, 15 patients had synchronous recurrence, 11 metachronous, and 5 both synchronous and metachronous. Average number of recurrence was 3 (maximum 6 times). In addition, we performed immunohistochemical staining of proteins produced by DNA mismatch repair genes (MLH 1, MSH 2, PMS 2, and MSH 6) and microsatellite instability (MSI) assay.
Results: We found total of 467 somatic mutations of 58 SMGS in 83 samples (cut-off level of allelic fraction-AF above 5%). We also performed immunohistochemical staining of repair genes and microsatellite instability assay. We then classified 83 tumor tissue samples from 31 patients into 4 groups proposed by TCGA and ICGC international collaborative study group. Our analysis revealed that multiple gastric tumors belonged to the three categories. (1) All recurrences in 2 patients are microsatellite instability high (MSI-H only) (2/31, 6%), (2) one tumor is microsatellite stable (MSS)/genetically CIN, but the recurrence is MSI-H (6/31, 19%), (3) all tumors are MSS and genetically CIN (23/31, 75%).
Of particular interest is that in one case with exceptionally frequent recurrence (6 times), microsatellite and immunohistochemical analysis revealed all these 6 tumors showed microsatellite instability high (MSI-H) and the methylation of the promoter region of MLH1.
Conclusion: The multiple gastric tumors belonged to three categories; all microsatellite instability-high (MSI-H) (2/31, 6%), mixture of MSS/CIN and MSI-H (6/31, 19%), all MSS and CIN (23/31, 75%).
It could be concluded as with multiple occurrence, principal genotypes may vary and modality of treatment should be modified according to the molecular types if the tumor advanced.
Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00
H. Pylori II – Hall X1

P1189 RISK OF OVERALL MORTALITY AFTER HELICOBACTER PYLORI TREATMENT IN PATIENTS WITH HYPERTENSION

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Introduction: Gastric cancer incidence and mortality in general population were reported to decrease after treatment of *Helicobacter pylori* infection. However, it was reported that overall mortality might be increased after *H. pylori* eradication about 9%. This finding should be studied before *H. pylori* eradication therapy is recommended in general population for gastric cancer prevention.
Aims and Methods: The aim of this study was to investigate whether the overall mortality is increased after the *H. pylori* treatment in patients with hypertension, who might have higher cardiovascular death risk than in general population. We used the database of Korean National Health Insurance Service-National Sample Cohort consisted of 1 million sample population. A total of 198,462 hypertension patients were selected between 2002 and 2010. Of these, 5,541 patients who received *H. pylori* eradication therapy (Hp-treatment group) were matched to 11,082 patients who did not receive *H. pylori* treatments (control group) at a 1:2 ratio by matching of age, sex, Charlson comorbidity index, the year when hypertension treatment started, and observation periods. The primary outcome variable was overall mortality that occurred at 6 months after the *H. pylori* treatment. The secondary outcomes were the specific mortalities due to the cardiovascular diseases, cerebrovascular diseases, and cancer. Cox-proportional hazard model was used to evaluate the mortality risk.
Results: In the matched cohort, the male proportion was 55.2% and proportion of person older than 60 years was 28.6%. In the Hp-treatment group, most of the patients (96.4%, 5,342/5,541 patients) were prescribed proton-pump inhibitor-clarithromycin containing triple therapy. During median follow-up periods of 4.8 years (interquartile range, 2.6–7.3 years), 229 patients (4.1%, 229/5,541) in the Hp-treatment group and 608 patients (5.5%, 608/11,082) in the control group died. Overall mortality was significantly lower in the Hp-treatment group than in the control group (adjusted hazard ratio [aHR] for overall mortality in the Hp-treatment group, 0.70; 95% confidence interval [CI], 0.60–0.81; $P < 0.001$). According to the cause of mortality, Hp-treatment group had significantly lower risk of mortality due to cerebrovascular disease mortality (aHR, 0.46; 95% CI, 0.26–0.82; $P = 0.008$) as compared with the control group. Overall cancer mortality risk was lower in the Hp-treatment group than in the control group with a borderline statistical significance (aHR, 0.75; 95% CI, 0.57–1.00; $P = 0.0502$). However, cardiovascular disease mortality (aHR, 0.96; 95% CI, 0.54–1.71; $P = 0.887$) was not different in both groups.
Conclusion: *H. pylori* treatment seems not be associated with an increase in overall mortality or cardiovascular mortality in patients with hypertension.
Disclosure: Nothing to disclose

P1190 MIGRATORY AND SOCIAL PARAMETERS INFLUENCING RESISTANT HELICOBACTER PYLORI INFECTION IN SOUTHERN CHINA: A MUNICIPALITY-WIDE MULTICENTER PREVALENCE STUDY

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Introduction: Southern China is witnessing increasing rates of *Helicobacter pylori* (*H.pylori*) eradication failure. Shenzhen, Guangdong province, is one of the rapidly-growing cities in China with a large migrant population. Risk factors for *H.pylori* resistance in relationship to the migratory environment of China have not been well-investigated.
Aims and Methods: Since September 2016, we recruited patients who tested ^{13}C-Urea breath test-positive after first-line *H.pylori* eradication from 5 hospitals located throughout Shenzhen in Southern China. Participants completed a questionnaire profiling potential risk factors of *H.pylori* infection, including geographical origin, educational status, source of drinking water, residential family size, and medication/smoking/alcohol history. All participants underwent an upper gastrointestinal endoscopy with three antral and two corpus biopsies obtained for *H.pylori* culture and antimicrobial susceptibility testing (Zhiyuan Medical Inspection Institute, Hangzhou, China) for 6 antibiotics: amoxicillin, clarithromycin, levofloxacin, metronidazole, tetracycline and furazolidone. Potential risk factors for antibiotic resistance were analyzed.
Results: In this interim analysis, we recruited 746 patients (52.4% male), with a mean age of 43.1 ± 12.5 years. 711 (95.3%) and 473 (63.4%) were born outside Shenzhen and Guangdong province respectively. Among 557 patients (74.7%) with a positive *H.pylori* culture, the antibiotic resistance for amoxicillin, clarithromycin, levofloxacin, metronidazole, tetracycline and furazolidone were 1.3%, 34.1%, 42.4%, 92.5%, 0% and 0% respectively. 313 patients (56.2%) were resistant to multiple antibiotics. Multivariate testing found a geographical origin from non-coastal cities to be independently associated with clarithromycin resistance (p = 0.006, OR 3.322, 95%CI 1.400–7.874), while patients' geographical origin provincial gross domestic product per capita of <20,000 USD showed borderline association (p = 0.070, OR 2.144, 95%CI 0.925–4.973). These two factors had no association with metronidazole or levofloxacin resistance ($p > 0.05$). Other significant factors include increasing age for resistance to clarithromycin (p = 0.007, OR 1.019, 95%CI 1.005–1.033), metronidazole (p = 0.002, OR 1.047, 95%CI 1.017–1.079) and levofloxacin ($p < 0.001$, OR 1.025, 95%CI 1.011–1.039) and prior antibiotic use for resistance to metronidazole (p = 0.024,

OR 2.132, 95%CI 1.106–4.098) Duration of migration to Shenzhen, population density of geographical origin and other social parameters showed no relationship with antibiotic resistance.
Conclusion: High rates of clarithromycin, levofloxacin and metronidazole resistance were noted among Southern Chinese patients with *H.pylori* eradication failure. Migratory and economic patterns may influence local epidemiological *H.pylori* resistance trends especially towards clarithromycin.
Disclosure: Nothing to disclose

P1191 PREVALENCE OF HISTOLOGIC ATROPHIC GASTRITIS AND INTESTINAL METAPLASIA IN THE CORPUS HAS DECREASED OVER 15 YEARS IN THE FEMALE IN KOREAN POPULATION

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Introduction: Recently the prevalence of *Helicobacter pylori* (*H. pylori*) infection has decreased to around 50% in Korea. Atrophic gastritis (AG) and intestinal metaplasia (IM) are the premalignant conditions for gastric cancer of which Korean incidence is the highest in the world.
Aims and Methods: The aim of this study is to investigate the trend of the prevalence and grades of AG and IM according to sex in Korean population. From March 2003 to February 2018, we prospectively enrolled 2002 subjects without significant gastroduodenal disease, which has been checked by esophagogastroduodenoscopy. Biopsies were taken from the lesser and greater curvatures of the antrum and mid-corpus, respectively, and CLOtest was also performed for diagnosis of *H. pylori*. Three periods were divided by 2003 to 2007, 2008 to 2012, and 2013 to 2018. AG and IM were scored histologically by using the Updated Sydney classification. Trend of the prevalence and grades of AG and IM were analyzed according to sex. In addition, multivariate logistic analysis was performed for the AG, IM depending on antrum and corpus.
Results: Total 2002 subjects were categorized by *H. pylori*-negative (n = 1220) and *H. pylori*-positive (n = 782). In each period *H. pylori*-positivity decreased as following: 49.2% (149/303) during the 2003 to 2007, 40.2% (207/515) from 2008 to 2012, and 36.0% (426/1184) from 2013 to 2018 ($P < 0.001$). In the case of male, *H. pylori*-positivity decreased as following: 51.6% (48/93) during the 2003 to 2007, 38.2% (83/217) from 2008 to 2012, and 36.3% (174/480) from 2013 to 2018 ($P = 0.014$). In the case of female, *H. pylori*-positivity decreased as following: 48.1% (101/210) during the 2003 to 2007, 41.6% (124/298) from 2008 to 2012, and 35.8% (252/704) from 2013 to 2018 ($P = 0.001$). By using chi-square test and linear-by-linear association analysis according to period, female prevalence of AG at corpus ($P = 0.001$ and $P < 0.001$) and IM at corpus ($P < 0.001$ and $P < 0.001$) were gradually decreased from 2003 to 2018, different from male (table). In the multivariate logistic analysis, old age [odds ratios (ORs), 4.117; $P = 0.001$ and 8.188; $P < 0.001$ for ages in the 40 ~ 59 and ≥60], Period (OR, 0.628; $P = 0.024$ and 0.471; $P = 0.005$ from 2008 to 2012 and from 2013 to 2018), and *H. pylori* infection (OR, 3.467; $P < 0.001$) were statistically significant in AG at corpus. AG at antrum and IM at corpus had also similar results. In case of IM at antrum old age (OR, 5.154, $P < 0.001$ and 8.899, $P < 0.001$ for ages in the 40 ~ 59 and ≥60) and *H. pylori* infection (OR, 1.491; $P = 0.008$) and smoking status (OR, 1.738; $P = 0.011$) were statistically significant.
Conclusion: Significantly decreased prevalence and grades of AG and IM at corpus only in female in spite of decreased *H. pylori* infection regardless of sex suggests that sex or gender-specific characters such as eating habits including salty or spicy foods are related with the development of AG and IM.
Disclosure: Nothing to disclose

P1192 HELICOBACTER PYLORI INFECTION AND AUTOIMMUNE DISEASES: A POPULATION STUDY IN PRIMARY CARE SETTING

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Introduction: *Helicobacter pylori* (Hp) infection is common worldwide, with a global prevalence over 50%, but with substantial geographical variations. Prevalence rates also differ according to ethnicity, socio-economic status, and age, being more prevalent with advancing age. Hp has been defined as a carcinogen class I due to its capacity to induce antrum atrophy that progressively extends to the entire stomach, with subsequent development of gastric metaplasia and eventually adencarcinoma. Patients affected by autoimmune diseases have an higher risk of developing other autoimmune conditions such as autoimmune gastritis (AG); although AG has a different pathogenesis, the relationship between Hp and the development of this condition in patients affected by autoimmune diseases has not been well established yet.
Aims and Methods: The aim of this study was to assess the prevalence of Hp infection in a cohort of patients with at least one of these non-gastric autoimmune diseases: Hashimoto's thyroiditis (HT), celiac disease (CD), rheumatoid arthritis (RA), psoriatic arthritis (PA), Sjögren's syndrome (SS) and vitiligo (VI). Records of patients affected by any of the mentioned autoimmune conditions were evaluated as part of a larger study involving the determination of several biochemical parameters, including dosing of anti-Hp IgG antibodies (Biohit Oyj, Finland). A cut-off value of IgG > 30 EIU was considered positive, indicating Hp infection.

Abstract No: P1191
Table 1: Grades and prevalence for atrophic gastritis and intestinal metaplasia in the antrum and the corpus from 2003 to 2018

		2003–2007	2008–2012	2013–2018	p-value	linear by linear association
Total	AG grade	0.58(0.706)	0.40(0.650)	0.54(0.800)	0.004	0.833
Antrum	Prevalence (%)	46.8%(130/278)	32.7%(127/388)	36.9%(263/712)	0.001	0.030
Total	IM grade	0.51(0.837)	0.37(0.677)	0.47(0.795)	0.017	0.817
Antrum	Prevalence (%)	31.4%(95/303)	26.0%(134/515)	30.7%(363/1184)	0.119	0.621
Total	AG grade	0.42(0.738)	0.28(0.632)	0.29(0.672)	0.018	0.024
Corpus	Prevalence (%)	28.1%(77/274)	20.2%(83/410)	18.3%(149/815)	0.002	0.001
Total	IM grade	0.38(0.730)	0.23(0.565)	0.23(0.598)	0.001	0.002
Corpus	Prevalence (%)	24.4%(74/303)	16.1%(83/515)	15.2%(180/1184)	0.001	0.001
Male	AG grade	0.74(0.774)	0.35(0.634)	0.57(0.800)	<0.001	0.603
Antrum	Prevalence (%)	57.6%(49/85)	27.6%(45/163)	39.5%(121/306)	<0.001	0.105
Male	IM grade	0.58(0.913)	0.39(0.699)	0.55(0.856)	0.034	0.401
Antrum	Prevalence (%)	34.4%(32/93)	26.7%(58/217)	34.8%(167/480)	0.100	0.321
Male	AG grade	0.46(0.801)	0.29(0.664)	0.38(0.772)	0.220	0.779
Corpus	Prevalence (%)	28.9%(24/83)	19.2%(33/172)	22.3%(73/328)	0.217	0.441
Male	IM grade	0.49(0.816)	0.24(0.593)	0.35(0.742)	0.015	0.580
Corpus	Prevalence (%)	31.2%(29/93)	16.6%(36/217)	21.7%(104/480)	0.016	0.332
Female	AG grade	0.50(0.662)	0.44(0.660)	0.52(0.800)	0.418	0.558
Antrum	Prevalence (%)	42.0%(81/193)	36.4%(82/225)	35.0%(142/406)	0.248	0.113
Female	IM grade	0.48(0.802)	0.36(0.662)	0.41(0.746)	0.189	0.556
Antrum	Prevalence (%)	30.0%(63/210)	25.5%(76/298)	27.8%(196/704)	0.528	0.767
Female	AG grade	0.40(0.710)	0.28(0.608)	0.23(0.590)	0.009	0.003
Corpus	Prevalence (%)	27.7%(53/191)	21.0%(50/238)	15.6%(76/487)	0.001	<0.001
Female	IM grade	0.32(0.685)	0.21(0.543)	0.14(0.458)	<0.001	<0.001
Corpus	Prevalence (%)	21.4%(45/210)	15.8%(47/298)	10.8%(76/704)	<0.001	<0.001

Results: Biochemical evaluation of anti-Hp antibodies was performed in 609 patients with autoimmune diseases (mean age 52.4 ± 14.3); Hp infection was found in 139 (22.8%): 118/527 (22.4%) of TH patients, 3/25 (12.0%) of CD patients, 5/13 (38.5%) of RA patients, 7/21 (33.3%) of PA patients. In patients with two or more coexisting autoimmune diseases, Hp infection was observed in 2/7 subjects with HT and CD, 2/4 patients with HT and PA, 1/3 subjects with HT and RA, and in 1/4 subjects with HT and VI. No cases of Hp infection were found in the 4 patients affected with SS.
Conclusion: The overall prevalence of Hp infection in the population of patients with autoimmune diseases was 22.8%, which is significantly lower than the medium value reported for the Italian general population and is partly due to the lower mean age of patients with autoimmune diseases. This data seems to confirm previous reports of a lower prevalence of Hp infection in patients with autoimmune diseases compared to the general population of the same age.
Disclosure: Nothing to disclose

P1193 NATURAL HISTORY OF GASTRIC ULCER IN A 25 YEARS FOLLOW-UP: ROLE OF HELICOBACTER PYLORI INFECTION AND NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

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Introduction: *Helicobacter pylori* (H.p.) remains the main cause of gastric ulcer (GU); however, the role of nonsteroidal anti-inflammatory drugs (NSAIDs) is quickly increasing worldwide.
Aims and Methods: The aim of the present study was to assess the natural history of GU related to H.p. or NSAIDs aetiology, evaluating clinical presentation, recurrence rate and complications occurred during a long-term follow-up.
We conducted a retrospective follow-up study of 256 consecutive patients (M/F = 134/122, mean age 57 yrs, range 20–84 yrs) with endoscopically diagnosed gastric ulcer. After baseline EGD, during a 25 years follow-up clinical assessments every 6 months and at least one EGD with biopsies and H.p. evaluation were performed. Each episode of recurrence of symptoms lasting more than 5 days was investigated by means of EGD. Enrolled subjects were divided into 4 groups according to H.p. infection and intake of NSAIDs.
Results: Overall, 172 patients (67%) with GU had history of H p. infection and 72 pts (28%) were NSAID takers. 115/172 pts H.p.+ did not use NSAIDs. NSAID takers H.p.-negative were only 15 (6%). H p. negative individuals not taking NSAIDs were 67 (26%) and H.p.+ pts with associated NSAIDs use were 57 (22%). At the beginning, the majority (85%) of the pts was symptomatic and presented epigastric pain (30%) and/or heartburn (29%) and/or dyspepsia (28%), whilst 14% presented bleeding as first symptom ($p < 0.0001$). Epigastric pain was the single most important starting symptom in H.p.+ pts in comparison with H.p.- ($p < 0.0001$). There were no significant differences in presenting complaints in NSAIDs+ and NSAIDs- pts. Undergoing EGD, 233 were diagnosed for gastritis, 15 resulted affected by duodenal ulcer, and 3 cases of gastric cancer were discovered. Within 3 years 33% of pts were symptom-free, but in H.p+ NSAIDs+ the persistence of symptoms in comparison with the other groups was prolonged (<0.002). At the end of the follow-up, 90% was asymptomatic and in 207/256 the ulcer disappeared. The recurrence rate was 18% (46/256) and haemorrhagic complications occurred in 5% of pts, more frequent among HP+NSAIDs+ pts (42%).
Conclusion: This study confirms that the natural history of GU depends on the cause and assesses the pathological role of both H.p. and NSAIDs and their frequent (22%) association. There is a synergism between H.p. infection and NSAIDs use for the development of GU bleeding and the persistence of symptoms. A long-term follow-up assessed that GU patients can be symptoms-free.
Disclosure: Nothing to disclose

P1194 HELICOBACTER PYLORI INFECTION AMONG PHYSICIANS OF DIFFERENT REGIONS OF RUSSIAN FEDERATION

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Introduction: Russia belongs to countries with high prevalence of *Helicobacter pylori* (*H.pylori*) infection ranging from 50% to 92%. Epidemiological studies on *H. pylori* infection among Russian physicians of different regions of country have not been carried out to date.
Aims and Methods: To evaluate the prevalence of *H.pylori* among physicians according to the different regions of Russian Federation by using 13C-urea breath test.
Results: 1154 doctors from 14 different regions of Russian Federation were examined. High prevalence of *H. pylori* (59%) among physicians was found. The lowest prevalence of infection was found in Saratov (38.5%), the highest incidence of infection was recorded in Krasnodar (76.2%). The prevalence of *H. pylori* in the group of doctors under the age of 30 y. o. was 45.2%, in the group of 51–60 y. o. — 65.2%, respectively. 20% of specialists refused to take part in the testing, 50% of doctors noted that they would not take antibiotics if an infection was detected. Treatment for eradication *H. pylori* among 619 of *H. pylori*-positive physicians was received only in 114 (18.9%) doctors and therapy achieved elimination of the infection in 69.2% cases.
Conclusion: The first observation epidemiological study on *H. pylori* infection among Russian physicians showed differences in infection rates in various regions of Russia with an average of 59%. The low awareness of physicians about their own *H.pylori* status and lack of internal conviction in the appropriateness of self-diagnosis and eradication of *H. pylori* was revealed.
Disclosure: Nothing to disclose

P1195 IS HELICOBACTER PYLORI ERADICATION RELATED TO REFLUX ESOPHGITIS? CORRELATION WITH GASTRIC ACID SECRETION

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Introduction: Gastroesophageal reflux disease (GERD) is largely diffuse in general population. No clear relationship has been established between GERD and the eradication of *H. pylori* (H.p.) infection, although some papers support the onset of esophagitis in patients in whom the infection has been cured.
Aims and Methods: Aim of this study was to investigate the relationship between the cure of H.p. infection and the onset of esophagitis in a long follow-up taking into account the Maximal Acid Output (M.A.O.). A group of 450 patients was recruited (M = 343, F = 107, mean age 42.89 ± 11.8 yrs, range 18–80yrs), all H.p.+ (U.B.T.). All patients underwent to gastric acid aspiration test for measuring B.A.O. in basal conditions and M.A.O. after maximal stimulation with pentagastrin (i.m. 6 μg/kg) in order to determine secretory status and were classified accordingly as: normo-secretory (group A) or hypersecretory (group B).
Patients were treated with standard triple therapy for H.p. eradication and two months later they underwent to esophagogastroduodenoscopy with bioptic sampling to evaluate the presence of lesions, the state of the gastric mucosa and the eradication of H.p. In addition, all of them were subjected to a blood sampling for serum pepsinogen I and G17 determination. We excluded from the study patients tested negative for H.p. infection in U.B.T, patients on antisecretory treatment and patients who denied informed consent.
Results: All patients were divided in two groups according with the secretory status after the results of gastric juice collection:
Group A) Normosecretory status: 135/450 patients (30%) with low or normal acid secretion (M.A.O. 5–25 mEq/h);
Group B) Hypersecretory status: 315/450 patients (70%) with elevate gastric acid secretion (M.A.O. >25 mEq/h).
Eradication rate was elevated, with 320 of 450 (71%) treated patients achieving H.p. eradication. Esophagitis was diagnosed in a total of 157/450 patients (34.9%), and was significantly more frequent in patients in whom eradication was achieved when compared against patients with persistent infection (150/320, 46.9% vs 7/130, 5.4%, respectively, $p = 0.0001$).
In Group A cured patients were 96/135 (71.1% Group A1) versus 39/135 (29.9% Group A2) of patients with persistent infection. In the latter group of subjects, esophagitis was found in 22.2% (30/135) patients, in particular 30 out of 96 (31.2%) in Group A1 developed esophagitis compared to 0% in Group A2. On the other hand, in Group B, cured patients were 224/315 (71.1% Group B1) versus 91/315 (28.9% group B2). In the latter, esophagitis was observed in 127/315 subjects (40.3%) and subdividing them according to the success of eradication therapy, in group B1 53.6% (120/224) of patients developed esophagitis against 7.7% (7/91) in Group B2, $p = 0.0001$.
Comparing patients with hyper (Group B1) and normal (Group A1) acid secretion, in whom H.p. eradication therapy was effective, a statistically significant increase in the occurrence of esophagitis, can be noted in group B1 (120/224 53.6%) against 30/96 31.2% in group A1 $p = 0.0001$.
No statistically significant difference was found in the development of esophagitis in patients with persistent infection when they were divided according to secretory status in group A2, 0/39 (0%) versus Group B2 7/91 (7.7%) $p = 0.077$.
Conclusion: This study shows statistically significance relationship between H.p. eradication and onset of esophagitis particularly in the group of hypersecretory status subjects.
Disclosure: Nothing to disclose

P1196 OPTIMIZATION OF 13C UREA BREATH TEST THRESHOLD LEVELS FOR THE DETECTION OF *HELICOBACTER PYLORI* INFECTION IN A NATIONAL REFERRAL LABORATORY

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Introduction: Threshold values for C13-urea breath test (C13-UBT) positivity may be affected by sociodemographic factors, host factors such as C13 excretion kinetics, bacterial factors and laboratory factors including urea dose. Manufacturer-recommended cutoffs for C13-UBT assays may not be applicable in all settings. Optimizing C13-UBT cut-offs may have profound public health ramifications.
Aims and Methods: We aimed to determine the optimal threshold for C13-UBT positivity in our population. Consecutive test samples collected at our central laboratory from patients undergoing a first-time C13-UBT between 1st January 2010 and 31st December 2015 were included. The difference between values at 30 min and at baseline (T30-T0) was expressed as delta over baseline (DOB). Cluster analysis was performed on the C13-UBT test results to determine the optimal cut-off point with minimal interclass variance.
Results: 234,831 patients (87,291 (37.2%) male, age 39.9 ± 19.9) underwent a first-time C13-UBT, including 124,701 (53.1%) negative and 110,130 (46.9%) positive tests, using the manufacturer-recommended cutoff of 3.5 DOB. Cluster analysis determined an optimized cut-off of 2.74 DOB, representing an additional 2180 (0.93%) positive subjects who had been previously categorized as negative according to the manufacturer-specified cutoff of 3.5 DOB. Mean positive and negative DOB values were 19.54 ± 14.95 and 0.66 ± 0.51, respectively. The cut-offs for male and female subjects were 2.23 and 3.05 DOB, respectively. Threshold values for <45 year-olds, 45–60 year-olds and >60 year olds were 2.67, 2.55 and 2.93 DOB, respectively. Of the 2180 (0.93%) patients with DOB 2.73–3.49, 289 (13.3%) performed a subsequent C13-UBT and 140 (48.4%) remained positive when tested at 20.3 ± 14.4 months.
Conclusion: Major referral laboratories should optimize threshold values for C13-UBT positivity for their geographical location. Different cut-off values should be applied for male and female subjects.
Disclosure: Nothing to disclose

P1197 CLARITHROMYCIN RESISTANCE AND FEMALE GENDER AFFECT *HELICOBACTER PYLORI* ERADICATION FAILURE IN CHRONIC GASTRITIS

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Introduction: *Helicobacter pylori* infection affects 54.4% of population in Korea. The eradication rate of the first-line triple therapy (a proton pump inhibitor, clarithromycin, and amoxicillin) for *H. pylori* infection has gradually decreased in Korea. The eradication failure is influenced by host-related, bacterial, and environmental factors. It has been reported that the clarithromycin (CAM) resistance rate gradually increased from 17.2% to 23.7% between 2003 and 2012 in Korea. Clarithromycin resistance is considered the most important factor of eradication failure and the *CYP2C19* polymorphism is also related to the *H. pylori* eradication.
Aims and Methods: We aimed to evaluate whether clinical parameters, clarithromycin resistance, and *CYP2C19* genotype can affect the eradication failure. A total of 203 patients with *H. pylori*-positive chronic gastritis were consecutively enrolled. All the participants received a diagnosis of *H. pylori* infection by a rapid urease test or detection of *H. pylori* genomic DNA from gastric mucosal tissues. They received clarithromycin-based triple therapy for 7 days. A clarithromycin resistance test was performed by detection of A2142G and A2143G point mutations in *H. pylori* 23S rRNA using a dual-priming oligonucleotide PCR. The *CYP2C19* genotype was examined for polymorphism G681A of exon 5 and G636A of exon 4 by PCR with restriction fragment length polymorphism. The patients were classified into three groups by *CYP2C19* genotype: rapid metabolizers (RM), intermediate metabolizers (IM) and poor metabolizers (PM). Eradication was assessed by a ^{13}C-urea breath test 4 weeks after treatment.
Results: Of 203 patients, 190 completed the study. The eradication rate was 64.0% according to intention-to-treat analysis and 68.4% by per-protocol analysis. *CYP2C19* genotypes were identified as follows: 75 poor metabolizers, 75 intermediate metabolizers, and 40 rapid metabolizers. Nonetheless, this polymorphism was not significantly associated with eradication failure ($p = 0.682$). Clarithromycin resistance was detected in 33/190 patients (17.4%), and their eradication rate was zero. Clarithromycin resistance (odds ratio 19.13, 95% confidence interval 9.35–35.09) and female gender (odds ratio 1.73, 95% confidence interval 1.15–4.25) were significantly associated with eradication failure. The other clinical parameters such as age, cigarette smoking, alcohol intake, the body-mass index, hypertension, and diabetes were not significantly associated with eradication.
Conclusion: Clarithromycin resistance and female gender are factors affecting *H. pylori* eradication failure in patients with chronic gastritis.
Disclosure: Nothing to disclose

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P1198 A MOLECULAR DIAGNOSTIC TEST USING REVERE BLOT HYBRIDIZATION ASSAY FOR IDENTIFICATION OF GENOMIC MUTATION RESPONSIBLE FOR ANTIBIOTICS RESISTANCE OF *HELICOBACTER PYLORI*

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Introduction: The rapid identification of antibiotics-resistance of *H. pylori* is important to eradicate *H. pylori* infection. The aim of this study was to examine a newly designed revere blot hybridization assay (REBA) for identification of antibiotics-resistance by using *H. pylori* genomic mutations.
Aims and Methods: REBA for identification of genomic mutations responsible for antibiotic-resistance of H. pylori was developed: clarithromycin resistance (23s rRNA A2143G, A2142G and A2142C), fluoroquinolone resistance (gyrA Codon 87 C261G/A, and Codon 91 A272G and G271A/T), tetracycline resistance (16s rRNA AGA nt, 965–967 TTC). DNA extracted from *H. pylori* strains and other bacterial species. Polymerase chain reaction and REBA was performed.
Results: For diagnostic accuracy, a test using twelve samples of *H. pylori* strains and clones were performed, and findings of PCR-REBA were consistent with those of prepared samples. In cross-reactivity test using 26 other bacterial species, no cross reactivity was observed among bacterial species. For validation of findings of PCR-RBHA, data of direct DNA sequencing of seven samples of *H. pylori* strains were performed. Findings of PCR-REBA were consistent with those of direct DNA sequencing data.
Conclusion: REBA showed a good performance of rapid and accurate identification of antibiotics-resistance of *H. pylori*. It may become an effective diagnostic test for tailored eradication treatment of *H. pylori*.
Disclosure: Nothing to disclose

P1199 EVALUATION OF THE RIDAGENE *HELICOBACTER PYLORI* REAL-TIME PCR ASSAY COMPARED TO CULTURE FOR THE DETECTION OF CLARITHROMYCIN RESISTANCE IN AN IRISH CENTRE

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Introduction: *H. pylori* antimicrobial susceptibility testing is important for determining the prevalence of antibiotic resistance in a given population, in order to recommend the most appropriate treatment regimens. Furthermore, it provides the opportunity to tailor an individual patient's therapy. As traditional culture-based approaches are time-consuming, recently developed molecular methods provide a more rapid alternative for the detection of *H. pylori* and its resistance to antibiotics.
Aims and Methods: Our aim was to evaluate the Ridagene *H. pylori* real-time PCR assay compared to culture-based methods for the detection of clarithromycin resistant *H. pylori* infection.
Following ethical approval and receipt of informed consent, gastric biopsy samples of patients diagnosed with *H. pylori* infection by the rapid urease test (RUT) were processed for culture and clarithromycin susceptibility testing using Etest strips (Biomerieux, France). DNA was isolated from biopsies using the QiaAmp DNA Mini Kit (Qiagen, UK) and analysed for the 3 most common clarithromycin-mediating point mutations (A2146C, A2146G and A2147G) using the Ridagene *H. pylori* real-time PCR assay (R-Biopharm AG, Germany).
Results: In all, samples from 131 RUT- and culture-positive patients (mean age 47.4 ± 14.2 years; 46.6% female) were analysed. The Ridagene assay detected *H. pylori* DNA in 96.9% ($N = 127/131$) of samples. Using biopsies that were both culture- and *H. pylori* DNA-positive, the rate of clarithromycin resistance detected by culture-based methods was significantly higher than that of the Ridagene assay (51.2% ($N = 65/127$) vs 38.6% ($N = 49/127$), respectively; $X^2 = 4.1$; $P = 0.04$). Results were concordant from both methods in 80.3% ($N = 102/127$) of cases. The sensitivity and specificity of the Ridagene assay

compared to culture for the detection of clarithromycin resistance were 67.7% (95% CI: 55.0–78.8%) and 91.9% (95% CI: 82.2–97.3%), respectively. The positive predictive value was 89.8% (95% CI: 78.9–95.4%) and the negative predictive value was 73.1% (95% CI: 65.5–79.5%).
Conclusion: Although the Ridagene assay is rapid and easy to use, the low sensitivity compared to culture for the detection of clarithromycin resistance in our cohort limits its use to cases where culture-based methods are unsuccessful. Further studies are required to characterise the full range of clarithromycin resistance-mediating mutations present in our patients.
Disclosure: Nothing to disclose

P1200 THE USEFULNESS OF LINKED COLOR IMAGING AND THE POTENTIAL OF AUTOMATIC DIAGMOSIS SYSTEM FOR DIAGNOSIS OF *H. PYLORI* INFECTION

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Introduction: Linked Color Imaging (LCI) is a novel image-enhanced endoscopy to enhance the slight difference in mucosal color. The lighting in LCI mode emphasizes hemoglobin related information. Using the latest LASEREO system (VP-7000&LL-7000) and latest endoscopy (EG-L600ZW7, EG-L600WR7) (FUJIFILM Co., Tokyo, Japan), we expected LCI to enhance the diffuse redness in Hp positive patients and support the diagnosis of active Hp infection. However, the endoscopic diagnosis of Hp infection does not have objective indicators; it depends on physician's experience. Therefore, it is necessary to establish universal methods for the endoscopic diagnosis of Hp infection, such as computer-aided diagnosis.
Aims and Methods: The aims of this study are (1) to evaluate the diagnosability of our artificial intelligence (AI) system for Hp infection and (2) to evaluate the usefulness of LCI for diagnosis of Hp infection compared to the conventional endoscopy with white-light image (WLI).
In our new AI system, LCI images were classified into two types based on the slight difference of the red color, high hue images (red-purple) and low hue images (red-orange). Then, the presence or absence of Hp infection was learned by machine learning for each type of LCI image. The trained classifiers gave us the diagnosis of Hp infection automatically. We retrospectively analyzed 133 patients with Hp positive (55 patients) or negative (78 patients) those were examined with WLI and LCI at Asahi University Hospital from December 2016 to January 2018. The presence of Hp infection was determined by more than two different examinations: histologic examination, serum antibody test, stool antigen test, ^{13}C-urea breath test. The absence of Hp infection was determined by the ^{13}C -urea breath test at least 2months after Hp eradication therapy. For this study, we used 3 endoscopic images per patient, which were taken from lesser curvature or greater curvature of middle to lower of gastric body. Three LCI images were read into AI system, and randomly arranged 3 LCI and 3 WLI images were made a judgment of Hp-positive/negative by 3 endoscopists, A: an expert involved in the development of LCI, B: a gastroenterology specialist, C: a senior resident.
Results: The levels of accuracy/sensitivity/specificity of diagnosis of Hp infection by AI system with LCI were 82.0%/74.5%/85.9%, respectively. On the other hand, those of diagnosis by A with WLI and LCI were 78.9%/74.5%/82.1%, and 88.0%/85.5%/89.7%, respectively. Those of diagnosis by B with WLI and LCI were 75.9%/58.2%/88.5%, and 87.2%/78.2%/93.6%, respectively and diagnosis by C with WLI and LCI were 74.4%/69.1%/78.2%, and 85.7%/85.5%/85.9%, respectively.
The accuracy and sensitivity of diagnosis with LCI was significantly higher than those of WLI by all three endoscopists ($p = 0.018$–0.048). There was no significant difference between diagnosis of physicians and AI system. The kappa value of variability among 3 physicians for LCI (kappa value: between A&B = 0.86, A&C = 0.71, B&C = 0.72) was higher than that for WLI (kappa value: between A&B = 0.58, A&C = 0.57, B&C = 0.65). There were 7 cases (5%) that were wrongly diagnosed by both 3 physicians and AI system.
Conclusion: LCI had significantly higher accuracy and sensitivity of diagnosis of Hp infection compared to conventional WLI. We recommend LCI mode for screening of Hp infection in routine endoscopy as costless and convenience.
The AI system could diagnose the Hp infection with great accuracy. Learning more images, our new proposed AI system will be able to support an inexperienced physician.
Disclosure: Nothing to disclose

P1201 SPANISH PRIMARY CARE SURVEY ON THE MANAGEMENT OF *H. PYLORI* INFECTION: PERCEPTIONS, ACCESS TO INFORMATION AND CONTINUOUS MEDICAL EDUCATION

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Introduction: The preferences and decisions of Primary Care physicians in the management of *H. pylori*, or their access to different health technologies (i.e. diagnostic methods), courses and information have not generally been taken in consideration, even though Primary Care physicians currently manage this infection in most of the cases.
Aims and Methods: To evaluate the perceptions, access to continuous medical education and information of Spanish Primary Care physicians. A multidisciplinary committee formed by *H. pylori* experts from the Spanish Association of Gastroenterology (AEG) and the three societies of Primary Care in Spain (SEMFyC, SEMERGEN and SEMG) designed an online survey registering 140 variables regarding demographics, type of practice, continuous education received, preferences on management and access to health technology. Survey was submitted via e-mail to the members of the three societies. Responses were anonymously codified. Truncated responses were included up to last question answered. Responses were weighted by province, gender, age and type of practice. Categorical variables were represented as percentage and 95% confidence interval (CI), numerical variables as mean and standard deviation (for normal distribution) or median and inter-quartile range (IQR) (if not normal). Survey was performed using the AEG-REDCap platform.
Results: A total of 1,581 responses were received between December 2017 and March 2018. After removing blank and duplicate responses 1,425 were valid for analysis (representing 5% of all Primary Care doctors in Spain). Of them, 66% (95%CI = 64–68%) were women and the average age was 48 years (SD = 11). 59% were from urban context, 20% from semi-urban and 21% from rural. 93% provided public practice. No respondent bias was identified in the known variables. 48% of physicians had read at least one Maastricht consensus, and 21% had read Maastricht V. 87% of doctors had read at least one national or international guideline or consensus on *H. pylori* or dyspepsia. 34% had attended a continuous education course related to *H. pylori*, the majority of them in the last four years (median 2, IQR = 1–4 years). Course access was region dependent, ranging from 18% in Andalucia to 65% in Madrid. Only 16% of doctors responded they knew local *H. pylori* prevalence, 63% did not know and 21% knew that there was no data or it was outdated. Local prevalence reported by those who "knew" was higher than the prevalence expected by those who "did not know" (43% vs. 32%). Information on resistance to clarithromycin rates showed similar patterns: only 13% reported knowing them, and 21% reported there was no data or outdated, and expected resistance was lower (16%) than reported (23%).
Conclusion: Although Spanish Primary Care physicians seem relatively updated through literature, continuous medical education updates are region dependent and should be extended nationally. Lack of knowledge on, and underestimation of, prevalence and resistance rates are due both to lack of educational updates as well as lack of scientific studies in the literature.
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P1202 EVALUATION OF CURIAN HPSA FLUOROMETRIC ASSAY. A NOVEL, RAPID IMMUNOASSAY FOR THE DETECTION OF *HELICOBACTER PYLORI* ANTIGENS IN HUMAN STOOL

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Introduction: Stool antigen has become a widely acceptable method for detection of *H. pylori*. This non-invasive method provides an alternative to the more invasive techniques of biopsy. Gastric disease attributed to *Helicobacter pylori* includes chronic gastritis and peptic ulcer disease. The recent Maastricht V[1] Consensus Report indicates that serology tests performance may be variable due to geographic location and recommends the use of the stool antigen tests as an aid in the detection of *Helicobacter pylori* disease in the primary care setting.
The purpose of this study was to evaluate the sensitivity and specificity of a novel, rapid immunoassay compared to the gold standard method of detection. Curian HpSA Fluorometric (RUO), is an innovative, rapid, qualitative, immunoassay that utilizes fluorescent technology for the detection of *Helicobacter pylori* antigens in human stool specimens. The test uses monoclonal anti-*Helicobacter pylori* antibodies for both capture and detection. For clear interpretation, the Curian Analyzer (reader) is used to report results.

Aims and Methods: The Curian HpSA Fluorometric (RUO) assay was compared using 95 prospective positive stools and 53 retrospective negative stools characterized by UBT, Histology and Culture (Gold Standard). Samples were acclimated to room temperature and tested according to the Curian HpSA (RUO) Package Insert.
Results: The Curian HpSA Fluorometric assay (RUO) demonstrated Sensitivity of 94.73% and Specificity of 98.11% compared to the gold standard for diagnosis of *Helicobacter pylori* infection. Overall correlation was 95.95%.
Conclusion: The Curian HpSA Fluorometric (RUO) assay performance demonstrated comparable sensitivity and specificity compared to the gold standard for detection of *H. pylori*. The 20 minute, rapid, qualitative assay provides the end user with accurate interpretation of results without subjective review. Curian HpSA Fluorometric is a 20 minute rapid test for the accurate, non-invasive detection of *Helicobacter pylori* in human stool specimens.
Disclosure: Nothing to disclose

P1203 EFFICACY OF VONOPRAZAN-BASED THERAPY COMPARED TO PROTON PUMP INHIBITOR (PPI) IN *H.PYLORI* ERADICATION THERAPY

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Introduction: PPI-based therapy is one of the most popular *H.pylori* eradication therapies in the world. However, first-line eradication rate is decreasing in Japan, because *H.pylori* acquired resistance to antibiotics. It is known that most antibiotics are not effective under strong acid secretion. So in order to improve the eradication rate, gastric acid secretion must be reduced more rapidly and strongly.
Vonoprazan is newly developed potassium competitive acid blocker (P-CAB) and more effective in reducing gastric acid secretion than PPI.
Aims and Methods: The aim of this study is to clarify the efficacy of Vonoprazan-based eradication therapy and compare to PPI-based therapy.
The subjects were 1215 patients who were diagnosed as *H.pylori* infection in our institution from June 2014 to December 2017 using blood antibody positive. These patients were grouped into three; Vonoprazan group (VPZ) and Rabeprazole group (RPZ) and Lansoprazole group (LPZ). We evaluated retrospectively first-line and second-line eradication rate and statistical analysis.
Each first-line regimen of VPZ was 7days, Vonoprazan 20mg bid + AMPC750mg bid + CAM and second-line regimen was 7days, Vonoprazan 20mg bid + AMPC750mg bid + MNZ250mg bid.
Each first-line regimen of RPZ was 7days, Rabeprazole 10mg bid + AMPC750mg bid + CAM. Second-line regimen of RPZ was 7days, Rabeprazole 10mg bid + AMPC750mg bid + MNZ250mg bid.
Each first-line regimen of LPZ was 7days, Lansoprazole 30mg bid + AMPC750mg bid + CAM, second-line regimen of LPZ was 7days, Lansoprazole 30mg bid + AMPC750mg bid + MNZ250mg bid.
Results: The number of first-line regimen of VPZ patients was 350, and eradication was achieved in 321 patients (91.7%). RPZ patients was 309, and eradication was achieved in 229 patients (74.1%), and LPZ patients was 378, and eradication was achieved in 301 patients (79.6%) respectively. Eradication rate of VPZ is higher than RPZ and LPZ ($P < 0.0001$ and < 0.0001 respectively).
The statistically number of second-line regimen of VPZ patients was 40, and eradication was achieved in 34 patients (85.0%).
RPZ patients was 65, and eradication was achieved in 60 patients (92.3%), and LPZ patients was 70, and eradication was achieved in 61 patients (87.1%) respectively. There were no significant difference in second-line regimen.
Adverse events such as rash, diarrhea, 6.9% in VPZ, 16.2% in RPZ, 6.3% in LPZ.
Conclusion: Vonoprazan-based regimen was superior to conventional PPI (Rabeprazole and Lansoprazole) in eradication rate of *H.pylori*. In addition, it was a safe regimen on the issue of adverse events.
Disclosure: Nothing to disclose

P1204 EFFICACIES OF DIFFERENT PROTON PUMP INHIBITOR-BASED 14-DAY BISMUTH-CONTAINING QUADRUPLE REGIMENS FOR THE INITIAL ERADICATION OF *HELICOBACTER PYLORI* IN THE SOUTHEAST COASTAL REGION OF CHINA: AN OPEN-LABEL, RANDOMIZED CLINICAL TRIAL

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Introduction: *Helicobacter pylori (H. pylori)* is reported to be associated with a range of gastrointestinal diseases, such as gastritis, peptic ulcer, gastric cancer, and mucosa-associated lymphoid tissue lymphoma. Although the prevalence of *H. pylori* infection has decreased on a global scale, it remains a serious concern in China with a prevalence of 66% among rural populations and 47% among urban populations. The Kyoto global consensus report on *H. pylori* gastritis has defined it as an infectious disease and suggested that all populations infected with *H. pylori* should receive eradication treatment. Therefore, the selection of a cost-effective regimen for the initial eradication of *H. pylori* is urgently needed in China for the consideration of regional prevalence and cost-benefit ratio.
Standard triple regimens have failed to reach 80% efficacy and 14-day bismuth-containing (BQ) regimen is the most commonly used regimen in China currently according to a real-world Asia-Pacific *H. pylori* survey. Resistance rates towards amoxicillin and furazolidone in the southeast coastal region of China were 0.1% and 0.1%. Furthermore, as a component of BQ regimens, proton pump inhibitor (PPI) plays an important role in the eradication of *H. pylori.*
Aims and Methods: We aimed to evaluate the efficacy and safety of different PPI-based 14-day BQ regimens for the initial eradication of *H. pylori* and to provide credible evidence to justify the clinical use of PPIs. In total, 175 eligible patients were enrolled and randomly assigned to 14-day BQ regimens consisting of colloidal bismuth pectin (0.4g), amoxicillin (1000mg), furazolidone (100mg) and a PPI, all twice a day. The PPIs used in the five regimens were Group A (SOMAC, pantoprazole sodium enteric-coated capsules, 40mg), Group B (Pantoloc, pantoprazole enteric-coated tablets, 40mg), Group C (Takepron, lansoprazole enteric-coated capsules, 30mg), Group D (Nexium, esomeprazole magnesium enteric-coated tablets, 20mg), and Group E (Pariet, rabeprazole sodium enteric-coated tablets, 10mg). *H. pylori* status was reassessed by ^{13}C urea breath test on day 56 and negative status indicated the success of eradication treatment. Gastrointestinal symptoms and stool type in patients were assessed on day 0 and day 56 using a simplified Gastrointestinal Symptom Rating Scale (GSRS) and Bristol Stool Scale (BSS). Parenteral adverse effects and compliance were recorded simultaneously. Patients who took less than 80% of the total dose were poorly compliant.
Results: The total eradication rate of 14-day BQ regimens was 86.9% (152/175) and 95.6% (152/159) by intention-to-treat (ITT) and per-protocol (PP) analysis, respectively. The efficacies of groups A, B, C, D, and E by ITT analysis were 91.4% (32/35), 85.7% (30/35), 88.6% (31/35), 85.7% (30/35), and 82.9% (29/35), respectively ($p > 0.05$). In the PP analysis, the efficacies were 97.0% (32/33), 93.8% (30/32), 93.9% (31/33), 100% (30/30), and 93.5% (29/31), respectively ($p > 0.05$). The total GSRS score decreased significantly from day 0 to day 56(5.48 ± 0.321 vs. 2.76 ± 0.238, $p < 0.01$), and 12 of 15 gastrointestinal symptoms were observed to have prominent remission ($p < 0.05$). The stool type was improved distinctly after eradication treatment ($p < 0.01$). The rate of total parenteral adverse effects was 15.7% (25/159) and the total rate of poor compliance was 5.0% (8/159).
Conclusion: 14-day BQ regimens consisting of amoxicillin and furazolidone are effective and safe for the initial eradication of *H. pylori*. Efficacies of different PPI-based 14-day BQ regimens showed no significant difference.
Disclosure: Nothing to disclose

P1205 APPARENT INTRACELLULAR *HELICOBACTER PYLORI* DETECTION BY IMMUNOHISTOCHEMISTRY AS INDEPENDENT RISK FACTOR FOR FAILURE OF FIRST-LINE ERADICATION THERAPY

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Introduction: *Helicobacter (H.) pylori* is considered as an extracellularly living bacterium; however, the microorganism can also be found in canaliculi of parietal cells resembling intracellular occurrence by immunohistochemistry, or even in the cytoplasm of surface epithelial cells, parietal cells and chief cells. Using immunohistochemical staining we have been able to observe that the detection of apparent intracellular *H. pylori* (aiHp) has been associated with reduced eradication rates after antimicrobial therapy.
Aims and Methods: Considering antimicrobial resistance, we aimed to investigate the impact of aiHp detection on the success rate of the first-line eradication therapy.
Paraffin-embedded gastric corpus biopsies of 52 *H. pylori*-infected patients, in which the pathogen was found by immunohistochemistry, not only extracellularly but also apparently intracellularly, and of matched controls with solely extracellular *H. pylori* (eHp) occurrence were analysed. All patients were naïve to treatment and have received antimicrobial therapy consisting of amoxicillin, clarithromycin and PPI. Further inclusion criteria were the occurrence of a second corpus biopsy obtained between two and four months after the first endoscopy and a positive PCR result of the first biopsy. The PCR was targeting a *H. pylori*-specific sequence of the 23S rRNA gene, which includes the region of potential point mutations associated with resistance to clarithromycin.
Results: The overall eradication rate was 78.8% by eHp versus 46.2% by eHp/aiHp cases; in clarithromycin susceptible cases the respective values were 89.5% and 57.1%. Logistic regression analysis revealed that both resistance to clarithromycin and apparent intracellular detection are highly significant ($p \leq 0.001$) and independent predictors of eradication failure with an odds-ratio (95% CI) of 5.2 (2.1–12.7) and 4.3 (1.8–10.3), respectively. Out of 13 aiHp cases that failed eradication with a clarithromycin sensitive strain in the first biopsy, 12 (92.3%) developed a resistance associated mutation.
Conclusion: Occurrence of aiHp was clearly shown to be an independent risk factor for failure of the first-line eradication therapy. Our data suggest the importance of immunohistochemical staining for *H. pylori* in corpus biopsies; aiHp should be taken into consideration with regard to therapy options.
Disclosure: Nothing to disclose

P1206 PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): IMPACT OF RESISTANCE ON EFFICACY.

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Introduction: The specific impact of antibacterial resistance on *Helicobacter pylori* eradication treatments is a fundamental factor in designing management strategies.

Aims and Methods: Our aim was to evaluate the effect of *H. pylori* resistance in different first-line treatments by European Gastroenterologists in their routine clinical practice. A Local Coordinator was selected from each country with more than 10 *H. pylori* references in PubMed. Each Coordinator selected a representative group of recruiting investigators from his/her country. An e-CRF was created on AEG-REDCap to systematically register all adult patients infected with *H. pylori*. Variables included: *H. pylori* diagnostic test used, use of culture and susceptibility testing, or molecular tests for the evaluation of antibiotic resistance.

Results: Resistance data was available in 677 treatment-naïve patients. Although culture and antibiotic susceptibility testing were not systematically performed and more data is needed to draw definite conclusions of the effect of resistance to some antibiotic combinations, the data from the present study show that resistance affected nearly all prescribed combinations (data shown in table). The negative impact of resistance was more marked in triple therapies, in which clarithromycin resistance halved (89 vs. 44%) the efficacy of triple therapy with clarithromycin and amoxicillin.

Conclusion: Triple therapies are greatly affected by single resistance to their constituent antibiotics. Non-bismuth quadruple therapies appear to be unaffected by single resistance but may be affected by dual clarithromycin-metronidazole resistance.

	No resistance		Clarithromycin		Metronidazole		Dual (C + M)	
	N	%E	N	%E	N	%E	N	%E
PPI+C+A	345	88.7%	23	43.5%	137	83.2%	7	57.1%
PPI+C+A+M	34	94.1%	11	90.9%	11	81.8%	5	80.0%
PPI+C+M	20	80.0%		NA		NA		NA
PPI+C+A+T seq	218	88.5%	29	86.2%	218	84.9%	123	84.6%
PPI+C+A+B	3	100%		NA		NA		NA
PPI+C+A+M seq	36	86.1%	7	71.4%	27	59.3%	8	62.5%
PPI+A+M	49	87.8%	25	84.0%	5	80.0%	1	100%
PPI+A+L	5	100%	5	100%	14	85.7%	13	84.6%
PPI+M+Tc+B s.c	26	88.5%	7	85.7%	22	86.4%	12	75.0%
PPI+C+A+T	24	91.7%	24	100%	24	100%	14	100%
PPI+M+Tc+B	3	100%	10	90.0%	6	100%	5	100%

N – total resistant patients, NA – not applicable/unknown, PPI – proton pump inhibitor, Conc – concomitant, Seq – sequential, C – clarithromycin, M – metronidazole, A – amoxicillin, L – levofloxacin, B – bismuth, Tc – tetracycline, s.c. – single capsule

[Table 1]

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions and is an advisor of Mayoly.

P1207 META-ANALYSIS OF BISMUTH QUADRUPLE THERAPY IN SINGLE CAPSULE FOR THE ERADICATION OF *HELICOBACTER PYLORI*

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Introduction: Single-capsule bismuth quadruple therapy (scBQT) plus a proton pump inhibitor (PPI) has been proposed as first alternative and rescue therapy for the eradication of *Helicobacter pylori*.

Aims and Methods: To perform a meta-analysis evaluating the efficacy and safety of scBQT as any line of treatment. Studies were selected up to January 2018. Efficacy was estimated using the generic inverse variance method, and safety through the incidence rate of adverse events (AEs).

Results: In total, 20 studies (2,685 patients) were included in the analysis. Intention-to-treat (ITT) efficacy was 92% (95%CI = 89–95%, 14 studies, $I^2 = 87\%$) in first-line, 91% (95%CI = 87–95%, 9 studies, $I^2 = 75\%$) in second-line and 80% (95%CI = 77–8%, 5 studies, $I^2 = 0\%$) in third-line. There were no significant differences per type or dosage of PPIs across treatment lines. In clarithromycin and metronidazole resistant infection, the ITT efficacy in first-line was 92% (95%CI = 88–97%, 3 studies, $I^2 = 0\%$) and 93% (95%CI = 89–97%, 4 studies, $I^2 = 0\%$) respectively. In patients previously treated with clarithromycin, ITT efficacy was 93% (95%CI = 89–98%, 6 studies, $I^2 = 63\%$). The incidence of AEs was 46% (95%CI = 36–56%, 16 studies, $I^2 = 90\%$), and mostly mild.

Conclusion: Treatment with Single-Capsule Bismuth Quadruple Therapy for 10 days represents a highly effective option (≥ 90%) in first and second-line, regardless of the type and dose of PPI, even in patients with clarithromycin or metronidazole resistant strains or in those who were previously treated with clarithromycin.

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions. Dr. Nyssen has no conflict of interests.

P1208 PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): EXPERIENCE WITH SINGLE CAPSULE BISMUTH QUADRUPLE THERAPY IN 1,200 PATIENTS

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Introduction: Bismuth quadruple therapy with a PPI, bismuth salts, tetracycline and metronidazole has resurfaced in Europe thanks to a new single-capsule formulation.

Aims and Methods: Our aim was to evaluate the efficacy and safety of the single-capsule bismuth quadruple therapy in the European Registry on *Helicobacter pylori* management. International multicenter prospective non-interventional registry starting in 2013 aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists. National coordinators were selected from each country to identify a representative group of recruiters. All infected adult patients were systematically registered at an e-CRF by AEG-REDCap. Variables included: Patients' demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat and per-protocol analyses were performed. Data monitoring was performed to ensure the quality of the data.

Results: So far, 21,302 patients from 27 European countries have been evaluated. Of these, 1,258 have been treated with single capsule bismuth quadruple therapy, of which 1,231 have finished follow-up. Of them, 1,148 have been prescribed following the technical sheet (10 days, 3 capsules q.i.d.) Average age was 52 years, 66% were women, and 18% had peptic ulcer. Results are shown in the Table. The majority of cases (60%) were naïve to *H. pylori* treatment. PPI type or dose did not influence eradication rate. 33% of cases suffered from adverse events (severe in 3%, and only 1% withdrew treatment due to adverse events). Only two serious adverse events were reported: hospitalization due to diarrhea and an allergic reaction treated with anti-histamine drugs, both solved without complications.

	ITT			PP			Compliance
	Hp-	N	%	Hp-	N	%	%
First-line (naïve)	610	666	92	602	633	95	96
Second-line	243	273	89	240	260	92	96
Third-line	124	151	82	120	142	85	95

ITT: intention-to-treat; PP: per-protocol.
[Table 1]

Conclusion: Treatment with single capsule bismuth quadruple therapy achieves *H. pylori* eradication in approximately 90% of patients by intention-to-treat in clinical practice, both in first- and second-line, with a favorable safety profile.

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions and is an advisor of Mayoly.

P1209 OUTCOMES OF FURAZOLIDONE-BASED QUADRUPLE THERAPY FOR *HELICOBACTER PYLORI* INFECTION AND PREDICTORS OF FAILED ERADICATION

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Introduction: With the increasing antibiotic resistance to *Helicobacter pylori* (*H. pylori*) worldwide, traditional triple therapies have become increasingly ineffective, with some studies reporting eradication rates as low as 50%. High antibiotic-resistant rate is one of the most important reasons. Selecting optimal therapies for antibiotic-resistant *H. pylori* infection has become an important global public health task. Compared to high rates of resistance observed with clarithromycin, metronidazole, and levofloxacin, *H. pylori* to furazolidone remains low in China. Although a number of studies with limited sample size demonstrate high efficacy of furazolidone, amoxicillin-based quadruple therapy (FABQT) for treatment of *H. pylori*, data on the impact of adverse events are not well described. Predictors of failed *H. pylori* eradication other than the choice of regimen or poor medication adherence are largely unknown. Therefore, we performed a retrospective study of patients who received FABQT for treatment of *H. pylori* at our center.

Aims and Methods: The aim of the study is to evaluate the outcome of furazolidone-based quadruple therapy for treatment of *H. pylori* and identify predictors of failed eradication. Patients with *H. pylori* infection treated with furazolidone, amoxicillin, bismuth, and proton pump inhibitor therapy (from January 2015 to December 2015 in Sir Run Run Shaw Hospital,Hangzhou, China) and received ^{13}C-urea breath test >4 weeks after treatment were evaluated. *H. pylori* eradication rate, treatment-related adverse events, and predictors of failed eradication, including age, gender, education levels, prior treatment history, smoking and alcohol status during treatment, PPI types, bismuth dose, treatment duration, diagnosis according to endoscopy and medication adherence were evaluated. Intention-to-treat (ITT) and per-protocol (PP) analyses were used to assess the H. pylori eradication rates. Categorical variables were compared using the χ^2 test or Fisher's exact student *t*-test. Univariate and multivariate analysis were performed to identify predictors of failed *H. pylori* eradication.

Results: Of the 992 patients treated and retested for *H. pylori*, the overall eradication rates were 95% (95%CI 94–96%) by intention-to-treat (ITT) and 95% (95%CI 94–97%) by per protocol (PP) analyses. *H. pylori* eradication rates as primary therapy were 95% (95%CI 94–97%) and 96% (95%CI 94–97%), while as rescue therapy were 91% (95%CI 87–96%) and 91% (95%CI 86–96%) per ITT and PP analyses, respectively. Among the 859 patients who completed the study protocol, 144 (17%) reported treatment-related adverse events including 24 (3%) leading to premature discontinuation of therapy. In the multivariate analysis, poor medication adherence (AOR = 6.7, 95%CI 2.8–15.8), >2 previous *H. pylori* treatments (AOR = 7.4, 95%CI 2.2–24.9), alcohol consumption during therapy (AOR = 4.4, 95%CI 1.5–12.3), and possibly smoking during therapy (AOR = 1.9, 95%CI 0.9–4.3) were associated with failed *H. pylori* eradication. Age, gender, education level, PPI type, bismuth dose, therapy duration, and the indication for treatment were not associated with failed *H. pylori* eradication.

Conclusion: Furazolidone-amoxicillin quadruple therapy in high clarithromycin-resistant area for *H. pylori* demonstrated high eradication rates as primary and rescue therapy with a favorable safety profile. Patient education targeting complete abstinence from alcohol and improved medication adherence may further optimize *H. pylori* eradication.
Disclosure: Nothing to disclose

P1210 CONCOMITANT VERSUS SEQUENTIAL THERAPY FOR THE TREATMENT OF HELICOBACTER PYLORI INFECTION: A TUNISIAN RANDOMIZED PROSPECTIVE STUDY

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Introduction: The objective of this study is to compare, in Tunisia, a region with 15% mean local resistance to clarithromycin, the efficacy rates of the concomitant versus the sequential *H. pylori* eradication therapy.
Aims and Methods: Our prospective randomized study included 152 patients with newly diagnosed H. pylori infection, randomized to receive a 10-day concomitant or 10-day sequential therapy. Treatment outcome was assessed by histopathological examination at least 6 weeks after therapy. Only patients per protocol (PP) ($n = 106$) were analyzed for eradication rates. Secondary end points included patient compliance and safety.
Results: The concomitant therapy group achieved statistically significant higher eradication rates when compared with the sequential treatment group in the PP analysis (49.1% versus 32.7%, $p = 0.001$), after adjusting for age, gender and the presence or not of ulcer and/or non-ulcer dyspepsia. Both groups displayed medium compliance rates (71.4%, 95% CI 97%-100% with sequential vs. 75.4%, 95% CI 98%-100% with concomitant). Regarding treatment safety, major adverse events that led to the discontinuation of both regimens were few, with no statistical difference between the two groups (36.8% for the concomitant therapy group and 30.6% for the sequential therapy group). However, diarrhea, dizziness, headache and anorexia were related with concomitant therapy with statistical significance ($p = 0.03$, 0.002, 0.000, 0.002, respectively).
Conclusion: Concomitant therapy led to statistically significant higher eradication rates over sequential therapy with moderate efficacy. Both therapies showed moderate compliance and an acceptable safety profile. The 10-day quadruple concomitant scheme should be the adopted for first-line *H. pylori* eradication in Tunisia.
Disclosure: Nothing to disclose

P1211 SINGLE-CAPSULE BISMUTH-BASED QUADRUPLE THERAPY AS SECOND-LINE OR SALVAGE TREATMENT FOR HELICOBACTER PYLORI INFECTION: A NEW WINDOW OF OPPORTUNITY IN A SOUTH-EUROPEAN COUNTRY?

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Introduction: *Helicobacter pylori* (*H. pylori*) infection is highly prevalent in Portugal and its eradication is formally recommended in multiple circumstances. However, the indiscriminate use of antimicrobials has led to a drastic rise in antibiotic resistance, with failure of traditional eradication schemes. Bismuth was not available in this South-European country, but a single-capsule bismuth-based quadruple treatment became recently available. This study aims to determine whether this quadruple regimen is useful as a second-line or salvage therapy.
Aims and Methods: This was a multicentric, retrospective study, with most patients included in a prospective database but without any direct intervention of the investigation team before or during treatment. All consecutive patients that were treated with bismuth-based quadruple therapy as second-line or salvage treatment between July-2017 and February-2018 were enrolled. Their medical records were reviewed and clinical and laboratorial parameters, as well as data on treatment efficacy and adverse events were retrieved. Patients were also contacted by telephone after treatment in order to confirm compliance (considered as adequate when at least 90% of prescribed medication was taken), adverse events and global satisfaction with this specific therapy.
Results: A total of 73 subjects were included (female – 74%; mean age – 56 ± 13.6 years). Patients had previously completed a mean of 2 eradication schemes (1 to 5): triple clarithromycin-based – 45.2%; sequential – 28.8%; concomitant – 17.8%; fluoroquinolone-based – 16.4%; rifabutine-based – 2.7%. The proton pump inhibitor of choice was esomeprazole (32.9%), followed by omeprazole (31.5%). Compliance was achieved in 87.7% and the overall eradication rate was 87.7% (95% confidence interval: 78.9–93.9). Treatment-related adverse effects were experienced by 22 patients (30.1%), being mild in 8, moderate in 6 and severe in 8. The main drawbacks of the treatment in the patient's perspective were its' high price (26%) and the adverse effects (17.8%). Failure to eradicate *H. pylori* was correlated with the following: previous rifabutine-base scheme (28.6% vs. 0%) and higher number of previous treatment regimens (2.6 ± 1.2 vs. 1.7 ± 0.7).
Conclusion: In this South-European country a single-capsule bismuth-based quadruple therapy is an excellent alternative in patients who have failed previous eradication schemes, with acceptable compliance and side effects.
Disclosure: Nothing to disclose

P1212 HIGH-DOSE CLARITHROMYCIN WITH P-CAB PLUS AMOXICILLIN TRIPLE THERAPY REGIMEN IS MOST RECOMMENDED ON 1ST *H.PYLORI* ERADICATION REGIMEN; A MULTICENTER CENTER PROSPECTIVE CASE STUDY

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Introduction: It has been believed that drug resistance is the most important cause of eradication failure on Amoxicillin (AMX) and Clarithromycin (CLR) based *H.pylori* (Hp) eradication therapy for a long time. Unfortunately, we have been permitted to prescribe only AMX and CLR as antibiotics of 1st eradication in Japan. So far, several proton pomp inhibitors (PPIs) have been used in Hp eradication therapy, most of reports said that the success rate of eradication about 70% regardless of CLR dose (400 or 800 mg/day) in Japan. Recently the ratio of CLR resistance in Japan comes up to over 30 %, we need to overcome CLR resistance on Hp eradication. On the other hand, recently it is considered that the stability of continuous gastric acid suppression is more important factor rather than CLR resistance. At the point of gastric acid suppression, we have been used so strong acid suppressive drug P-CAB (Potassium-Competitive Acid Blocker) rather than conventional PPIs. Since Feb. 2015, we have used P-CAB instead of previous PPIs in AMX and CLR based Hp eradication therapy to improve success rate of eradication.
Aims and Methods: The aim of this study is to elucidate the importance of CLR dose on success rate of P-CAB Vonoprazan (VPZ)-based triple therapy regimens. This study is a multicenter center (8 hospitals), prospective case study from Jan. 2012 to Jan. 2018. A total of 3,471 patients (Hp positive) were enrolled. Mean age of the patients was 52.1 years old. Fisher's exact test was used in all statistical analyses. Regimen of VAC (400 or 800) was VPZ (40 mg/day) b.i.d., AMX (1,500 mg/day) b.i.d. plus CLR (400 or 800 mg/day) b.i.d. for 7 days. The judgement of success or failure on the eradication therapy had been done with urea breath test on 3 months after eradication therapy to avoid false negative results. We compared which is better CLR 400 or 800 mg/day on P-CAB based triple therapy regimens of Hp eradication and checked their adverse events.
Results: The average success rate of VAC regimens was 91.0 % (3,032/3,332 = 91.0%, PPS). Success rate of VAC 800 showed significantly high (1,301/1,331 = 97.7%, PPS) rather than VAC 400 (1,762/2,001 = 88.1%, PPS) ($p < 0.001$). It was noteworthy that the average success rate of VAC 800 regimens (238/251 = 94.8 %) were significantly high rather than the average success rate of VAC 400 regimens (207/249 = 83.1%) ($p < 0.001$) on CLM resistance group. These results suggest that using high dose CLR with VPZ (P-CAB) plus AMX regimen is better on Hp eradication triple therapy regimen to overcome CLR resistance. Although its mechanism is unclear, the rapid and potent gastric acid-inhibitory effect of VPZ would provide a good environment for effective antibacterial action. VPZ has been available for Hp eradication since 2015, and the efficacy of first-line eradication therapy in Japan has dramatically improved.
Conclusion: High-dose CLR with P-CAB plus AMX triple therapy regimen is much better on Hp eradication therapy even if CLR resistance. We have been able to expect significantly high success rate (more than 97 %) as Hp 1st eradication therapy. This regimen is most recommended on 1st eradication regimen.
Disclosure: Nothing to disclose

P1213 THE HELICOBACTER ERADICATION ASPIRIN TRIAL (HEAT): RECRUITMENT AND DEMOGRAPHICS OF THE RANDOMISED PATIENT POPULATION

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Introduction: The Helicobacter Eradication Aspirin Trial (HEAT) is a multicentre, double blind, randomised controlled trial investigating whether *Helicobacter pylori* eradication reduces the incidence of hospitalisation for peptic ulcer bleeding (1). Participants are subjects aged over 60, taking low dose aspirin for at least four months at the time of recruitment; all participants were recruited from primary care. *H. pylori* positive participants were randomised to receive one week active trial treatment (lansoprazole 30mg, clarithromycin 500mg and metronidazole 400mg twice daily) or placebo. Recruitment to the trial started in 2012 and completed in 2017; follow-up is endpoint driven and is ongoing.

Aims and Methods: Participants are followed up using a bespoke web-based trial management system that communicates directly with HEAT Toolkit software downloaded at participating GP practices, which issues MIQUEST (2) queries searching follow-up criteria. The primary endpoint of the study is the rate of hospitalisation due to definite or probable peptic ulcer bleeding. The study will end when 87 adjudicated events have occurred. Events are tracked by accumulating information from MIQUEST searches of GP databases via the HEAT toolkit, patient contact, review of national secondary care admission and mortality data.

Results: HEAT is being conducted in practices across the whole of the UK with 188,428 invitation letters sent from 1,208 GP practices. A total of 37,247 positive responses were received, representing a 20% response rate. Of those, 30,025 patients were consented to the study of whom 5,356 *H. pylori* positive patients were randomised. The percent of *H. pylori* positive patients varied from 13% to 39% throughout the country. Multiple deprivation scores applied to the data indicated an increase in response with less deprivation, but a decrease in the number of randomised patients.

The mean age at randomisation for all participants was 73.6 ± 7.0 (SD) years, and 73.8% of participants are male. Only 7.2% of participants are smokers although 52.9% are ex-smokers. A total of 15% of the randomised patients have withdrawn from the trial, and 100 patients have died so far.

Conclusion: The trial methodology has shown that recruitment of large numbers of patients from primary care is attainable, with the assistance of the NIHR Clinical Research Network, and could be applied to other outcomes studies at relatively low cost.

Last year, there were almost 17,000 hospital admissions for gastric ulcers (3) and more than 1,850 recorded deaths for gastric and duodenal ulcers (4). If successful, the study will help to reduce NHS costs and improve health outcomes by reducing hospital admissions, increasing patient safety and preventing premature deaths.

Disclosure: Nothing to disclose

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TUESDAY, OCTOBER 23, 2018 09:00–17:00

Small Intestinal II – Hall X1

P1214 IMBALANCE OF TREG/TH17 IN RAT NSAID-INDUCED INTESTINAL INJURY

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Introduction: Non-steroidal anti-inflammatory drugs (NSAIDs) are some of the most commonly prescribed drugs in the world. However, recently its gastroduodenal complications, especially intestine injury has attracted people's attention. The pathogenesis is not yet completely clear, therefore there is no effective treatment measures. Treg/Th17 have been described as two distinct subsets from Th1 and Th2 cells and have the opposite effects on autoimmunity. Treg/Th17 balance controls inflammation and may be important in the pathogenesis of inflammatory bowel disease and other autoimmune diseases. However,there are few studies on the imbalance of Treg/Th17 in NSAIDs induced intestinal injury.

Aims and Methods: We aimed to explore whether there's an imbalance of Treg/Th17 in NSAIDs induced intestinal injury.

20 Male SD rats weighing 180–200g were randomly divided into 2 groups. The control group was given 1ml100 $g^{-1}d^{-1}$ saline by gavage; the experimental group was given of diclofenac sodium 10 $mgkg^{-1}d^{-1}$ by gavage, the rats were sacrificed 5 days later. Assessed the gross and pathological injury of the intestine, the Th17 and Treg were detected by flow cytometry; Foxp3, RORγt were detected by RT-qPCR and IL-6, TGF-β, IL-17A, IL-10 were detected by ELISA.

Results: 1. The injury of small intestine:Multiple ulcers were seen in the small intestine mucosa of the experimental group, the mucosal were evidently congestion and edema. H&E staining revealed that the villous were edema and necrosis,massive inflammatory cells were observedin the lamina propria. 2. The proportion of Th17 and Treg cells in the mesenteric lymph node: The percentage of IL-17^+T cells and $CD25^+Foxp3^+$ cells in gated $CD4^+$ T cells both significantly increased in the experimental groups ($P<0.05$). However the ratio of $CD25^+Foxp3^+$Treg/IL-17^+T cells decreased significantly in the experimental group ($P<0.05$). 3. The specific transcription factor RORγt of Th17 and Foxp3 of Treg. The expression of RORγt-mRNA significantly increased ($P<0.01$), and the Foxp3-mRNA expression level also increased,although it was not statistically significant ($P>0.05$), while the ratio of Foxp3/RORγt decreased ($P>0.05$). 4. The IL-6 and IL-17A levels in the experimental group increased significantly ($P<0.05$), while the IL-10 expression was significantly decreased ($P<0.05$), although the TGF-β1 expression was decreased, it was not statistically significant ($P>0.05$). 5. Pearson correlation analysis: The injury scores has a significant negative correlation with Treg/Th17, Foxp3/RORγt, IL-10, TGF-β1 ($P < 0.05$), and has a significant positive correlation with IL-6, IL-17A ($P < 0.05$).

Conclusion: There is an imbalance of Treg/Th17 in NSAID induced intestine injury, immune imbalance may be involved in the pathogenesis of NSAID induced intestinal injury.

Disclosure: Nothing to disclose

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P1215 TERMINAL ILEITIS: WHEN IS IT NOT CROHN'S DISEASE?

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Introduction: Terminal ileitis (TIS) is defined as inflammation of the terminal ileum (TI) signified by ulcers, erosions, oedematous/erythematous mucosa. It can be idiopathic or secondary to crohn's disease (CD), infections and medications. The aim of this study was to assess the outcome of patients with idiopathic terminal ileitis (ITI).

Aims and Methods: Patients with TIS and no history of CD (ITI group) were compared to patients with terminal ileum Crohn's disease (TICD). Patients with a recent history of gastroenteritis, NSAIDs and angiotensin receptor blockers use were excluded.

Results: 23 patients with ITI (mean age 39 years; 57% females) were compared to 27 patients with TICD (mean age 39 years; 59% females).

Reasons for small bowel capsule endoscopy (SBCE) in the ITI group included: abdominal pain (52%), bloating, nausea, vomiting (48%), diarrhoea (39%), persistent iron deficiency anaemia (22%), weight loss (4%), rectal bleeding (4%), low b12 and calcium (4%). All patients in the CD group had a SBCE to assess disease activity.

In patients with ITI, 17% had evidence of minor findings on colonoscopy including erosions/aphthous ulcers with histology showing non-specific inflammation in 2 patients (n = 4 50%).

In tandem, all patients with ITI (5) who underwent small bowel (SB) MRI had a normal investigation compared to the TICD group in whom MRI SB was abnormal in 75%.

Similarly the mean faecal calprotectin (FC) (160 vs 99 ug/g $p = 0.791$) and CRP (13 vs 7 mg/L; $p = 0.209$) were higher in the TICD group compared to the ITI group, although these did not reach statistical significance.

The mean number of ulcers on (SBCE) in TI were significantly less in the ITI group (3) than in those with TICD (5) ($p = 0.005$). There was luminal narrowing in 2 patients (7%; $p = 0.493$) and mucosal oedema in 10 patients with TICD (37%; $p = 0.001$) with CD. Whereas patients with ITI had more aphthous/small ulcers, patients with TICD had more circumferential, deep, large, linear ulcers ($p = 0.018$).

Follow-up data with an average of 9 month was available for 78% (18) of the ITI group. 80% of those who underwent a repeat SBCE showed an improvement in the findings which corresponded to an improvement in CRP (3 previously 7mg/L; $p = 0.523$). At follow-up 39% improved clinically without treatment whilst 33% were treated as IBS. One patient who was treated with budesonide, improved.

Conclusion: Patients with ITI demonstrated a lower CRP, FC, and a normal MRI. SBCE findings for the ITI group were milder compared to TICD group and they were more likely to improve over time without treatment. Milder findings on SBCE can further reassure physicians to treat patients with a small number of ulcers in TI conservatively.

Disclosure: Nothing to disclose

P1216 *H. PYLORI* INFECTION MAY INDUCE SMALL INTESTINAL MUCOSAL INJURY

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Introduction: *Helicobacter pylori* (*H. pylori*) infection is a primary cause of gastric ulcer, duodenal ulcer, and gastric cancer. Capsule endoscopic studies for healthy volunteers revealed that 5–10% of healthy volunteers had small intestinal mucosal breaks. Many infectious disease and immunological disease are known to cause small intestinal mucosal injury. However, the etiology of small intestinal mucosal breaks in healthy volunteers, who have suffered from no such diseases and/or medicated no drugs, is unclear. In the studies of healthy volunteers, the several subjects brought into the act as healthy volunteers having an infection of *H. pylori*. Because *H. pylori* infection is seen as not having small intestinal influence, subjects infected with *H. pylori* are included in the studies. *H. pylori* infection is main cause of duodenal ulcer. In fact, it is undeniable that *H. pylori* infection has an impact on small intestinal mucosa. The aim of the study was to investigate whether there is an association between *H. pylori* infection and small intestinal mucosal injury.

Aims and Methods: This study was a retrospective study at the Nippon Medical School Hospital from January 2008 through March 2016. Patients aged 20–85 years were selected from a general pool of subjects who underwent capsule endoscopy for current or past obscure gastrointestinal bleeding. The background included age, gender, history, treatment with NSAIDs and/or acid suppressant (PPI, or histamine H2-receptor antagonist), final diagnosis, and *H. pylori* infection were investigated. Patients infected with *H. pylori* had a positive result by at least one diagnostic method: the serum antibody of *H. pylori*, ^{13}C-Urea breath test, or *H. pylori* antigenic agent of the stool within before and after 30 days capsule endoscopy examination. Patients diagnosed with inflammatory disease, malignant tumor, etc. were excluded. All subjects' video images were re-evaluated by two skilled reviewers to count small intestinal mucosal breaks. Eligible analyzable patient variables were compared between patients infected *H. pylori* and uninfected patients.

Results: Ninety-two patients (30 infected *H. pylori*/62 uninfected) were eligible for the study. By multivariate analysis of variables regarding the number of small intestinal mucosal breaks, patients treated with NSAIDs had more small-intestinal mucosal breaks than patients untreated NSAIDs (38%:8/21 vs. 18% 13.71P = 0.009), and the possible association was detected between patients infected *H. pylori* and uninfected patients 67%:14/21 vs. 37%:26/71; (P = 0.056). In comparing between patients infected *H. pylori* and uninfected patients, the rate of patients with small intestinal mucosal breaks was greater in patients infected *H. pylori* (7%:14/30 vs. 11%:7/62; P = 0.001). After excluding the patients treated with NSAIDs, the number of small intestinal mucosal breaks was also statistically greater in patients infected *H. pylori* than in uninfected patients (1.16 ± 1.51 vs. 0.38 ± 0.62; P = 0.001).

Conclusion: There is high possibility that *H. pylori* infection induces small intestinal mucosal injury.

Disclosure: Nothing to disclose

P1217 EVIDENCE FOR IMMUNE ACTIVITY IN FUNCTIONAL DYSPEPSIA AND THE IRRITABLE BOWEL SYNDROME: A SYSTEMATIC REVIEW

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Introduction: Functional dyspepsia (FD) and the irritable bowel syndrome (IBS) are functional gastrointestinal disorders (FGIDs), for which there are no explicit pathological changes identified on routine endoscopy. There is evidence in the literature of a dysregulated gastrointestinal immune response potentially driving the onset and continuation of symptoms such as early satiety, bloating, abdominal pain and nausea in FD and IBS, however the mechanisms by which this occurs has not been fully characterised.

Aims and Methods: We systematically reviewed the FD and IBS literature in order to collate the evidence for immune activation in common FGIDs. Our review focused on answering the research question: 'Do IBS and FD have clinically definable immune profiles?' We aspired to elucidate the cell types and associated molecules that may be implicated in the subtle inflammatory phenotype observed in these conditions. A search of seven literature databases was conducted using the following keywords and phrases: 'immun*', 'functional gastrointestinal disorder', FGID, 'functional dyspepsia', 'non-ulcer dyspepsia', 'idiopathic dyspepsia', 'irritable bowel syndrome', and IBS. References were then screened for suitability based on defined inclusion and exclusion criteria. Data presented relating to immune effectors such as cytokines and cellular populations were collated for analysis.

Results: The 51 papers determined to meet stringent selection criteria for this review provided evidence of specific alterations in the systemic and local immune systems in both FD and IBS. In addition to duodenal eosinophilia (FD) and increased colonic mast cells (IBS), variations in circulating IL-6 and IL-10 cytokine activity, along with increases in circulating $\alpha4^+\beta7^+$ gut-homing T cell number appear to be linked to the pathophysiology of both FD and IBS. There seems to be no change in the proportion of either circulating or local $CD3^+$ lymphocyte numbers in either condition. Patients with FD have higher peripheral proportions of both activated ($CD45RO^+$) and naïve ($CD45RA^+$) T lymphocytes, however there is debate in the literature regarding the proportions of small intestinal mast cells in this condition suggesting disease heterogeneity. There was evidence for a peripheral B cell activation in IBS patients, with studies reporting increased expression of activation markers ($CD80^+$, $CD86^+$) and higher IgG expression, suggestive of antigen presentation and reaction. Further to this, increased numbers of activated T lymphocytes ($CD45RO^+$) were reported in the colon of IBS patients.

Conclusion: Evidence from the literature suggests that underlying immune activity in FD and IBS is likely related to subtle alterations in the activation status of the cellular populations at both the systemic and local level, rather than an influx of newly recruited cells. Heterogeneity among subgroups of patients with either FD or IBS complicate studies in the field. It is evident that well-characterised patient cohorts including sufficient participant numbers will be required to elucidate the interplay of immune mechanisms that drive the development of FGIDs.

Disclosure: Nothing to disclose

P1218 SYSTEMATIC REVIEW WITH META-ANALYSIS: PREVALENCE AND PREDICTORS OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN IRRITABLE BOWEL SYNDROME

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Introduction: SIBO is common among patients with IBS, and symptoms of IBS are relieved after treatment of SIBO with antibiotics. The reported prevalence of small intestinal bacterial overgrowth (SIBO) among individuals with irritable bowel syndrome (IBS) is highly variable,ranging 4% to 84%, which may be related to the testing methods performed to diagnose SIBO.

Aims and Methods: The primary aim of the study was to evaluate overall and test-specific pooled prevalence of SIBO among individuals with IBS. The secondary aims were to determine the pooled odds ratio (OR) of SIBO among individuals with IBS compared to controls, and also to examine predictors associated with SIBO among patients with IBS. PubMed, Cochrane Library, and EMBASE through July 2017 were searched to identify studies evaluating the prevalence of SIBO in IBS. The pooled prevalence of SIBO among individuals with IBS and the pooled odds ratio (OR) of SIBO among those with IBS compared to healthy controls was calculated. Predictors of SIBO among IBS patients were also evaluated.

Results: Fifty studies (8,398 IBS, 1,432 controls) met the inclusion criteria. Overall pooled prevalence of SIBO in IBS was 38% (95%CI 32–44%) and was higher among individuals with IBS (OR = 4.7, 95%CI 3.1–7.2) compared to controls. The pooled prevalence of SIBO in IBS was higher in studies diagnosed by breath tests (40%, 95%CI 33–46%) compared to cultures (19%, 95%CI 8–30%). Furthermore the prevalence of SIBO was higher in studies diagnosed by LBT (47%, 95%CI 39–56%) compared to GBT (31%, 95%CI 24–38%). Among those with IBS, female gender (OR = 1.5, 95%CI 1.0–2.1), older age (standard mean difference = 3.1 years, 95%CI 0.9–5.4), and IBS-diarrhea (OR = 1.7, 95%CI 1.3–2.3) compared to other IBS subtypes increased the odds of SIBO; proton pump inhibitor (PPI) use (OR = 1.1, 95%CI 0.7–1.7) was not associated with SIBO.

Conclusion: More than one-third of IBS patients tested positive for SIBO, and the odds of SIBO in IBS were increased nearly five-fold. The prevalence of SIBO varied according to the diagnostic modality performed. Female gender, older age, and IBS-diarrhea, but not PPI use, were associated with SIBO among individuals with IBS.

Disclosure: Nothing to disclose

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P1219 BREATH TESTS FOR SMALL INTESTINAL BACTERIAL OVERGROWTH DIAGNOSIS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Small intestinal bacterial overgrowth (SIBO) is a syndrome characterized by increased colonization of the small bowel by colonic bacteria. Despite jejunal culture remains the diagnostic mainstay, in clinical practice the diagnosis is achieved by glucose breath test (GBT) or lactulose breath test (LBT). Therefore we performed a meta-analysis aimed to estimate pooled sensitivity and specificity of breath tests for SIBO diagnosis.
Aims and Methods: We searched in main databases (PubMed, Scopus, ScienceDirect, EMBASE) articles using the following keywords: (Small intestinal OR bacterial overgrowth) AND (breath test OR diagnosis OR lactulose OR glucose). Only studies in which breath tests were compared to culture of jejunal aspirate were selected. Data were entered the MetaDisc 1.4 software to calculate pooled sensitivity, specificity, positive and negative likelihood ratio (LR) and summary of area under the curve (SROC), as well as their 95% confidence intervals (CI).
Results: Twelve studies, enrolling 630 patients overall were selected. GBT showed a pooled sensitivity of 58.3% (95% CI 51.4–64.9%), a specificity of 83.5% (95% CI 79.1–87.2%), a positive LR of 2.7 (95% CI 1.6–4.7), a negative LR of 0.5 (95% CI 0.4–0.8) and a SROC of 0.76.
LBT had a sensitivity of 42.0% (95% CI 31.6–53.0%), a specificity of 70.6% (95% CI 61.9–78.4%), a positive LR of 1.3 (95% CI 0.7–2.2), a negative LR of 0.8 (95% CI 0.6–1.1) and a SROC of 0.56.
Conclusion: Breath tests do not show excellent performances in comparison to the gold standard. However, keeping into account that SIBO is a benign disease that in most cases requires a simple antibiotic therapy, they can be considered as a surrogate test to replace the invasive one. In this context, GBT has a better sensitivity and specificity than LBT and, therefore, should be preferred.
Disclosure: Nothing to disclose

P1220 THE CHANGING AND CHALLENGING FACE OF PROTON PUMP INHIBITORS -RELATED SMALL INTESTINAL BACTERIAL OVERGROWTH

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Introduction: In the last decade the relationship between proton pump inhibitors (PPI) and small intestinal bacterial overgrowth (SIBO) has covered an extensive, controversial interest in the literature, with meta-analysis confirming this association (1,2).
Aims and Methods: To update, in our experience, this phenomenon from a temporal point of view, comparing two periods: 2005–2010 *vs* 2012–2017. This dichotomy was chosen based on an increased interest on this issue in the literature from 2010 on.
Methods: From November 2012 to November 2017, 970 consecutive out-patients entered the study. 458 were eligible for Glucose Hydrogen Breath test for SIBO diagnosis (GHBT) (388 on PPI; 70 pts off PPI for at least 5 years: 50 IBS, 20 Control). This cohort of patients (group A) was compared to that of 450 out-patients studied in 2010, for the prevalence of SIBO (group B) (3) and to that of 1056 out-patients studied in 2011 for the epidemiology of the use of PPI in the period 2005–2010 (group C) (4). GHBT was assessed by Breath Tracker digital microlyzer. Symptoms frequency and intensity (abdominal pain, bloating, diarrhea) were recorded by means of a visual analogue scale. Exclusion criteria: neoplasia, malabsorption diseases, metabolic/hormonal disturbances, use of antibiotics, laxatives, neurological treatment. Long-term continuous PPI therapy (LTc) was defined >9 months/yr for at least 2 yrs. Medium-term T (MT): 6–8 months/yr for at least 2 yrs. Short-term T (ST):1–5 months/yr for at least 2 yrs. Statistical analysis were carried out by SPSS software.
Results: Mean age and gender distribution in the group A, B and C were comparable (46 ± 18 SD, 39 ± 20, 45 ± 21 yrs; M: 55%, 57%, 59%). The use patterns of PPI in the 2 period were:
*LTc MT *ST
2005–10 79% Not evaluated 21%
2012–17 25% 35% 40%. * $P < 0.001$
SIBO in group A e B was as follows:
LTc MT ST IBS C
Group A 50% 19% 17% 18% 5%
Group B 68% 22% 14% 20% 5%
Conclusion: 1) LTc treatment has decreased significantly from 79% to 25%, leaving room to a MT (35%) and ST (40%) patterns of therapy.
2) Although the frequency of SIBO in LTc in group A remains high (50%), it involves only 25% of pts on PPI, practically "saving" those on MT and on ST modalities.
3) Informed medical culture, increased awareness of potential side-effects and financial restraints from Health Institutions may be the reasons for such changes.
Disclosure: Nothing to disclose

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P1221 SERUM REGENERATING ISLET-DERIVED 3-ALPHA PREDICTS THE EVOLUTION OF POTENTIAL COELIAC DISEASE INTO OVERT COELIAC DISEASE

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Introduction: Potential coeliac disease (PCD) is a form of coeliac disease (CD) characterized by positive coeliac antibodies, but normal duodenal mucosa. Currently, there are not noninvasive biomarkers able to predict the onset of villous atrophy in PCD patients. Serum regenerating islet-derived 3-alpha (Reg3alpha) is a biomarker of mucosal damage in enteropathies, including CD.
Aims and Methods: The aim of this study was to determine whether serum Reg3alpha predicts the development of villous atrophy in PCD patients. We included 12 PCD patients who maintained gluten-containing diet and yearly underwent upper endoscopy with duodenal biopsies. Sera were taken from all these patients at the same time of upper endoscopy over their follow-up. Serum Reg3alpha was detected using a commercial ELISA kit.
Results: Along the follow-up, four out of the 12 PCD patients developed an overt CD so that they started gluten-free diet (GFD). In all these four PCD patients serum levels of Reg3alpha increased at or immediately prior to overt CD diagnosis (median 32.30 ng/ml, range 13.62–42.59 ng/ml) in comparison to baseline concentrations (median 18.33 ng/ml, range 10.83–25.25 ng/ml). In addition, serum levels of Reg3alpha were down-regulated by at least 12 months of GFD (median 11.14 ng/ml, range 4.73–26.12 ng/ml) at similar concentration to baseline in these four patients. Low levels of serum Reg3alpha (median 15.00 ng/ml, range 0.77–25.59 ng/ml) were found in the remaining eight PCD patients.
Conclusion: In a relatively small sample of PCD patients, when considering that PCD is quite rare, we demonstrated that serum Reg3alpha predicts the evolution of PCD into overt CD. These findings suggests that Reg3alpha can identify PCD patients who should undergo upper endoscopy to confirm overt CD, thus reducing time- and cost-consuming procedures.
Disclosure: Nothing to disclose

P1222 SCREENING FOR COELIAC DISEASE

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Introduction: Coeliac disease (CD) is a lifelong autoimmune disease affecting about 1% of the population, although many are undiagnosed. Coeliac disease is caused by an abnormal immune response, in genetically susceptible individuals, against gluten proteins from wheat, rye and barley. We screened for coeliac disease in a previous cross-sectional population-based study (1). In the current study we screened for coeliac disease antibodies in seven additional population-based studies from our biobank.
Aims and Methods: The aim was to determine coeliac disease prevalence, as reflected by coeliac disease antibody positivity, in the eight Danish studies from the biobank at Center for Clinical Research and Disease Prevention and evaluate a possible change over time. The studies are listed in the table below. In total, we screened serum samples from 16.779 participants collected between 1976 and 2012 for tissue transglutaminase (TTG) IgA/IgG and deamidated gliadin peptide (DGP) IgG.
Results: The results of the screening are listed in the table below, both for the coeliac disease antibody positivity (IgA/IgG-TTG≥7 U/ml and/or IgG-DGP≥10 U/ml) and the additional cut-off of only TTG≥10 U/ml.
Conclusion: The coeliac disease antibody positivity was around 1 % in all the 8 studies. We found no marked changes of the prevalence over time.
Disclosure: Conflict of interest: The study was supported by the Tryg Foundation (7-11-0213), Dansk Cøliaki Forening (the Danish Celiac Disease Patient Organization), The Novo Nordisk foundation (NNF160C0022464), Independent Research Fund Denmark and Thermo Fisher Scientific, Allerød, Denmark. Thermo Fisher Scientific, performed the coeliac disease screening.

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Abstract No: P1222
Table 1

Study	Examination year	n	Coeliac disease antibody positivity (IgA/IgG-TTG≥7 U/ml and/or IgG-DGP≥10 U/ml)	Only TTG (IgA/IgG-TTG≥10 U/ml)
The 1936-cohort study, 40 years	1976–1977	1,038	0.8 % (8/1038)	0.2 % (2/1038)
The Monica-1 study	1982–1984	1,839	0.9 % (17/1839)	0.3 % (5/1839)
The 1914-cohort study, 70 years	1984–1985	798	0.9 % (7/798)	0.4 % (3/798)
The Monica-2 study	1986–1987	1,274	0.9 % (12/1274)	0.5 % (7/1274)
The Allergy90 study	1990–1991	1,101	1.0 % (11/1101)	0.3 % (3/1101)
The Monica-3 study	1991–1992	2,009	0.9 % (19/2009)	0.3 % (7/2009)
The Inter99 study	1999–2001	6,423	1.2 % (77/6423)	0.4 % (28/6423)
The Health 2006 study, 5-year follow-up	2011–2012	2,297	0.8 % (18/2297)	0.5 % (12/2297)
Total		**16,779**	**1.0 % (169/16779)**	**0.4 % (67/16779)**

P1223 SERONEGATIVE COELIAC DISEASE: CLINICAL FEATURES AND PREVALENCE AMONG COELIAC PATIENTS

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Introduction: Seronegative coeliac disease (SCD) is characterized by villous atrophy (VA) responding to a gluten-free diet (GFD) but without both/either IgA/IgG endomysial (EMA) and IgA/IgG tissue-transglutaminase (tTG) antibodies [1]. The quality of data on the epidemiology of SCD is limited due to the rarity of the condition and the confusion pertaining to the nomenclature. Prevalence of SCD among coeliac patients was historically reported to be as high as 10–20% [1–5]. However, more recently it has been shown to be around 2% of all coeliac patients [6,7]. In SCD age at diagnosis has been reported to be higher than in seropositive CD, classical presentation more common, while results for sex are discordant [3, 6–8]. We think we should distinguish true SCD in which reasons for seronegativity include early disease, late disease (with possible refractory CD), dermatitis herpetiformis and first degree familiarity for CD. Masked SCD is a second group of patients which display seronegativity at diagnosis because immunosuppressants or a GFD had already been started prior to antibody testing. Finally, a third group is that of patients with total IgA deficiency (serum IgA $\leq$ 2 standard deviations below normal age-adjusted means) in whom the finding of positive IgG EMA/tTG should support the diagnosis of conventional seropositive CD and not that of SCD [1].
Aims and Methods: To define prevalence and clinical features of patients affected by true SCD, masked SCD and CD+IgA deficiency among all the coeliac patients directly diagnosed in two referral centers for CD (Sheffield, UK and Pavia, Italy) from 01/2010 to 12/2017. IgA positive EMA/tTG and a VA while on a gluten-containing diet allowed the diagnosis of conventional seropositive CD. For IgA deficient patients class IgG antibodies were tested. HLA DQ2/DQ8 positive patients with IgA and IgG negative EMA/tTG and a certain degree of VA responsive to a GFD met the criteria for true SCD. VA and negative IgA/IgG EMA/tTG due to concomitant GFD or immunosuppressants allowed diagnosis of masked SCD.
Results: 692 coeliac patients (229M, mean age at diagnosis 42 ± 17 years, 154 classical) were directly diagnosed in 7 years. 24 patients (4M, 47 ± 17 years, 17 classical) had negative IgA and/or IgG EMA/tTG at diagnosis (prevalence 3.47%). In this group true SCD was diagnosed in 17 of them (prev 17/692 = 2.45%, 2M, 50 ± 17 years, 12 classical). 5 had masked SCD (prev 5/692 = 0.72%, 1M, 40 ± 19 years, 3 classical, 4 on a GFD and 1 on steroids and azathioprine at time of diagnosis) and showed positive serology after discontinuation of immunosuppressors or during gluten challenge. Finally, 2 patients had positive IgG EMA/tTG in the context of total IgA deficiency (prev 2/692 = 0.29%, 1M, mean age 35 ± 12 years, all classical). Classical presentation and female sex were statistically more common ($p < 0.001$) in the 24 seronegative patients and in true SCD than in conventional seropositive coeliacs (668, 225 M, 42 ± 17 years, 137 classical). Age at diagnosis was higher in true SCD than in the group of seropositive CD ($p = 0.50$) and masked SCD ($p = 0.70$), but not statistically significant.
Conclusion: We proposed a redefinition of the diagnostic categories of SCD. Our partial data show that true SCD is rare among coeliac patients, being this result in accordance with the high sensitivity of EMA/tTG. SCD is characterized by peculiar clinical features allowing the distinction from seropositive CD. With the recruitment of a larger sample size we think we will be able to see if prevalence of this condition has changed over the years.
Disclosure: Nothing to disclose

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P1224 ADULT COELIAC DISEASE REMISSION ASSESSMENT: DOES A D1 BIOPSY INCREASE THE DETECTION OF VILLOUS ATROPHY?

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Introduction: The diagnosis of Coeliac disease (CD) requires the presence of villous atrophy on duodenal biopsy. The duodenal bulb (D1) has been shown to be a sensitive site for detecting villous atrophy (VA) in newly diagnosed CD. However there is a scarcity of data from those with established CD.
Aims and Methods: In patients with established CD, we aim to determine whether D1 biopsies improved the identification of VA compared to biopsies from the second part of the duodenum (D2) alone. 251 patients with established CD were prospectively recruited from the endoscopy department at the Royal Hallamshire Hospital between 2013 and 2017. All patients were undergoing repeat gastroscopy to assess dietary adherence, with one biopsy taken from D1 and four from D2. Biopsies were classified according to Marsh criteria. We assessed concordance of histology between the D1 and D2 sites, and 95% confidence intervals were calculated for all results using a binominal distribution.
Results: 251 patients were recruited (70.5% female, age range 17–81 years, median age 53 years) having been on a gluten-free diet for a median duration of 6 years. Concordant results: 35.1% (n = 88, 95% CI = 29.16–40.96) had normal duodenal biopsies in both D1 and D2; 32.3% (n = 81, 95% CI = 26.49–38.05) had VA in D1 and D2; 18.3% (n = 46, 95% CI = 13.54–23.11) had raised intra-epithelial lymphocytes (IELs) only in both D1 and D2. Disconcordant results: 4.4% (n = 11, 95% CI = 1.85–6.91) had VA in D1 but not D2; 2.4% (n = 6, 95% CI = 0.50–4.28) had raised IELs in D1 but normal histology in D2. 2.8% (n = 7, 95% CI = 0.75–4.83) had VA in D2 but normal histology in D1; 4.8% (n = 12, 95% CI = 2.14–7.42) had IELs in D2 but normal histology in D1.
Conclusion: VA was confined to the duodenal bulb in 4.4% of patients with established CD. Thus a D1 biopsy in addition to distal duodenal biopsies increases the likelihood of detecting VA, although the significance of isolated VA in the bulb in patients on a gluten-free diet is yet to be determined.
Disclosure: Nothing to disclose

P1225 EFFECTS OF BLINDED ACUTE AND SUB-ACUTE GLUTEN CHALLENGE ON EXTRA-INTESTINAL AND GASTROINTESTINAL SYMPTOMS IN NON-COELIAC GLUTEN SENSITIVITY VERSUS HEALTHY CONTROLS

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Introduction: Non-coeliac gluten sensitivity (NCGS) is characterised by gastrointestinal (GI; e.g. bloating) and extra-intestinal (e.g. fatigue) symptoms that subjectively disappear after dietary exclusion of gluten, in the absence of coeliac disease. Previous research has shown that a 3-day exposure to gluten increases depression scores in self-reported NCGS patients, however acute effects of gluten were not investigated (Peters et al., 2014).
Aims and Methods: We aimed to investigate the effect of single-blind acute and sub-acute administration of 16g gluten on psychological and GI symptoms in healthy volunteers (HV) and NCGS patients.
Sixteen grams of gluten or whey protein (placebo) were mixed in 250mL of low fat, unsweetened yoghurt, which was consumed as an acute challenge. GI symptoms (bloating, cramps) were assessed using visual analogue scales (VAS;

100mm) every 15' until 180' after administration. At the same time points, extra-intestinal symptoms (fatigue, tension, depression) were assessed using VAS derived from the Profile of Mood States Questionnaire. Participants then consumed two gluten-free or gluten containing (8g) muffins at different time points per day for the following 5 days, as a sub-acute challenge. GI symptoms (ordinal values; zero until 7) and extra-intestinal symptoms (VAS) were scored at the end of each day. After a washout period of 2 weeks, participants crossed over to the alternative dietary arm. Responses over time (compared to pre-administration for the acute challenge and compared to the mean of the 2 days before the intervention period for the sub-acute challenge) were analysed using (generalized) linear mixed models.

Results: Twenty HV (3 men, 29.7 ± 2.6 years) and 10 NCGS patients (4 men, 32.9 ± 3.1 years) completed the study. After acute administration of gluten compared to placebo, fatigue scores increased in NCGS patients ($p = 0.015$), but not in HV ($p = 0.74$). Similarly, NCGS patients had higher tension scores after gluten compared to placebo ($p = 0.043$), contrary to HV ($p = 0.31$). Acute challenge of gluten did not alter depression scores compared to placebo ($p = 0.41$). After 5 days of sub-acute administration, no significant differences in fatigue scores were observed between healthy controls and NCGS patients ($p = 0.70$) nor between conditions ($p = 0.48$), but tension and depression scores were higher in both groups after gluten compared to placebo ($p = 0.053$ and 0.076, respectively).
Immediately following the acute challenge, NCGS patients showed more bloating ($p < 0.0001$) and pain ($p = 0.019$) compared to HV, regardless of whether gluten or placebo was ingested. This continued during the sub-acute challenge where GI symptoms increased in the NCGS patients compared to healthy controls (abdominal pain: $p = 0.038$, bloating: $p = 0.015$), regardless of gluten versus placebo intake.

Conclusion: These findings provide new insights into NCGS, which might be characterised by acute gluten-induced increases in extra-intestinal symptoms such as fatigue, rather than GI symptoms. During a sub-acute challenge, using the same dose spread over two different time points per day for five consecutive days, GI symptoms were elevated in the patient group regardless of gluten versus placebo intake. Further, there was a tendency towards higher levels of tension and depression after gluten intake regardless of patient versus control status. Further research on the mechanisms underlying these effects as well as other (dietary) factors involved in symptom generation in NCGS is warranted.

Disclosure: Nothing to disclose

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P1226 IS SEROLOGY PREDICTIVE OF PERSISTING VILLOUS ATROPHY IN PATIENTS WITH ESTABLISHED COELIAC DISEASE?

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Introduction: Monitoring of mucosal remission is essential in Coeliac Disease (CD) to assess adherence in patients with persisting symptoms and to prevent complications. However, duodenal biopsies are invasive, expensive and poorly tolerated by many patients. Recent work has suggested that an IgA-tissue transglutaminase (tTG) < 1.2 U/mL may predict mucosal healing in those with established CD, reducing the need for gastroscopies and biopsies in some patients.

Aims and Methods: This study examines whether the combination of serological markers may be used as a surrogate marker for the detection of villous atrophy (VA) in known CD patients. We undertook a prospective analysis of known CD patients diagnosed in a university hospital. All patients underwent a gastroscopy, with four biopsies taken from the second part of the duodenum, and one from the duodenal bulb. Serological markers were assessed at the time of endoscopy. tTG, IgA-endomysial antibodies (EMA), IgA-antigliadin antibody (IgA AGA) and IgG-anti-gliadin antibody (IgG AGA), and their performances in isolation and in combination were compared to histological outcomes.

Results: 107 patients (67.3% female, median age 53 years (20–81 years)) that were on a gluten-free diet for a median duration of 6 years were included. The performance of the different serological markers to detect VA, both in isolation and in combination are shown in Table 1. The performance of tTG using the previously used cut-off of < 1.2u/ml produced a sensitivity of 38.5%, a specificity of 73.8%, a positive predictive value of 64.9% and a negative predictive value of 43.7% to detect VA.

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
tTG	39.0% (CI 29–48%)	97.0% (CI 89–99%)	88.9% (CI 64–98%)	70.8% (CI 61–81%)
EMA	40.5% (CI 26–57%)	96.9% (CI 88–99%)	89.5% (CI 65–98%)	71.6% (CI 61–80%)
IgA AGA	47.5% (CI 32–64%)	95.5% (CI 87–99%)	86.4% (CI 64–96%)	75.3% (CI 65–84%)
IgG AGA	37.5% (CI 23–54%)	90.0% (CI 80–96%)	68.2% (CI 45–85%)	71.6% (CI 61–80%)
EMA + tTG	33.3% (CI 20–50%)	98.5% (CI 91–100%)	93.3% (CI 66–100%)	30.4% (CI 21–41%)
IgA + IgG AGA	28.6% (CI 16–45%)	100% (CI 93–100%)	100% (CI 70–100%)	68.4% (CI 58–77%)
IgA or IgG AGA + EMA	28.6% (CI 16–45%)	100% (CI 93–100%)	100% (CI 70–100%)	68.4% (CI 58–77%)
IgA or IgG AGA + tTG	31.0% (CI 18–47%)	100% (CI 93–100%)	100% (CI (72–100%)	69.1% (CI 59–78%)

[Ability of serological markers to detect villous atrophy]

Conclusion: This study is the first to evaluate the combination of serological markers to detect VA in patients with established CD. Our findings oppose recent work that serology may be used as a surrogate marker of mucosal healing in known CD.

Disclosure: Nothing to disclose

P1227 BIOPSY AVOIDANCE STRATEGY IN ADULT COELIAC DISEASE

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Introduction: Currently, the diagnosis of adult Coeliac disease (CD) requires the presence of villous atrophy (VA) on duodenal biopsy. However, biopsies are expensive, invasive and poorly tolerated by many patients. Paediatric ESPGHAN guidelines support a diagnosis of CD when immunoglobulin-A anti-tissue transglutaminase (IgA tTG) antibody titres are greater than 10 times the upper limit of normal (ULN) and combined with supportive criteria. This study examines whether serological testing alone could be sufficient for diagnosis in adult patients, thus avoiding the need for gastroscopy and duodenal biopsies.

Aims and Methods: The aim of this study was to assess whether an IgA tTG value of greater than 10 times the ULN could produce a 100% positive predictive value (PPV) for the detection of VA. We performed a prospective analysis of CD patients diagnosed in a university hospital. Symptoms of CD, VA on biopsy, IgA-endomysial (IgA-EMA) antibodies, tTG and Human Leukocyte Antigen (HLA) genotype were used for analysis. We then compared the tTG antibody level against small bowel histology.

Results: 443 CD patients (66.8% female, median age 41 years, range 15–84 years) were diagnosed between 2008 and 2016. 56.9% ($n = 252$, 95% CI = 52.12–61.53) had a tTG value of greater than 10 times the ULN, and 100% of these patients had VA on biopsy. 292 fulfilled ESPGHAN guidelines for features of malabsorption (diarrhoea = 157, weight loss = 45 and anaemia = 190). Of these symptomatic patients, 70.4% ($n = 179$, 95% CI = 64.86–76.08) had a tTG value $10 \times$ ULN. The proportion reaching the $10 \times$ tTG threshold was 55.4% ($n = 87$, 95% CI = 47.64–63.19) for diarrhoea, 60.0% ($n = 27$, 95% CI = 45.69–74.31) for weight loss, and 74.2% ($n = 141$, 95% CI = 67.99–80.43) for anaemia. Of the 151 patients who did not experience malabsorptive features, 49.0% met the $10 \times$ ULN tTG level ($n = 74$, 95%CI = 41.03–56.98). The sensitivity of tTG antibodies and EMA antibodies for predicting VA was 93.2% (95% CI = 90.89–95.57) and 90.7% respectively (95% CI = 88.05–93.44). Combined tTG and EMA was 98.6% (95% CI = 97.67–99.72). All patients had compatible HLA typing, thereby failing to add any further diagnostic value.

Conclusion: An IgA tTG level of greater than 10 times the ULN had a PPV of 100% for detecting VA. Using this threshold, 56.9% of patients would have been correctly diagnosed with CD and avoided duodenal biopsy. Symptoms and HLA typing did not add any supportive information. This study provides evidence that a biopsy avoidance strategy may be implemented into adult gastroenterological practice.

Disclosure: Nothing to disclose

P1228 HUMAN LEUCOCYTE ANTIGENS COELIAC HAPLOTYPES: FROM ETIOLOGICAL FACTORS TO DIAGNOSTIC APPROACHES

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Introduction: Celiac disease (CD) is an autoimmune enteropathy caused by gluten ingestion in genetically susceptible individuals. Genetic susceptibility to CD has been associated with human leukocyte antigen (HLA)-DQ2 heterodimer, encoded by the DQA1*05 and DQB1*02 genes. Our aim was to investigate whether the DQB1*02 allele could influence anti-tissue transglutaminase (tTG) titres in adult patients with CD.
Aims and Methods: A total of 75 patients with established CD, tested for tTG antibodies at diagnosis, were typed for HLA- DQA1, and -DQB1 genes, and divided according to the number of DQB1*02 alleles: group 1, homozygous; group 2, heterozygous; group 3, no gene.
Results: We report that the mean of tTG antibody indexes was not significantly higher in group 1 patients than in group 2 (118.90 ± 93.98 *versus* 142.45 ± 100.24, $P = 0.529$), or group 3 patients (90.74 ± 91.87 *versus* 142.45 ± 100.24, $P = 0.221$). Nevertheless, patients in group 1 showed more severe histological lesions (Marsh3a-c) compared to those in the other groups. When assessing disease phenotype, the carriage of 2 copies was associated with the presence of anaemia, abdominal pain, weight loss, and chronic diarrhoea.
Conclusion: The study demonstrates that tTG titers are not significantly influenced by the number of HLA-DQB1*02 copies. Moreover, individuals with at least 1 HLA-DQB1*02 allele tend to have a higher degree of histological damage and different clinical features compared to those carrying other alleles.
Disclosure: Nothing to disclose

P1229 PERSISTENT VILLOUS ATROPHY AMONG ADULT CELIAC DISEASE PATIENTS ON A GLUTEN-FREE DIET: IS THERE A ROLE FOR SEROLOGY?

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Introduction: Tissue transglutaminase (tTG) antibodies are hallmarks of CD diagnosis. The aim of our study was to assess whether serum IgA- tTG tests are useful to detect villous atrophy in patients with CD treated with gluten free diet (GFD).
Aims and Methods: We performed a prospective study using the information entered into a structured database including adult patients diagnosed with CD hospitalized at the Institute of Gastroenterology and Hepatology, adherent to GFD for at least 12 months after diagnosis. Data from adult patients with CD (diagnosed between January 10, 2010 through December 10, 2015) with biopsy, and serological tests (IgA/IgG-tTG antibodies) were retrieved from a computerized database. Results of non-invasive tests were compared with the persistence of villous atrophy on follow-up biopsy.
Results: The study group included 81 adult patients with a female: male ratio of 3:1, mean age 40.02 ± 12.14 years. When assessing the serological parameters, IgA-tTG levels (61.45 ± 76.458 u/mL *vs* 162.02 ± 106.179 u/mL, $P = 0.001$) correlated with intestinal villous atrophy (Marsh 1–2 *vs* Marsh 3a-c) in CD patients, with a sensitivity of 82.56% and a specificity of 91.78% for mucosal atrophy upon diagnosis (AUC = 0.909; IC95%: 0.86–0.95). Follow-up biopsy and serology testing were available for 47(74.6%) treated patients. Twenty one patients had variable degrees of villous atrophy, and IgA-tTG assay was 51% sensitive and 67.3% specific in identifying Marsh 3 lesions among patients allegedly adherent to a GFD with normal IgA-tTG levels.
Conclusion: Increased IgA-tTG levels in the treated population may reflect quantity and frequency of gluten exposure. The diagnostic accuracy of IgA-tTG antibodies for detecting persistent villous atrophy on a GFD is limited, showing relatively high specificity, but low sensitivity. Consequently, the majority of patients with villous atrophy on a GFD had normal levels of IgA- tTG.
Disclosure: Nothing to disclose

P1230 HLA TYPING AND CELIAC DISEASE IN ROMANIANS

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Introduction: Celiac disease (CD) is considered to have a high heritability involving HLA genes, which provide the genetic risk to develop the disease. The aim of the study was to investigate whether the genetic profile influences age of onset and diagnosis in CD.
Aims and Methods: High- resolution class 2 HLA genotyping was performed in a sample (n = 75) of North-Eastern Romanian residents residents with CD to determine the contribution of DQA1 and DQB1 on the age of diagnosis. The complete inpatient and outpatient medical record of each candidate were carefully reviewed. Age of onset was the age at which the patient first complained of symptoms subsequently explained by CD. Age at diagnosis was established as the date of interpretation of the initial intestinal biopsy or positive serology. Depending on the heterodimers inherited, 3 study groups were identified and compared: high risk (DQ2.5/DQ2.5, DQ2.5/DQ2.2, DQ2.5/DQ8, DQ8/DQ8), moderate risk (DQ2.5/X, DQ2.2/X, DQ8/X, DQ2.2/DQ2.2), and low risk (DQ7/X, DQ7/DQ7, DQX/DQX).
Results: A total of 32 (42.6%) patients had high-risk heterodimers. The age at diagnosis and the age of onset of patient symptoms attributable to CD were associated with the number of copies of DQB1*02. Mean age at diagnosis was significantly higher among patients in the low-risk group compared to those in the high-risk group (46.83 ± 7.93 *versus* 37.72 ± 12.39, $P = 0.004$). Disease severity (at least 10-pound weight loss and diarrhea) was found to be associated with high risk haplotypes, and the number of copies of DQB1*02.
Conclusion: Both HLA- DQA1*05 and DQB1*02 alleles are associated with earlier disease onset, diagnosis and disease severity.
Disclosure: Nothing to disclose

P1231 USEFULNESS OF DOUBLE-BALLOON ENTEROSCOPY FOR DIAGNOSIS OF MECKEL'S DIVERTICULUM

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Introduction: Meckel's diverticulum (MD) is a congenital malformation of the gastrointestinal tract. The number of reports of MD observed by balloon assisted enteroscopy is increasing since the development of the double-balloon enteroscopy (DBE) and single-balloon enteroscopy. The present case series describes 14 patients with MD in whom DBE was useful for diagnosis.
Aims and Methods: Thirteen retrograde and one anterograde DBE were performed for fourteen patients (11 men, 3 women) with MD at Kobe City Medical Center General Hospital from May 2004 through Octorber 2017.
Results: DBE diagnosed MD in thirteen out of fourteen patients (92.3%), but one of them (inverted MD) was misdiagnosed as a lipoma. MD was identified using iodinated contrast medium through the scope during anterograde DBE in one patient. Abdominal computed tomography was performed in all fourteen patients and revealed abnormalities in eight (61.5%), but MD was suspected in only two cases (14.5%). Technetium-99 m pertechnetate scintigraphy and capsule endoscopy were carried out in six and four patients, revealing MD in one and two patients (16.7%, 50%) respectively. Surgery was performed in thirteen patients, and endoscopic resection was carried out in one patient (inverted MD) by DBE. Ulcer formation was found in or near MD in eight patients.
Conclusion: Compared with other modalities such as CT scan, Technetium-99 m pertechnetate scintigraphy and capsule endoscope, DBE is excellent for the diagnosis of MD because direct observation of both MD and ulceration is possible. This study shows that DBE is highly useful in the diagnosis of MD either alone or in combination with other methods. In addition, endoscopic resection using DBE could be one method of treatment of inverted MD.
Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00
Nutrition II – Hall X1

P1232 ENDOSCOPIC GASTRIC MUCOSAL ABLATION (EGMA) FOR WEIGHT LOSS: THE FIRST HUMAN CASE REPORT

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Introduction: Morbid obesity is an increasing common chronic health problem in the world including in China. Currently, Laparoscopic Sleeve Gastrectomy (LSG) is the most favored surgical bariatric procedure for the treatment of morbid obesity**.** The LSG procedure requires removal of the greater curvature of the stomach along with its blood vessels and nerves.
Inspired by the complication esophageal stenosis after large area Endoscopic Submucosal Dissection (ESD) for the treatment of early esophageal cancer, we hypothesized that ablation of a sufficiently large area of the gastric mucosa might result in permanent contracture and a reduction in gastric volume. We therefore performed Endoscopic Gastric Mucosal Ablation (EGMA) using pigs as an animal model to confirm our hypothesis (manuscript in preparation). EGMA resulted in shrinkage of the pig stomach producing a reduction in gastric volume. Based on the success with animal experiments, we performed EGMA on an obese patient.
Aims and Methods: The patient was a 38-yr-old obese woman (BMI 37.2 kg/m^2) with type 2 diabetics (blood glucose level 15–20 mmol/L) who required 25 units of Insulin and 850 mg of metformin both twice a day. Her total gastric volume was 787.70 mL measured by CT scan before the procedure. EGMA procedure was performed under general anesthesia with endotracheal intubation. A cap-based single-channel endoscope (GIF-Q260J; Olympus, Tokyo, Japan) was used for the procedure. Endoscopic Submucosal Dissection (ESD) and Endoscopic Mucosal Resection (EMR) procedures were performed to resect the mucosal layer of the fundus and body of the stomach. The goal was to resect 80% of the circumference of the anterior, posterior, greater curvature mucosal layer of the stomach (Figure 1a). Small portions of mucosa (mucosal islands) were left to promote wound healing and regeneration of the gastric mucosa after the procedure

(Figure 1b). Coagulation forceps were used to coagulate any bleeding or potential bleeding sites in the submucosal and muscular layer and to prevent recurrent bleeding (Soft coagulation 50W, ICC 200; ERBE Erbotom, Germany).
The patient then remained fasting for 3 days followed by a liquid diet for days 4 through 7. A proton-pump inhibitor (40 mg esomeprazole sodium injection) was given intravenously for 7 days. A semi-liquid was given for day 7 to 15 after which a normal diet was resumed.
Results: The post-procedure period was not associated with bleeding, severe abdominal pain, nausea or vomiting. After the procedure her blood glucose level decreased to normal without anti-diabetic drugs. One week after the procedure, gastroscopy showed a large area of ulceration on the greater curvature of the stomach covered by yellow plaque. One month after the procedure, the area of the ulcer was noticeably smaller, the mucosal islands were wider, and the plaque was white and clean. The BMI had decreased to 31.8 kg/m^2. There were no major adverse events and complications during the procedure or during the 18 months follow-up.
Conclusion: EGMA appears to be an effective, safe, and less invasive restrictive-type bariatric procedure with low technical complexity and complications.
Disclosure: All authors were involved in this work, agreed to submit it for UEG Week 2018, and assumed responsibility for the accuracy and completeness of the data. The authors declare that there are no conflict of interest.

P1233 ALT REDUCTION IN GERIATRIC PATIENTS WHO HAVE UNDERGONE BARIATRIC SURGERY

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease. Treatment recommendations include weight reduction, with a number of studies showing that bariatric surgery to lose weight leads to an improvement in NAFLD in obese patients. Alanine aminotransferase (ALT) has been used as a marker to monitor NAFLD, and reductions in ALT have been demonstrated with weight loss. To date, there have been no studies looking at reduction in ALT in geriatric patients who have undergone bariatric surgery.
Aims and Methods: The aim of this study was to see if geriatric patients who have undergone bariatric surgery show the same improvement in ALT as seen in younger, bariatric patients. This is a retrospective study of 90 morbidly obese, adult patients, divided into two arms based on age. Patients were labeled as geriatric if they were 65 years of age or greater at the time of surgery and non-geriatric if they were 64 years of age or below at the time of surgery. There were 45 patients in each arm, and patients were BMI and sex matched and followed for one year. All patients either underwent laparoscopic roux-en-y gastric bypass (RYGB) or laparoscopic sleeve gastrectomy. Gender, age, pre-surgical body mass index (BMI), percent weight loss and pre and post-surgical ALT levels were recorded.
Results: Among the two different arms, 33% of patients were male and 66% were female. The average age in the non-geriatric group was 40.4, and the average age in the geriatric group was 67.9. The pre-surgical BMI was 40.8 and 40.7 in the non-geriatric and geriatric groups, respectively. In the non-geriatric group, 49% of patients underwent a RYGB and 51% underwent a sleeve gastrectomy. In the geriatric group, 40% of patients underwent a RYGB and 60% underwent a sleeve gastrectomy. There was no significant difference in frequency of sleeve gastrectomy vs RYGB between these two groups ($p = 0.40$). Percent weight loss in the non-geriatric group was 29% and 24% in the geriatric group ($p < 0.001$). The non-geriatric patients had an average pre-surgical ALT of 47.4 and average post-surgical ALT of 31. The geriatric patients had an average pre-surgical ALT of 49 and had an average post-surgical ALT of 28.8. Percent decrease in ALT levels was 25.3% in the non-geriatric group and 33.5% in the geriatric group, respectively ($p = 0.222$). The non-geriatric group had 9 out of 45 patients with elevated pre-surgical ALT, and the geriatric group had 14 out of 45 patients with elevated pre-surgical ALT ($p = 0.23$). In both the non-geriatric and geriatric groups, all patients who had a pre-surgical ALT above the upper limit of normal had normalization of ALT after bariatric surgery.
Conclusion: Our study shows that geriatric, morbidly obese patients have a reduction in ALT after bariatric surgery, similar to what is seen in younger, morbidly obese patients who have undergone bariatric surgery. As ALT can be used as a marker to monitor NAFLD, this suggests that geriatric patients likely have a reduction in NALFD after bariatric surgery.
Disclosure: Nothing to disclose

P1234 ORAL AND EXTRA-ORAL BITTER TASTE RECEPTOR EXPRESSION IN A MODEL OF ANTIBIOTIC-INDUCED DYSBIOSIS

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Introduction: Antibiotic treatment is associated with weight gain and risk for obesity. The mechanisms driving this association are not clear. However, dysbiosis has been identified as a potential causative factor for weight gain. Procedures that impact diet, weight, and the gastrointestinal microbiota, such as gastric banding surgery, have been linked to modified expression of taste receptors on the tongue. Taste receptors are expressed throughout the gastrointestinal tract, and so may be involved in detecting dietary compounds, appetite control and gut motility.
Aims and Methods: We, therefore, aimed to assess how antibiotic-induced dysbiosis influenced expression of *tas2r114, tas2r116 and tas2r138,* three broadly tuned bitter taste receptors, on the tongue and in the colon in a mouse model**.** Mice (8/group) received amoxicillin and clavulanate (five day course), or control treatment. Three days post-treatment colon and tongue tissues were collected, RNA was isolated (TRIZOL) and expression of *tas2r114, tas2r116 and tas2r138* assessed by qPCR.
Results: Expression of each receptor assayed was increased in the colon following antibiotic treatment (*tas2r114* 1.0 ± 0.18 vs 3.39 ± 0.44 relative expression units (REU), $p = 0.001$; *tas2r116* 1.0 ± 0.2 vs 6.57 ± 1.41 REU, $p = 0.0001$; *tas2r138* 1.0 ± 0.20 vs 2.1 ± 0.40 REU, $p = 0.05$). However, expression of *tas2r116* and *tas2r138* expression was reduced on the tongue following antibiotic treatment (*tas2r116* 1.0 ± 0.36 vs 0.09 ± 0.02. REU, $p = 0.03$; *tas2r138* 1.0 ± 0.19 vs 0.4 ± 0.08 REU, $p = 0.04$). Expression of *tas2r144* was not significantly different between the two groups.
Conclusion: The change in expression of taste receptors found may lead to reduced sensation of bitter dietary compounds on the tongue, and increased enteroendocrine signalling in the colon. Further studies are required, to assess the duration of effects, how altered mRNA expression translates into changed protein expression levels, and the consequences for the host.
Disclosure: Nothing to disclose

P1235 COMBINED USE OF *LACTOBACILLUS* AND *BIFIDOBACTERIA* PROBIOTIC STRAINS WITH NANOCERIA REDUCE CHOLESTEROL LEVEL IN OBESITY MOUSE MODEL

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Introduction: Probiotic strains *Lactobacillus* and *Bifidobacteria* demonstrated efficacy to reduce weight of animals and cholesterol level, changed liver morphology and modulated gut microbiota on obesity mice model in our recent study [1]. New updated prebiotic concept supposes perspectives to search for new substances. Our recent studies have shown starin-specific properties of *Lactobacillus* and *Bifidobacteria* probiotic actitvity [2] and suggested nanoceria to be used as potential prebiotics to enhance their probiotic properties (unpublished data).
Aims and Methods: The aim of this study was to evaluate the possibility of combined use of nanoceria and *Lactobacillus* and *Bifidobacteria* strains in monoculture and compositions to reduce cholesterol level on obesity model in mice. Previously studied probiotic strains *Lactobacillus acidophilus* IMV B-7279, *L. casei* IMV B-7280, *L. delbrueckii* subsp. *bulgaricus* IMV B-7281, *Bifidobacterium animalis* VKL, *B. animalis* VKB and cerium dioxide nanoparticles (size 3–7 nm) were used in the study. We used female mice of two lines and age groups: 6–8 weeks (18–24 g) BALB/c line mice, and 11–12 months (20–26 g) CBA line mice. Animals were divided into fifteen groups to test probiotic strains and nanoceria. All groups except the control received a special fat-enriched diet during three weeks before the experiment. Animals orally received probiotic strains and nanoceria in various compositions. One group of intact animals was used as a control. Cholesterol level and weight of mice were studied during 30 days.
Results: We revealed that all studied probiotic bacteria and composition of *B. animalis* VKL/*B. animalis* VKB/*L. casei* IMV B-7280 decreased the weight of obese BALB/c mice and concentration of different cholesterol types; adding nanoceria to the probiotic strains of *L. casei* IMV B-7280, *B. animalis* VKB and *B. animalis* VKL in monoculture and composition more effectively reduced levels of free, bound and ester cholesterol in serum. The rate and intensity of this process depends on the age of animals, as well as the type and concentration of the drug. The combination of 0.01 M nanoceria and probiotic strain *L. casei* IMV B-7280 oral administration resulted in the fastest decrease in cholesterol levels to the indicators of control groups of mice both in young and adult animals. The level of total cholesterol in the blood serum after tretement with *L. casei IMV B-7280* orally decrease to 7.37 ± 0.25 mmol/L, after treatment with 0.01 M CeO_2 + *L. casei IMV B-7280* orally 3.50 ± 0.47 mmol/L vs 7.83 ± 0.11 mmol/L in intact animals.
Conclusion: Combined use of nanoceria as prebiotic substance and probiotic strains *L. casei* IMV B-7280, *B. animalis* VKB and *B. animalis* VKL in monoculture and combination reduce weight and the level of free, bound and ester cholesterol in serum of young and adult obese mice. This can provide novel insights for using of probiotics compositions and nanomaterials considered as safe and effective prebiotic substances.
Disclosure: Nothing to disclose

References

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P1236 ^{68}GA-NODAGA-EXENDIN-4 PET/CT FOR IMAGING OF BETA CELLS IN PATIENTS AFTER ROUX-EN-Y GASTRIC BYPASS (RYGB) SURGERY

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Introduction: After undergoing RYGB, remission of type 2 diabetes (T2D) occurs in >60% of patients. The mechanism behind this remission is not completely understood. Beta cell activity (BCA) and beta cell mass (BCM) could possible play a role. While RYGB is beneficial for the health and quality of life of most patients, a rare complication is hyperinsulinemic hypoglycaemia. Also here the mechanism is still unclear, but a role for BCA and BCM is hypothesized.
Measuring BCA and BCM could provide useful information on the role of beta cells in patient responses to RYGB and possibly offer predictive value. Exendin-4, a stable analogue of glucagon-like peptide-1, specifically accumulates in the beta cells. ^{68}Ga-exendin-4 PET/CT can be used to quantify BCM *in vivo* and could help to study the role of BCM in changes of glycemic control after RYGB.
Aims and Methods: BCA and BCM were compared between patients with different responses after RYGB. Patients with complete remission of T2D (responders) and without complete remission of T2D (non-responders) after RYGB were included as well as patients with hypoglycaemia after RYGB.
BCA was measured by an arginine stimulation test and either an oral glucose tolerance test (in responders and non-responders) or a standard meal tolerance test (in the hypoglycaemia patients). BCM was measured in all patients as pancreatic uptake of ^{68}Ga-exendin-4 by quantitative analysis of PET/CT scans.
Results: In total, 12 responders and 12 non-responders will be included. So far, four responders and four non-responders were included. Preoperative patient characteristics and postoperative weight loss were comparable between the groups. The BCM was 37% lower in the non-responders (131 ± 78 kBq) compared to the responders (206 ± 90 kBq), although not statistically significant ($p = 0.25$). BCA was significantly lower in the non-responders compared to the responders, with an arginine stimulated acute C-peptide response of 0.4 ± 0.2 and 0.9 ± 0.3 nmol/l, respectively ($p = 0.02$).
In total, 8 hypoglycaemia patients and 8 matched controls will be included. At this moment, three hypoglycaemia patients have completed the study and in these patients the mean BCM was 226 ± 69 kBq.
Conclusion: These preliminary data show that measuring BCM in vivo is possible using ^{68}Ga-exendin-4 PET/CT. The data suggest that BCM is lower in patients with incomplete remission of T2D compared to those with complete remission. Furthermore, BCM in patients with hypoglycaemia seems to be even lower than in patients with remission of T2D after RYGB. These data may suggest a role for BCM in patient response to RYGB.
Disclosure: Nothing to disclose

P1237 LIRAGLUTIDE TREATMENT IN OBESE DIABETIC PATIENTS MODULATES GAS PRODUCTION DURING LACTULOSE BREATH TEST: A NEW POTENTIAL TREATMENT TO MODULATE GUT MICROBIOTA

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Introduction: Colonic bacteria fermentation produces hydrogen (H2) and methane (CH4), which can be easily measured using breath test method. Breath tests (BT) represent a valid and non-invasive diagnostic tool in many gastroenterological disorders. C13 Octanoic Acid breath test, is used to analyze gastric emptying, often altered in various gastrointestinal disorders.
To date the link between diabetes and intestinal microbiota is well known.
Liraglutide is a human GLP-1 analogue approved for type 2 diabetes, to reduce glycosylated hemoglobin (HbA1c) and achieve better effects on glucose control. Delayed gastric emptying has been previously associated with Liraglutide treatment.
So far it has never been analyzed colonic gas production, with lactulose breath test, before and after Liraglutide treatment.
Aims and Methods: Ten obese diabetic patients (age 63.8 ± 12.6; HbA1C 8.1 ± 1.4 %; weight: 105.4 ± 19.1 kg), candidates to receive GLP1-analogs therapy, where included in the study. All subjects underwent, before (B) and after 6 weeks of treatment (PT) with liraglutide 1.2 mg, metabolic evaluation including glucose, HbA1c, glucose self-monitoring, Lactulose Breath test (LBT) and Octanoic Acid breath test in our Gastroenterology Unit.
Methane and Hydrogen production, by the area under the time-concentration curve calculation (AUC), and the peak value were calculated, during LBT. Gastric emptying was assessed by C13 Octanoic Acid BT.
Results: All subjects experienced a significant weight loss (6% of the basal body weight; BMI B: 37 ± 5.1 kg/m^2, BMI PT: 27.4 ± 1.5 kg/m^2 p: 0.05), as well as a significant reduction of fasting plasma glucose (B FPG pre: 149.4 ± 15 mg/dl, FPG PT: 98.2 ± 23 mg/dl p: 0.09) and a Hb1Ac (HbA1C B: 8.1 ± 1.4 %, HbA1C PT: 5.5 ± 1% p: 0.01). Methane and Hydrogen production (AUC) and peak value were significantly reduced by Liraglutide in the post-treatment group; moreover, the LBT revealed that Liraglutide is able to significantly slow down the Oro-cecal transit time (OTT). Also Gastric emptyng was significantly reduced after Liraglutide treatment.
Conclusion: These results confirm the effect of Liraglutide on delayed gastic emptying and suggest that the glucose lowering effect of this molecule, may be potentially mediated by modulation of intestinal gas production, and OTT. These new findings could represent a new potential effect of Liraglutide treatment on the modulation of Gut Microbiota, underlying new potential mechanisms of microbiota-mediated metabolic effects.
Disclosure: Nothing to disclose

P1238 ROLE OF DIETARY INTERVENTION IN CLINICAL IMPROVEMENT OF NONALCOHOLIC FATTY LIVER DISEASE PATIENTS

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the main cause of liver diseases worldwide that poses heavy health-related metabolic problems associated with the increasing trends of obesity and diabetes. NAFLD is affected with lifestyle practices including nutrition and sedentary life. Therefore, the common treatment is weight loss through dietary restrictions and practicing exercise. However, there is no consensus regarding the best diet to treat NAFLD, not merely focusing on weight loss but to improve the metabolic health of patients.
Aims and Methods: The aim is to study the role of dietary intervention program including dietary and exercise plan in the clinical improvement of NAFLD.
110 patients were recruited from the hepatology outpatient clinic in the Main Alexandria University Hospital and diagnosed as NAFLD based on Ultrasound examination and exclusion of other causes of acute and chronic liver disease like post viral, alcoholic, autoimmune and metabolic liver diseases. Also, patients who have diabetes mellitus, cirrhosis, or receiving hormonal treatment were excluded. Assessment of dietary intake, dietary habits, lifestyle practices, body composition measurements, laboratory investigations, clinical examination and evaluation of liver fat with ultrasound based hepatorenal index calculations was done. For 12 weeks, each patient received individualized dietary plan based on Mediterranean diet restricted in carbohydrates (40–45%), moderate in fat (35–40%) and protein (15–20%). Physical exercise including aerobic training and abdominal exercises 5 times/week and resistant training 1–2 times/weeks.
Results: The dietary intake of carbohydrate and energy were decreased, while the percent of fat intake were increased. This was associated with reduction of liver fat among 70% of patients as assessed by reduction in HRI scores, improvement of serum transaminases as well as components of metabolic syndrome and gastrointestinal tract symptoms. Moderate reduction in body weight 5–6% with more loss of body fat (12%) and good preservation of muscle mass were observed.
Conclusion: Proper nutrition counseling based on Mediterranean diet restricted in total calories and carbohydrates, has significant impact on improving the metabolic health of NAFLD patients.
Disclosure: Nothing to disclose

P1239 SAFETY AND EFFICACY OF ELIPSE BALLOON IN OBESE ADULT PATIENTS: A SINGLE-CENTER PILOT STUDY IN AN ITALIAN TERTIARY HOSPITAL

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Introduction: Obesity represents a paramount clinical problem for short and long-term cardiovascular and metabolic complications, with consistent increasing incidence in many countries. Gastric balloon is a relevant non-surgical option for such patients, but the positioning and the removal requires endoscopic procedure

and sedation. ELIPSE balloon is a novel device that do not require endoscopy and/or sedation, since it is swallowed by the patients and spontaneously excreted after a progressive deflatation. We conducted a prospective pilot study at S. Giovanni Hospital in Rome, Italy, to evaluate safety and efficacy of ELIPSE balloon in obese adult patients.
Aims and Methods: Eleven consecutive patients (8 females), with mean age 40 ± 5 and BMI 40 ± 4, were included in the study. ELIPSE balloon was swallowed with water, filled with 560 mL of fluid. Patients were followed up by a nutritionist during the study. Body weight were recorded before ingestion and after excretion of the balloon, and potential adverse events were monitored at ingestion time and during follow up till the excretion of the balloon.
Results: All the patients successfully swallowed the device, and no major adverse event was recorded during the study. Minor and transient symptoms reported were: dyspepsia, vomiting, and diarrhea. All the patients spontaneously excreted the balloon after 16 ± 2 weeks. At the end of the study, all the patients had a significant weight loss (mean: 14 ± 5 Kg).
Conclusion: In a single-center pilot study, ELIPSE balloon has demonstrated safety and efficacy in adult obese patients. This device do not require endoscopy and sedation and may represent a feasible and effective option even in primary setting. Data confirming efficacy and safety of ELIPSE are increasing, and further studies will better clarify the positioning of this promising device for the treatment of obesity.
Disclosure: Nothing to disclose

P1240 CHANGES IN THYROID HORMONE LEVELS IN OBESE EUTHYROID PATIENTS UNDERGOING BARIATRIC SURGERY

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Introduction: An association between obesity and elevated levels of thyroid stimulating hormone (TSH) has been reported. One of the suggested mechanisms is the influence of adipokines, namely adiponectin. Bariatric surgery is a currently recognized technique for the treatment of obesity, with a favorable effect on weight loss; however, the impact of the postoperative period on thyroid function has not been clarified.
Aims and Methods: The aim of this study was to evaluate the changes in TSH and free thyroxine (fT4) in the obese population submitted to bariatric surgery.
Prospective analysis of patients undergoing undergoing Roux-en-Y gastric bypass (RYGB) by obesity. Clinical and laboratory data were analyzed before and 1 year after surgery. Patients with a known history of thyroid disease were excluded. Statistical analysis performed in SPSS V24.
Results: 38 patients were included; mean age was 43 ± 11.2 years, 80% were women and mean Body Mass Index (BMI) before surgery was 41.7 ± 5.4 kg/m2. After surgery, patients lost an average of 33.4% of their total body weight and 87.8% of BMI in excess. There was a significant reduction in weight (111 vs 73.7 kg) and BMI (41.7 vs 27.7 kg/m2) before and after surgery (p-0.00). There was also a reduction in FT4 and TSH levels before and after surgery (FT4 0.92 vs 0.87 mg/dL, p-0.02 and TSH 1.13 vs 1.04 μUI/mL, p-0, 14). There was a significant correlation between TSH levels and BMI before surgery (r = 0.37, p-0.021). After surgery, there was only a correlation in the female subgroup (r = 0.36, p-0.048). There was a significant reduction in TSH levels with increased levels of adiponectin (r = −0.39; p -0.04), but only in the subgroup of women.
Conclusion: There seems to be a reduction in thyroid hormone levels due to weight loss after bariatric surgery. Changes in adipokine production, such as adiponectin, in adipose tissue may explain some of the variation in TSH.
Disclosure: Nothing to disclose

P1241 DIAGNOSIS OF LACTOSE MALABSORPTION BY THIRD GENERATION HYDROGEN BREATH TEST: TIME IMPLEMENTATION AND SAMPLES DATA REVIEW

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Introduction: Hydrogen breath test using various substrates like glucose, lactulose, lactose and fructose are being used more and more to diagnose malabsorption and small intestinal bacterial overgrowth (SIBO). While glucose and lactulose hydrogen breath tests are more acceptable the diagnosis of SIBO, lactulose and fructose hydrogen breath tests are useful to diagnose various types of sugar malabsorption and lactose intolerance.
Technique and interpretation of different hydrogen breath tests are outlined in this review.
Aims and Methods: The third generation of hydrogen breath test monitors has reached a level of precision which makes such continuous air flow device (Gastrolyzer Bedfont, Scientific Ltd Harrietsham) or Heliprobe (Kilion, Mayoli Spindler) a helpful assist for diagnosis of gastrointestinal disorders.
Gases as H2, CH4 or CO2 are detected in a semi-conductor flow cell an displayed as ppm (part per million). The original sluggish development has now made room for a useful screening test in the cases where lactose intolerance is suspected.
Genetic test of lactose intolerance may help to differentiate patients with primary hypolactasia from those with lactose intolerance caused by secondary hypolactasia. Also it is useful for differing lactose intolerance from irritable bowel syndrome (IBS) which has very similar symptoms. So for the differentiation of adult-type hypolactasia from secondary causes of lactose intolerance, hydrogen breath testing (H2BT) might not need further genetic approach.
The third generation of H2BT is to prove and establish whether a simplified two or three sample test may reduce time, costs and staff resources without reducing the sensitivity of the procedure.
Data from 32 patients (20 males, 12 females) with a positive 4 h, nine samples H2BT were fully tested. Patients were stratified according to the degree of lactose malabsorption, the occurrence and type of symptoms. Sensitivity in the H2BT was tested taking into account two samples tests (0 and 120 min or 0 and 210 min) or three-sample tests (0 min,120 min and 180 min or 0 min 120 min and 210 min).
Results: Using a two sample test (0 min and 120 min or 0 min and 210 min) the false- negative rate was 35.6% and 27.8% respectively. With a three-sample test (0 min 120 min and 180 min or 0 min 120 min and 210 min) lactose malabsorption was diagnose in 94.6% (30 of 32) patients and in 97.1% (31 of 32) patients respectively. Of 20 patients with abdominal symptoms 5 (26.6%) and 2 (12.2%) would have false-negative results with 0 min and 120 min or 0 min and 210 min two-sample tests respectively. The three-sample tests, 0 min, 120 min and 180 min or 0 min, 120 min and 210 min, would have a false-negative rate of 5.9% and 2.1% respectively.
Conclusion: H2BT is an inexpensive, useful, simple and safe diagnostic test in the evaluation of lactose malabsorption. Standardization of the indications, performance and interpretation of the test still needs to be improved in clinical practice and research.
The third generation quantitative detection of rare gases with the breath expiration with three-sample H2BT is time and cost sparing without significant loss of sensitivity for the diagnosis both of lactose malabsorption and lactose intolerance
Disclosure: Nothing to disclose

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P1242 SINGLE DUODENAL MUCOSAL RESURFACING ELICITS IMPROVEMENTS IN GLYCAEMIC AND HEPATIC PARAMETERS IN TYPE 2 DIABETES MELLITUS: COMPLETE 1 YEAR RESULTS FROM THE FIRST PROSPECTIVE MULTICENTER STUDY

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Introduction: Abnormalities in duodenal mucosa, nutrient absorption and enteroendocrine cell population are thought to play a pathophysiological role in the development of insulin resistance in patients with type 2 diabetes (T2D). Duodenal exclusion via bariatric surgery confers an insulin sensitizing metabolic benefit that is, in part, weight-independent. Duodenal Mucosal Resurfacing (DMR) is an endoscopic procedure that entails catheter based circumferential mucosal lifting followed by hydrothermal ablation (targeted circumferential treatment area of 9–10 centimetres in length) and may confer similar metabolic benefits using a less invasive procedure. DMR has been shown to improve glycaemic control at 6 months in T2D patients in a single centre first-in-human study. Here we report the 12 month safety and efficacy data of all patients included in the first multicentre study involving DMR.

Aims and Methods: We conducted a single-arm, open-label, prospective, multicentre study in which T2D patients (HbA1c 7.5–10.0%; age 25–75y; BMI 24–40kg/m^2; using oral glucose lowering medication) received a single DMR procedure. Adverse events and impact on glycaemic control (HbA1c and fasting plasma glucose [FPG]), insulin resistance (HOMA-IR), and liver enzymes (AST and ALT) was determined at baseline and 1, 3, 6, 9, 12 months post DMR. Glucose lowering medication was kept stable for ≥ 6 months post DMR but could be adjusted according to care guidelines thereafter. We used ANOVA for repeated measurements with Bonferroni correction for the analysis of the multiple measurements after DMR. Values are mean ± SD.
Results: Baseline characteristics (n = 46) are 63% male, mean age of 55 years [range 31–69], mean T2D duration of 6 years [range 0.1–12]), and mean BMI 31.6 ± 4.3 kg/m^2. Additional baseline values are shown in Table 1. DMR was well tolerated in all 46 patients. Eight serious adverse events (SAEs) were reported, of which one was considered procedure-related and non were considered device-related. The single procedure-related SAE was mildly elevated body temperature (38°C) with an increase in C-reactive protein that started one day post-DMR and involved one extra day of hospitalization for observation. The 6 and 12 month post DMR follow-up values of HbA1c, FPG, HOMA-IR, weight, ALT and AST with significance levels (as compared to baseline) are shown in Table 1. Change at 12 months are: Δ HbA1c -1.0 ± 0.2% (p ≤ 0.001), Δ FPG -41 ± 8 mg/dL (p ≤ 0.001), Δ HOMA-IR -3.6 ± 0.9 (p = 0.005), Δ weight -2.7 ± 0.6kg (p = 0.003), Δ ALT -10 ± 2 (p = 0.005), and Δ AST -6 ± 2 (p = 0.002).

Measurement	Baseline	6 months	P-value*	12 months	P-value*
HbA1c [%]	8.6 ± 0.8	7.5 ± 0.8	≤0.001	7.5 ± 0.9	≤0.001
FPG [mg/dL]	196 ± 48	160 ± 40	≤0.001	156 ± 39	≤0.001
HOMA-IR	7.7 ± 5.6	5.0 ± 3.5	0.027	4.8 ± 3.0	0.005
Weight [kg]	91 ± 13	89 ± 12	≤0.001	90 ± 12	0.003
ALT [IU/L]	38 ± 22	29 ± 12	0.014	29 ± 16	0.005
AST [IU/L]	26 ± 10	21 ± 6	0.042	21 ± 6	0.002

*[Table 1. Baseline and 6 and 12 months values in complete population (n=46). *Following ANOVA repeated measurements Bonferroni correction.]*
Conclusion: The endoscopic DMR procedure was found to be safe and effective in 46 patients with suboptimally controlled T2D using oral glucose lowering medication. DMR elicited a substantial improvement in parameters of glycaemia as well as a decrease in liver transaminase levels up to 12 months post-procedure, suggesting considerable potential of DMR for the treatment of T2D.
Disclosure: This study was sponsored by Fractyl Laboratories Inc.

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P1243 DECIPHERING MICROBE-HOST COMMUNICATION BASED ON A DIETARY INTERVENTION WITH PARTIALLY HYDROLYZED GUAR GUM – THE PAGODA STUDY

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Introduction: Structural alterations of the intestinal microbiota and its metabolic capacities are associated with various disease states in humans. There is hope that remodeling of a dysbiotic microbiome towards a normal shape could improve health. Prebiotics are one possibility to beneficially modulate a dysbiotic microbiome. Despite increasing knowledge, mechanistic insight linking dietary fiber with health benefits, beyond the well-known role of short chain fatty acids (SCFA), is still scarce.
Aims and Methods: This study aimed to decipher novel mechanistic links between a dietary fiber intervention with partially hydrolyzed guar gum (PHGG) and structural and metabolic alterations of the human microbiome. We performed a clinical trial including 19 healthy volunteers (8m, 11f). Stool, serum and urine samples were collected weekly for 9 weeks allowing every study participant to serve as his/her own control. The study included three periods, namely a 3 week lead-in, a 3 week intervention, and a 3 week wash-out phase. During the 3 week intervention phase participants received daily dosing of 5g PHGG for 3 days followed by 10g PHGG for four days in the first week, proceeding with two weeks of 15g PHGG per day. A minute medical and nutritional history was taken for every participant at baseline, questions regarding abdominal symptoms were collected weekly and stool habits using the Bristol Stool Chart (BSC) were recorded on a daily basis. Alterations in the structural composition of the microbiome were assessed by 16S metagenomics using both V1-V3 and V3-V4 chemistry. Furthermore, stool metabolomics was studied by magnetic resonance spectroscopy. Data from metagenomics and metabolomics were linked using sparse regression matrices employing the 'Sparcc' software module.
Results: As expected, PHGG administration increased stool frequency and reduced stool consistency. Notably, this effect was more pronounced in males than females and persisted during the wash-out period. 16S sequencing revealed an increase in alpha-diversity during and also persisting after the intervention. Beta-diversity with respect to treatment periods was not different due to large inter-individual variability. NMR spectroscopy of the stool metabolome identified >30.000 signals, principal component analysis again revealed significant gender-specific differences and we identified >150 significantly changed metabolites before, during and after intervention. Interestingly, the concentration of SCFA showed an early peak that was not persistent, in contrast to numerous other metabolites.
Conclusion: In the PAGODA study, we show that a dietary intervention with PHGG induces beneficial and durable alterations of gut microbial structures along with changes in microbiota-derived metabolites. With more than 150 significantly regulated compounds we propose that microbe-host communication due to dietary fibers induced metabolites goes far beyond SCFA.
Disclosure: The study was supported by an unrestricted grant form Nestle Health Sciences to ARM. Otherwise there are no potential conflicts of interest regarding this study.

P1244 MICRONUTRIENT STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Micronutrient (MN) status in patients with inflammatory bowel disease (IBD) is important in evaluation of malnutrition. Malnutrition and weight loss are the most common causes of altered status of MN due to reduced food intake, enteric loss of nutrients and malabsorption. A wide range of vitamin and mineral deficiencies has been noticed in IBD patients, with varying degrees of clinical importance.
Aims and Methods: Aim of our study was investigate levels of micronutrients in patients with IBD, as well as assessment of possible correlation of micronutrients levels and disease activity.
A case-control study was preformed among 30 newly diagnosed IBD patients and the same number age, sex-matched healthy controls. All patients underwent a total colonoscopy with ileoscopy. Complete blood count was obtained in addition to inflammatory markers (CRP, erythrocyte sedimentation rate-ESR). Serum levels of selenium, zinc, copper and magnesium were measured spectrophotometrically, while serum iron was assesed with an electrochemiluminesence immunoassay. Mayo score and CDAI respectively were calculated for each patient.
Results: Serum levels of iron, zinc, magnesium and selenium were significantly lower ($P < 0.05$) in IBD patients than controls. There was no statistically significant difference in levels of copper between the two groups ($P > 0.05$). In patients group mean levels of iron (7.1 ± 8.2 μmol/L), zinc (23.6 ± 5.3 μmol/L), magnesium (0.6 ± 0.2 mmol/l) were reduced below the reference values, while the levels of copper (28.2 ± 24.1 μmol/L) were elevated. Serum values of iron and zinc levels negatively correlated with CDAI and Mayo score ($P < 0.05$), while the levels of copper and magnesium did not show significant correlation with CDAI and Mayo score ($P > 0.05$).
Conclusion: Our results suggest that deficiency of MN can be a result of the inflammatory process, so regular MN monitoring is essential, considering that zinc and iron deficiency could be potential indicators of disease activity.
Disclosure: Nothing to disclose

P1245 INFLUENCE OF INTRAGASTRIC AND INTRADUODENAL BITTER TASTANT ADMINISTRATION ON HUNGER RATINGS AND GUT PEPTIDE RELEASE IN HEALTHY CONTROLS

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Introduction: Intragastric (IG) administration of the bitter tastants denatonium benzoate (DB) or quinine hydrochloride (QHCl) decreases orexigenic gut peptide levels, and reduces hunger sensations. *In vitro* studies on human gastric tissue showed that DB stimulated somatostatin (SST) release.
Aims and Methods: We hypothesized that 1) the reduction in hunger ratings and orexigenic hormone levels is stronger after IG administration in comparison to ID administration, and 2) these differences are mediated by the inhibiting effect of released SST.

11 healthy female volunteers (age: 22 ± 0.7y; BMI: 21.7 ± 1.2kg/m^2) participated in a randomized, placebo-controlled crossover study. After an overnight fast, DB (1µmol/kg), QHCl (10µmol/kg) or placebo were given IG or ID via a feeding tube. A baseline blood sample was taken 10 min prior to administration. Following bloods samples were collected every 10 min after administration for a period of 2 hours. Hunger was rated at the same points on a visual analogue scale (VAS). *Ad libitum* milkshake intake was assessed at the end of the experiment and taste was scored on a VAS. Percentage change of SST and hunger were calculated from baseline. AUC of positive and negative peaks was calculated for both percentage change of hunger and SST. Net increment was calculated by subtracting the negative from the positive area. Data were analyzed using mixed models with planned contrast analysis. Comparisons of interest were QHCl vs placebo and DB vs placebo for both IG and ID administration together with the comparison between IG and ID for these differences. Observed p-values were corrected for multiple testing with stepdown Bonferroni.

Results: The net increment of hunger was significantly different after IG administration between QHCl and placebo (p = 0.03). There was no significant difference between the other comparisons. The net increment of SST, milkshake intake or taste showed no significant differences for the comparisons of interest.

Conclusion: Administration of QHCl has the potential to reduce hunger sensations in healthy female volunteers, but without significant effect on the amount of consumed milkshake and on taste scores. The effect was however, site specific as it was only seen after IG administration. SST release did not differ between the different treatments, suggesting that SST is not the inhibiting factor of orexigenic hormone secretion after IG bitter administration.

Disclosure: Nothing to disclose

P1246 VALIDATION OF SODIUM CONCENTRATION IN URINE USING POINT-OF-CARE TESTING; FEASIBILITY TO DETECT DEHYDRATION IN PATIENTS WITH AN ILEOSTOMY OR SHORT BOWEL

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Introduction: Excessive loss of water and sodium leading to dehydration is a frequent complication in patients with an ileostomy or those with a (near) short bowel syndrome (1). To maintain electrolyte and fluid balances in these patients, measurement of sodium concentration in a single portion of urine is a simple and helpful tool. In general a sodium of over >20 mmol/L rules out significant dehydration and/or sodium depletion (when not using diuretics and in the absence of significant renal disease). A direct measurement of sodium concentration in urine by means of POCT might enable patients to monitor their sodium status at home and as such might reduce complications like dehydration-related complaints such as general malaise, cramps and (eventually) problems such as kidney function loss provided that low urine sodium concentrations can be reliably measured. In this pilot study, the performance characteristics of the a home POCT tool, the Medimate Minilab, were validated.

Aims and Methods: The Medimate Minilab (Medimate BV) is a self test to measure sodium concentration in urine by means of POCT. The technology is based on microchip capillary electrophoresis combined with conductivity detection, consisting of disposable lab chips, the Medimate Lab Chip and a measurement device, the Medimate Multireader ®) (2). For validation, 50 ml of urine of xx subjects was collected and mixed with 5 ml of lithium containing buffer freshly collected urine was used to determine the limit of quantification (LOQ), imprecision and agreement with the academic laboratory reference, i.e. the Cobas 8000 ISE Roche system.

Results: Imprecision of urine samples was low: a maximum CV of 6.1% was determined in repeated measurements during five days. The smallest concentration of sodium that can be reliably measured with an acceptable imprecision was 17 mmol/L, i.e. well below the threshold of 20 mmol/l. The agreement with Sodium on the Cobas 8000 ISE system showed an overall positive bias of 23% with substantial deviation in individual points. The device was easy to handle, and found to be suitable for patients in a home setting. It is of essential importance that instructions are adequately followed, such as filling the cup to a certain volume (55 ml) of urine, to avoid falsely low results.

Conclusion: Our results suggest that home measurement of sodium concentration in urine of patients with intestinal failure to establish their hydration status seems feasible, given the high reporducability and threshold of measurements in the lower sodium concentration range observed with the current technology.

Disclosure: Nothing to disclose

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P1247 PREVALENCE AND IMPACT OF MALNUTRITION IN A GASTROENTEROLOGY DEPARTMENT. MALNUTRITION IMPAIRS HOSPITAL OUTCOMES

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Introduction: Hospital malnutrition is underestimated among physicians, even in gastroenterological settings.

Aims and Methods: To evaluate prevalence and impact of malnutrition in an Internal Medicine and Gastroenterology Department of an Italian large hospital (Fondazione Policlinico Gemelli, Rome). Patients were evaluated within 72 hours from admission according to Nutritional Risk Screening-2002 (NRS-2002) and European Society for Clinical Nutrition and Metabolism (ESPEN) criteria. Bioelectrical Impedance Analysis (BIA) derived Phase Angle (PhA) was used as a prognostic marker of length of stay and hospital mortality.

Results: In 10 months, 300 patients were enrolled. Male patients were 172 (57.3%), females were 128 (42.7%); mean age was 63.7 years (±17.6). The most frequent admission diagnoses were cancer (112 patients, 37.4%), followed by cirrhosis (43, 14.3%) and biliary diseases (31, 10.3%). 157 patients (52.5%) were at risk of malnutrition according to NRS-2002; 116 (38.7%) were malnourished according to ESPEN Criteria. Patients with a PhA <4.8° had a longer length of stay (10.9 ± 7.5 vs 8.9 ± 5.7: p = 0.018). PhA <4.8° significantly affected length of stay even when adjusted for other variables such as age, cancer, handgrip strength test and Nutritional Risk Screening-2002 < 3 (HR = 1.476; 95% CI: 1.102–1.976; p = 0.009). A Phase Angle <4.8° was independently associated with hospital mortality ($p < 0.005$).

Conclusion: Over half (52.5%) of gastroenterological patients were at risk of malnutrition and over a third (38.7%) are malnourished at admission. PhA may be used as a prognostic nutritional tool to identify patients at risk of worsening outcomes (length of stay and hospital mortality), who deserve to receive a specific nutritional support.

Disclosure: Nothing to disclose

P1248 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: DEALING WITH THE ISSUE OF DISLODGMENT

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Introduction: Percutaneous Endoscopic Gastrostomy (PEG) is widely accepted as an efficient mean to provide long term nutritional support. A soft inner bumper allows an easy external removal. Meanwhile, it similarly contributes to the growth of accidental dislodgment as a frequent complication of the procedure. The dislodgment rate is high and can lead to major harm and severe morbidity. We seek to acknowledge risk factors that commonly contribute to PEGs' accidental removal, thus allowing for a better selection of patients' individual vigilance care requirements.

Aims and Methods: We aimed to identify predictive factors for PEG's accidental dislodgment

Retrospective, unicenter study, including patients that underwent PEG procedure, from January 2014, to March 2017. Every patient had a 12 months minimum follow-up.

Statistical variables were chosen according to clinical experience and previous evidence in the literature. Univariate analysis allowed us to select variables with marginal association (p < 0.15) with the outcome variable, PEG dislodgment, which were then included in a logistic regression multivariate model. Finally the discriminative power was assessed using area under curve (AUC) of the receiver operating curve (ROC).

Results: We included 164 patients, 67.7% (111) were female and the mean age was 81 years. We report 59 (36%) PEG dislodgment and 13 (7.9%) early dislodgments. The variables with marginal association towards PEG dislodgment were hypoalbuminemia (p = 0.095); living at home (p = 0.049); living in a nursing home (p = 0.074); Cerebrovascular disease (CVD) (p = 0.028); weight fluctuation (p = 0.001); psychomotor agitation (p < 0.001); distance skin-bumper (p = 0.034) and irregular appointment follow up (p = 0.149).

We applied a logistic multivariate regression that specified the variables that remained statistically significant after model adjustment (CVD OR 4.8 [CI 95% 2.0–11.8]; weight variation OR 4.7 [CI 95%1.6–13.9] and psychomotor agitation OR 18.5 [CI 95% 5.2–65.6]).

Finally we report an excellent discriminative power (AUC ROC 0.797 [CI95% 0.719–0.875])

Conclusion: PEG is a common procedure and accidental dislodgment is a frequent complication. CVD, psychomotor agitation and weight fluctuation, by increasing this complication, are factors that would let us prudently select patients' individual vigilance care requirements.

Disclosure: Nothing to disclose

P1249 A NUTRITION SUPPORT TEAM REDUCES INAPPROPRIATE GASTROSTOMY CASE SELECTION AND ALL-CAUSE 30-DAY MORTALITY

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Introduction: Introduction: In 2004 the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report highlighted the high 30-day mortality related to Percutaneous Endoscopic Gastrostomy (PEG) insertion and the need for careful patient selection. Subsequent studies have demonstrated a higher mortality in certain patient groups, for example severe dementia. In 2010 the British Society of Gastroenterology (BSG) published guidelines recommending a nutrition support team (NST) to identify appropriate cases for PEG insertion.
A NST was set up in a district general hospital providing a review process for PEG referrals. Prior to this, patients were referred to neighbouring trusts for PEGs or to the radiology team for a per-oral inserted gastrostomy (PIG). A new standard operating procedure and dedicated electronic request form was created. A nutrition nurse was appointed to perform the initial vetting. Complex cases are discussed in a weekly nutrition multidisciplinary team (MDT) and subsequent ward round. Despite recommendations and evidence regarding PEG insertion, for many patients it remains a difficult clinical and ethical decision. Increasing bed pressures with an ageing population have complicated matters further. We have noted increasing demands for PEG to facilitate discharge to care homes.
Aims and Methods: Our aim was to assess whether the implementation of the NST led to improved patient selection and reduced 30-day all-cause mortality.
We conducted a retrospective analysis of all electronic PEG referrals and referral review notes held by the nutrition nurse between 1st December 2015 and 1st April 2017.
Results: We identified 136 referrals in total. Before the review process could be completed by the NST 8 patients died; 7 patients declined to have a PEG and 13 had already recovered their swallow and therefore these patients were excluded. 108 referrals were reviewed in full by the NST. Of the 108 referrals 81 were deemed suitable for gastrostomy insertion and 27 were not thought appropriate. 73/81 had PEGs placed. The remaining 8 were not placed due to suspicious findings during the procedure which required further investigation (1); agitation during endoscopy (1); recovered swallow prior to procedure (1); oesophageal stricture (1); and pharyngeal pouch (1); patient required referral on for radiologically inserted gastrostomy (RIG) (4). The 27 patients identified as inappropriate referrals were for the following reasons; not medically fit for procedure due to ongoing sepsis, other co-morbidities or low BMI (11); patient having end of life care (11); patient wishes to feed orally at risk (5). Of the total of those who did not proceed to PEG insertion, 22 patients died within 30 days (81.5%). In the group that did proceed to PEG 7 patients died within 30 days (9.6%): to our knowledge no deaths were related to PEG insertion.
Conclusion: Having a dedicated NST who review PEG referrals results in a significant reduction in mortality, inappropriate procedures and respects patient autonomy. It is important to maintain the NST and not let decisions surrounding gastrostomy be eroded by increasing pressures on the health care service.
Disclosure: Nothing to disclose

P1250 COMPOSITION OF THE MICROBIOME IN PATIENTS WITH SHORT BOWEL SYNDROME

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Introduction: Short bowel syndrome (SBS) is present when the length of the remnant small intestine after surgical resection is <200 cm. The decreased absorpting area and shortened transit-time increase the absorption of nutrients, electrolytes and water and lead to a permanent need for parenteral nutrition in many cases. The surgical shortening of the bowel causes a qualitative-quantitative change of the human microbiome. These alterations influence greatly the quality of life of the SBS-patients through the immun-, and nutritional status.
Aims and Methods: To investigate the composition of the microbiome of patients with SBS.
Patients >18 years old with SBS were included. After informed consent anthropometric parameters (weight, height, BMI, body composition- Inbody) were registered. To identify the microbiome-composing bacteria, stool samples were collected and the 16S rRNS (member of the subunit of procaryotic ribosome 30S) genetical sequencing was made. Beside evaluating the composition we calculated the Microbiome Diversity Index (MDI) comparing the diversity of the microbiome of patients with SBS to the data derived from the normal population.
Results: 5 female patients with SBS are under care at our clinic (mean age: 49 ± 13 év, mean bowel lenght: 81 ± 65cm, BMI:17.8 ± 2.1 kg/m^2), 3 of 5 patients are on parenteral nutrition permanently. The diversity is extremly reduced compared to the normal population (MDI: 5.5 ± 1.9, 0–30 between percentiles). The main phylum is Firmicutes, and Proteobacterium and Actinobacterium phyla are present, but the ratio of Bacterioides phyla is extremly low. Among Firmicutes the lactate-producing and -consuming bacteria (Lactobacillus, Bifidobacterium, Veillonella) form the majority of the microbiome.
Conclusion: The composition of microbiome of SBS patients differs largely from the normal population; the diversity is extremely reduced. Being able to enrich the diversity of bacteria in patients with SBS has probably therapeutical consequences.
Disclosure: Nothing to disclose

P1251 RAPID DIAGNOSIS OF BLOODSTREAM INFECTIONS IN PATIENTS ON HOME PARENTERAL NUTRITION

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Introduction: Home parenteral nutrition (HPN) patients have an increased risk of catheter-related bloodstream infections. Early identification of causative microorganism (s) is critical to optimize patient care and antimicrobial use. The droplet digital polymerase chain reaction (ddPCR) is a novel culture-independent molecular technique to rapidly identify pathogens in whole blood.
Aims and Methods: The aim of this study was to measure the diagnostic accuracy of the ddPCR in the HPN-setting in comparison with the current gold standard blood cultures. We analyzed a set of historically collected frozen blood samples from adult HPN patients with a suspected bloodstream infection, and compared these with blood cultures drawn on the same day. In a relative short procedure (± 4 hours), whole blood samples with possible DNA from microorganisms were isolated and analyzed with ddPCR. The analyses were independently performed by two research analysts, without knowledge of the blood culture results. Study outcomes included sensitivity, specificity, the positive- and negative predictive value, and the positive- and negative likelihood ratio of the ddPCR.
Results: In total, 40 blood samples were analyzed (Table 1). The sensitivity was 80% (95%CI 44–97) and the specificity 83% (95%CI 65–94). The positive- and negative predictive value were 62% (95%CI 40–79) and 93% (95%CI 78–98), respectively. The positive- and negative likelihood ratio were 4.8 (95%CI 2.0–11.3) and 0.24 (95%CI 0.07–0.84), respectively.

		Bloodculture		
		Positive	Negative	Total
ddPCR	Positive	8	5	13
	Negative	2	25	27
	Total	10	30	40

[Table 1]
Conclusion: ddPCR has an acceptable sensitivity and specificity for identifying pathogens from whole blood. At this moment, ddPCR seems to work especially well in predicting true negative results. A larger prospective study will be conducted to confirm these results.
Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 09:00–14:00
Liver and Biliary III – Hall X1

P1252 EFFECT OF ROSUVASTATIN ON HEPATIC STEATOSIS AND FIBROSIS IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS: A DOUBLE BLIND RANDOMIZED CLINICAL TRIAL

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Introduction: Non-alcoholic steatohepatitis is a serious and progressive disease, with no definitive treatment for it. Statins, as cholesterol-lowering drugs, are one of the treatments proposed for this disease.
Aims and Methods: The aim of the present study is to determine the effect of rosovatatin on steatosis and fibrosis in patients with non-alcoholic steatohepatitis. In this double-blind clinical trial, 44 patients with non-alcoholic steatohepatitis without metabolic syndrome, non-diabetic and BMI less than 30 were randomly divided into intervention (6 months daily 10 mg of rosuvastatin with nutrition and lifestyle education) and control (Placebo with the same protocol) groups. The condition of liver fibrosis and steatosis were evaluated by transient elastography (FibroScan) at the beginning and the end of the study.
Results: After 6 months, the percentage of steatosis in both groups was lower than the beginning of the study, which was significant in the intervention group ($P = 0.014$). At the beginning of the study, the liver fibrosis index in the control group was significantly lower than intervention group ($P = 0.01$) and at the end of the study, this difference was maintained between the two groups ($P = 0.002$). In the intervention group, the index of fibrosis decreased, although this difference was not significant ($P = 0.22$).
Conclusion: The use of rosuvastatin can affect the reduction of steatosis and may prevent the progression of liver fibrosis.
Disclosure: Nothing to disclose

P1253 MICRORNA-199A-3P PROMOTES THE ACTIVATION OF HEPATIC STELLATE CELLS AND LIVER FIBROSIS BY SUPPRESSING CAVEOLIN-2

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Introduction: There is limited therapy for liver cirrhosis although it constitutes a large proportion in the world. The activation of hepatic stellate cells (HSCs) is known as the key contributors to liver fibrosis/cirrhosis. MicroRNAs have been widely reported to regulate various diseases including liver fibrosis, and are promised to be novel therapeutic targets.
Aims and Methods: The aim of the study is to investigate the role of miR-199a-3p and its target caveolin-2(CAV2) in liver fibrosis and the underlying mechanisms. Rat HSCs was isolated by in situ perfusion with pronase and collagenase B, followed by Nycodenz density gradient centrifugation. We perform microRNA microarray to detect microRNA expression profile in quiescent and activated rat HSCs. We validated the microarray data by qPCR in rat HSCs, and further examine the expression in rat and human liver fibrotic tissues. Based on these results, the increased miR-199a-3p in both activated HSCs and liver fibrotic tissues was selected for further analysis. The human HSCs line, LX_2 and rat HSCs were transfected with miR-199a-3p mimics and antagomir, followed by qPCR and western blot to examine the expression of fibrotic markers. Moreover, MTT assay and colony formation experiment were used to detect the proliferation of HSCs. The targets of miR-199a-3p were predicted by Targetscan and miRanda. The effect of miR-199a-3p in vivo was assessed in mice liver fibrosis model induced by CCL_4.
Results: miR-199a-3p was dramatically up-regulated during HSCs activation and liver fibrotic tissues from both rat and human. Forced expression of miR-199a-3p in LX_2 and rat HSCs significantly increased fibrotic markers expression. Additionally, inhibition of miR-199a-3p reduced fibrotic markers expression. MiR-199a-3p suppressed CAV2 protein expression without mRNA repression. Further study reveled that CAV2 obviously inhibited fibrotic markers expression and the proliferation of HSCs. We then found the protein expression of TGFβRI, a key receptor in TGF-β signaling pathway, was reduced by CAV2. Interestingly, Twist1 could bind with the promoter sequences of human miR-199a-3p to drive miR-199a-3p expression in HSCs, then promoting liver fibrosis. More importantly, we provided evidence that antagomiR-199a-3p injection relieved mice liver fibrosis induced by CCL_4.
Conclusion: Our data indicate that miR-199a-3p mediates the regulation of liver fibrosis by suppressing CAV2 expression, and promoting TGF-β signaling pathway probably through increasing TGFβRI expression. Thus miR-199a-3p may represent potential targets for novel therapeutic strategies against hepatic fibrogenesis and also might evolve as biomarkers in the diagnosis of liver fibrosis.
References: none
Disclosure: Nothing to disclose

P1254 THE COMBINATION OF AN ANDROGEN, A BILE ACID AND AN EICOSANOID IS A PROMISING BIOMARKER FOR LIVER FIBROSIS IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver condition in the Western world and is considered a hepatic manifestation of the metabolic syndrome. It is associated with an increased risk of type 2 diabetes and cardiovascular diseases, and is characterized by an accumulation of lipids in the liver, which can lead to liver fibrosis and/or inflammation, eventually progressing to hepatocellular carcinoma. Although liver biopsy is still the gold standard for diagnosis and staging of patients with suspected NAFLD, it has many drawbacks, such as sampling errors, costs, and risks of complications. Furthermore, it is impractical for regular screening of patients because of the large number of individuals who have NAFLD. Therefore, tools for non-invasive assessment of disease severity are urgently needed.
Aims and Methods: The aim of this study was to identify novel non-invasive markers that are associated with key histology lesions of progressive NAFLD. Therefore, patients with biopsy-proven NAFLD (n = 74) and healthy controls (n = 62) were recruited; among the NAFLD patients, 13 had advanced fibrosis (≥F2) and 61 had no or mild fibrosis (F0-F1). EDTA plasma samples were obtained from blood by centrifugation and analyzed using gas chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry-based metabolomics. Statistical analysis was performed by multivariate (random forest, elastic net, and linear discriminant analysis) as well as univariate (analysis of variance) algorithms, and peak signals were compared to key histology lesions of NAFLD, i.e. fibrosis, activity, and steatosis.
Results: We identified a metabolite panel that successfully distinguishes between patients with fibrosis stage F≥2 and those with fibrosis stage F < 2. Our biomarker, consisting of an androgen, a bile acid and an eicosanoid, showed an area under the curve (AUC) value of 0.95 (sensitivity of 0.92, specificity of 0.90), outperforming current non-invasive diagnostic tests, including the measurement of caspase-cleaved keratin 18 levels (AUC = 0.68), the fibrosis-4 index (AUC = 0.80), and the enhanced liver fibrosis score (AUC = 0.82).
Conclusion: Our results proved that metabolomics is a powerful technology platform for studying complex disease mechanisms. By using whole metabolite profiling, we could identify a biomarker that is strongly associated with the stage of liver fibrosis in NAFLD patients. Since it provides an excellent performance in the detection of fibrosis in plasma samples from NAFLD patients, it can serve as a new non-invasive screening tool for NAFLD patients.
Disclosure: Nothing to disclose

P1255 PLGA NANOPARTICLES-BASED DELIVERY OF SRC KINASE SIGNALING PATHWAY INHIBITOR KX2-391 FOR THE TREATMENT OF NON-ALCOHOLIC STEATOHEPATITIS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) affecting about 25% of population, is becoming the leading and growing cause of mortality worldwide. The prevalence of NAFLD is growing rapidly due to western life style, and increasing incidences of diabetes and obesity. 30% of affected people develop liver Inflammation or non-alcoholic steatohepatitis (NASH) which further progresses to advanced fibrosis or cirrhosis to hepatocellular carcinoma. Currently, there is an unmet need for the effective and safe therapies for the treatment of this disease. Inflammatory macrophages play a crucial role in the pathogenesis of NASH and NAFLD. Therefore, molecular therapies inhibiting macrophage activation would be highly promising therapy for the treatment of NASH.
Aims and Methods: Transcriptome analyses in NASH patients and inflammatory macrophages revealed Src kinase, a tyrosine-protein kinase, as a prospective therapeutic target in inflammatory M1 macrophages. In this study, we investigated the implication of Src signaling pathway inhibition in inflammatory macrophages and NASH. We further developed a PLGA nanoparticles delivery system to deliver Src kinase inhibitor, for improved pharmacokinetic profile and therapeutic efficacy, to inhibit M1 macrophages thereby ameliorating liver inflammation and NASH.
To accomplish the goals of this project, we used KX2-391, a small-molecule Src kinase inhibitor. We tested the therapeutic efficacy and toxicity of KX2-391 in the differentiated inflammatory RAW macrophages and bone marrow derived macrophages. Thereafter, we synthesized PLGA nanoparticles to deliver Src kinase inhibitor (KX2-391) to increase the drug pharmacokinetics for the efficient treatment of liver inflammation. We investigated the efficacy of KX2-391-PLGA nanoparticles in differentiated RAW macrophages, bone marrow derived macrophages and murine precision cut liver slices (PCLS). Finally, we evaluated the therapeutic effects of KX2-391 and KX2-391-PLGA nanoparticles *in vivo* in Methionine Choline deficient (MCD)-diet NASH model.
Results: Analysis of livers from NASH patients showed a highly significant induction of Src kinase expression that correlated with the increasing NAS score as compared to normal livers as determined from transcriptome analysis (GEO accession number: GSE48452). Expression of Src kinase and M1-specific genes (iNOS, IL-1β, CCL2, Fcγ$R1) was found to be significantly upregulated in inflammatory macrophages. Src kinase pathway activation (Src phosphorylation) was confirmed in inflammatory macrophages. KX2-391 dose-dependently inhibited the phosphorylation of Src and pSTAT1 signaling pathway. Furthermore, KX2-391 significantly attenuated M1-induced Nitric oxide (NO) release (an indicator of M1 activation) and expression of M1 markers in RAW macrophages, BMDMs and murine precision cut liver slices (PCLS). PLGA loaded KX2-391 (KX2-391-PLGA) showed favorable size, stability, and drug entrapment efficiency. KX2-391-PLGA inhibited NO release and M1-specific markers expression in RAW macrophages and BMDMs. KX2-391 and KX2-391-PLGA showed significant inhibition of M1 macrophage markers in PCLS without inducing toxicity. Recently, we have performed an *in vivo* study on MCD diet-induced murine model of NASH and preliminary results suggests inhibition in liver inflammation as assessed by quantitative PCR. Further analyses are currently ongoing.

Conclusion: Inhibition of Src signaling pathway in inflammatory macrophages suggests a potential therapeutic approach to treat non-alcoholic steatohepatitis.
Disclosure: Nothing to disclose

P1256 THERAPEUTIC INHIBITION OF SYK KINASE IN MACROPHAGES USING PLGA NANOPARTICLES FOR THE TREATMENT OF NON-ALCOHOLIC STEATOHEPATITIS

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Introduction: Non-alcoholic steatohepatitis (NASH) is the leading cause of cirrhosis worldwide and is the most rapidly growing indication for liver transplantation. Macrophages are an important cellular component in the inflammatory milieu in NASH. The inflammatory and pro-fibrotic mediators produced by macrophages causes significant tissue injury leading to initiation and progression of many inflammatory diseases especially NASH. These inflammatory (classically-activated or M1) macrophages also recruit scar-forming fibrogenic myofibroblasts and inflammatory cells further driving liver injury to fibrosis, cirrhosis, and hepatocellular carcinoma. Therefore, inhibition of the inflammatory macrophages would be a promising approach to attenuate liver inflammation.
Aims and Methods: Bukong et al. have recently demonstrated the immunomodulatory role of spleen tyrosine kinase (SYK) pathway in alcoholic liver disease [1]. In this study, (i) we aim to study the implication of SYK signaling pathway in NASH and inflammatory macrophages; (ii) we investigated PLGA nanoparticles based delivery of SYK signaling pathway inhibitor as an highly effective and promising therapeutic approach for the treatment of NASH.
Methods: To accomplish the goals of this study, we used R406, a small-molecule Syk kinase inhibitor that blocks Fc receptor signaling pathway and reduces immune complex-mediated inflammation [2]. We tested the therapeutic efficacy of R406 in the differentiated inflammatory RAW macrophages. Thereafter, we synthesized PLGA nanoparticles to deliver SYK kinase inhibitor (R406) to increase the drug pharmacokinetics for the efficient treatment of liver inflammation in NASH. We investigated the efficacy of R406-PLGA nanoparticles in differentiated RAW macrophages and bone marrow-derived macrophages. Furthermore, we evaluated the therapeutic effects of R406 and R406-PLGA nanoparticles *in vivo* in Methionine Choline deficient (MCD)-diet NASH model.
Results: Analysis of livers from NASH patients showed a highly significant induction of SYK expression that correlated with the increasing NAS score as compared to normal livers as determined from transcriptome data analysis (GEO accession number: GSE48452). We observed significant upregulation of SYK expression and activation of SYK signaling pathway (SYK phosphorylation) in inflammatory macrophages. R406 dose-dependently inhibited LPS- and IFNγ-induced activation of SYK signaling pathway consequently resulting in inhibition of M1-induced nitric oxide (NO) release (M1 activation) and M1-specific markers (IL-1β, FcγR1, CCL2, iNOS, and IL-6) in RAW macrophages and bone marrow derived macrophages (BMDMs). R406 loaded PLGA nanoparticles (R406-PLGA) were successfully synthesized and were characterized for the size, charge, stability, and the drug entrapment efficiency. R406-PLGA inhibited NO release and M1-specific markers (IL-1β, FcγR1, CCL2, iNOS, and IL-6) in RAW macrophages and BMDMs. Finally, we performed an *in vivo* study on a typical murine model of NASH-associated liver inflammation and liver injury i.e. diet-induced (methionine-and-choline-deficient, MCD) model and further analyses are currently ongoing.
Conclusion: Inhibition of SYK signaling pathway using small molecule inhibitor and delivery of SYK inhibitor using PLGA nanoparticles can be a highly effective and potential therapeutic approach for the treatment of Non-alcoholic steatohepatitis.
Disclosure: Nothing to disclose

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P1257 THE SEQUENCE ANALYSIS OF NEW MITOCHONDRIAL GENE, MOTS-C, IN PATIENTS WITH THE NON-ALCOHOLIC STEATOHEPATITIS

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Introduction: In 2015, a new gene called as mitochondrial open reading frame of the 12S rRNA-c (MOTS-c) was found in 12S rRNA region of mtDNA. MOTS-c encodes a 16-amino-acid peptide. It has been reported that this new peptide reduces insulin resistance and obesity in experimental animal models. Insulin resistance and obesity are important components of non-alcoholic steatohepatitis. Therefore, variations in the MOTS-c gene may be responsible for insulin resistance in nonalcoholic steatohepatitis (NASH).
Aims and Methods: We aimed to find potential association between MOTS-c nucleic acid variations and NASH. DNA was isolated from the peripheral blood of 100 NASH patients and age and sex-matched 100 healthy controls. Primers were designed by using the Primer3 program for amplification of the MOTS-c gene (GenBank: KP715230.1). Whole MOTS-c gene was sequenced by using ABI 3500 Genetic Analyzer.
Results: We only detected one mutation in the NASH group. This mutation converts stop codon of MOTS-c gene to glycine amino acid. However, there was no variation found in the control group.
Conclusion: To the best of our knowledge, this is first human study is related to MOTS-c genetic variations in the NASH. We found that the MOTS-c gene is quite conserved, although mtDNA is highly variant. There was not found to be an association between NASH and MOTS-c genetic variations but this preliminary finding should be investigated in the different ethnic and geographical populations. This mutation may result a non-functional peptide formation longer than MOTS-c. In this case, our hypothesis is that, nonfunctional peptide can not activate AMPK pathway and so blood glucose levels may increase and insulin resistance may develop in skeletal muscles. However the effect of this mutation on MOTS-c peptide should be tested in the in-vitro study.
Disclosure: This study was supported by grants from Marmara University, Scientific Research Research Projects Committee (Project No:SAG-C-YLP-070617-0342).

P1258 THE RELATIONSHIP BETWEEN SMALL INTESTINAL BACTERIAL OVERGROWTH AND ENDOTOXEMIA LEVELS AND TLR2,TLR4 EXPRESSION IN PATIENTS WITH CIRRHOSIS

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Introduction: In cirrhotic patients, portal hypertension, hypohepatia, intestinal mucosal hyperemia and edema, dyskinesia, dysfunction of bile salt transporters and other factors could influence the species, colonization and metabolism of bacteria, leading to disbiosis of gut microbiota. While due to direct toxicity of endotoxin and inflammatory mediated-damage, intestinal dysbacteriosis could further aggravate liver damage. It has been found that TLR2,TLR4 and CD14 is the main endotoxin receptor. This study were to evaluate the effect of SIBO by lactulose hydrogen breath test, measure the plasma concentrations of endotoxin, and TLR2,TLR4 expression to determine the relationship among SIBO, endotoxemia and TLR2,TLR4 expression. Small intestinal bacterial overgrowth (SIBO) gets great attention because of its clinical significance in systemic and local complications in patients with liver cirrhosis, but there are still many controversies about the mechanisms.
Aims and Methods: We aimed to determine the frequency of SIBO in cirrhotics and correlate with endotoxemia, TLR2,TLR4 expression.
Between July 2015 and December 2016, there were 58 cirrhotic patients enrolled in our department. Based on the Child-Pugh classification, there were 18 cases of Child-Pugh grade A, 17 cases of grade B and 23 cases of grade C.36 males and 22 females, aged between32 and 75 years, with a mean age of 45.62 ± 12.50 years. The study involved 26 cases of healthy controls (16 men and 10 women; range, 23–78 year; mean age, 42.25 ± 14.18 year). Patients were included in the study if they had not been using any antibiotics, lactulose, antacids, or other drugs affecting gastrointestinal motility in the past 4 weeks. The serum endotox were tested by TAL chromogenic substrate Assay. The expression of TLR2,TLR4 on the surface of PBMC were tested by flow cytometry. Small-intestinal bacterial overgrowth was determined by LHBT. A rise of ^{3} 20p.p.m from basaline or a rise of ^{3}20 p.p.m from basaline in hydrogen by 90 min should be considered SIBO positive test. Hydrogen breath gross were also measured in all subjects who exhaled gas within 90 minutes (LHBT set-value). The LHBT set -value is expressed by the sum of the seven measured values in 90 minutes or before the second peak. In addition,it can be used as an indicator to indirectly reflect the growth of bacteria in the small intestine.
Results: Of the 58 cirrhotics, 25 (43.10%) had SIBO positive, compared to two (7.69%) control ($x^2 = 10.32$, $P = 0.001$). The LHBT intestinal set value,serum endotox level and the expression TLR2,TLR4 on the surface of PBMC in cirrhosis were obviously higher than the control group ($t = 11.573$, $P < 0.05$; $t = 9.958$, $P < 0.05$; $t = 12.380$, $P < 0.05$; $t = 10.319$, $P < 0.05$); It was shown by Pearson correlation analysis that LHBT intestinal set value was positive correlated with endotox level and the expression TLR2,TLR4 among cirrhotic patients and live cirrhosis with SIBO-negative.
Conclusion: Small-intestinal bacterial overgrowth was prevalent in patients with liver cirrhosis, and was related to the severity and complications of the liver disease. LHBT set-value as an indicator of bacterial contamination in the small intestine, it was significantly higher in liver cirrhosis than that in normal people, and it was positively correlated with the severity of symptoms. SIBO is associated with endotoxemia, and through TLR2,TLR4 signaling pathways lead to inflammatory damage, thereby involving in the developing cirrhosis. The early diagnosis and treatment of SIBO in liver cirrhosis will be possible to reduce complications, hold-up or delay the disease procession.
Disclosure: Nothing to disclose

P1259 MUCOSAL-ADHERENT *ESCHERICHIA COLI NF73-1* ISOLATED FROM A PATIENT WITH NON-ALCOHOLIC STEATOHEPATITIS INDUCES LIVER INJURY IN HIGH-FAT DIET MICE

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Introduction: It has been indicated that gut microbiota plays critical roles in non-alcoholic fatty liver disease (NAFLD). Our previous study has demonstrated that the abundance of *Escherichia* is significantly increased in fecal and mucosal microbiota in non-alcoholic steatohepatitis (NASH) patients. Our aim is to investigate the role of clinically isolated mucosal-adherent *Escherichia coli* (*E.coli*) strains in the development of NAFLD in high-fat diet (HFD) mice.
Aims and Methods: Colonic mucosa from one biopsy-proven NASH patient was obtained and cultured in Luria-Bertani (LB) medium, followed by planking on *E.coli* Chromogenic Medium. One hundred monoclone isolates were obtained and identified as *E.coli* through full-length 16s ribosomal RNA sequence and *E.coli*-specific gene uidA. Phylogenetic tree (maximum likelihood method) showed 3 clusters, which contained 73, 23, and 4 isolates respectively. They were named NF73-1 to NF73-73, NF23-1 to NF23-23, and NF4-1 to NF4-4. C57BL/6J mice were fed with HFD for 12 weeks. At 10th week, mice were treated daily with an oral administration of NF73-1, NF23-1, NF4-1 or LB for 2 weeks. In vitro, intestinal epithelial cells HT-29 were seeded on 12-well plates and treated with NF73-1, NF23-1, NF4-1 or LB.
Results: Compared with LB medium, NF73-1, NF23-1 and NF4-1 all increased NAFLD activity score (NAS). NF73-1 group showed the worst liver pathology and the highest NAS. In addition, Sirius-Red staining revealed that merely NF73-1 initiated hepatic fibrosis. Furthermore, bacterial load in liver was increased in NF73-1 and NF4-1 group, with NF73-1 higher. Consistently, highest mRNA levels of IL-6 and iNOS were observed in NF73-1 group, followed by NF4-1 and NF23-1 groups. The proportion of $CD11c^{+}MHCII^{+}$ $F4/80^{-}$ dendritic cells (DCs) in liver exhibited no significance among all groups. However, NF73-1, NF23-1 and NF4-1 all increased $IL\text{-}1\beta^{+}$DCs, and NF73-1 elevated $IL\text{-}6^{+}$ DCs in liver compared with other three groups, indicating enhanced hepatic immune responses of NF73-1 group. The mRNA and protein levels of MUC-2, Occludin and ZO-1 in colonic mucosa were markedly downregulated in NF73-1 treated mice compared with NF23-1 and NF4-1 groups. Similar with in vivo study, the mRNA levels of Occludin and ZO-1 in HT-29 cells were lowest in NF73-1 group.
Conclusion: Mucosal-adherent *Escherichia coli NF73-1* induces more serious liver injury than other isolates NF23-1 and NF4-1, indicating that NF73-1 might be a critical strain in NAFLD. Our research shed some light on diagnosis and treatment of NAFLD targeting specific bacterial strain.
Disclosure: Nothing to disclose

P1260 DOES THE COFFEE VIA GUT-LIVER AXIS PLAY A BENEFICIAL EFFECT ON LIVER DAMAGE?

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Introduction: Metabolic syndrome is one of the most important health issues worldwide. Its liver phenotype is called nonalcoholic fatty liver disease (NAFLD). We have previously demonstrated that high fat diet (HFD)-induced liver damage is reverted by coffee consumption thought a reduction of fat deposition in the liver and an amelioration of antioxidant and anti-inflammatory status.
Aims and Methods: We hypothesize that the first target organ of coffee is the gut, supporting the protective effect on the liver by modulating the gut permeability and contributing to the concept of relevant role of gut-liver axis. Twenty-four C57BL/6 mice were divided into 3 groups of 8 mouse each: one group received standard diet (SD: 3.3 Kcal/g, 5% from fat), one group received HFD (5.6 Kcal/g, 58% from fat), and a third group received HFD plus decaffeinated coffee solution (HFD+Coffee) for 12 weeks. Coffee daily dosage corresponded to 6 cups of espresso coffee or 2 cups of filtered coffee for a 70 kg person. At the end of treatment, hepatic histology was examined by H&E staining. Alanine-aminotrasferase (ALT), total cholesterol levels were measured in serum samples. Gene expression of PPAR-α and LXR-α was assessed in the liver. The expression of molecular mediators of fatty acids ABCA1, ABCG1, FFAR-1 and of gut permeability Zonulin and Claudin were evaluated in duodenum and colon by RT-PCR. Cecum fecal samples were collected for triglycerides and fatty acids analysis.
Results: Mouse body weight was significantly lower in HFD+Coffee group *vs* HFD ($p < 0.003$). Coffee treatment also reduced cholesterol and ALT serum levels ($p < 0.001$ and $p < 0.05$, respectively), and ameliorated liver macrovesicular steatosis ($p < 0.001$) and ballooning degeneration ($p < 0.05$). Coffee supplementation increased the expression of PPAR-α and LXR-α in the liver and upregulated the expression of ABCA1, ABCG1, FFAR-1, Zonulin, and Claudin in the duodenum and colon. The fecal cecum content of HFD+Coffee group showed higher levels of total triglycerides and fatty acids *vs* HFD group.
Conclusion: Coffee modulates the intestinal permeability and molecular expression of fatty acids mediators increasing fat oxidation and ameliorating fatty acids efflux. Coffee *via* of gut-liver axis exerts a beneficial effect on the liver reducing hepatic steatosis.
Disclosure: Nothing to disclose

P1261 A NOVEL AUTOMATIC DIGITAL ALGORITHM THAT ACCURATELY QUANTIFIES STEATOSIS IN NAFLD ON HISTOPATHOLOGICAL WHOLE SLIDE IMAGES

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Introduction: Progression from non-alcoholic fatty liver disease (NAFLD) to steatohepatitis is associated with severity of steatosis. Accurate assessment of hepatic steatosis in liver biopsy specimens is thus important. Steatosis is graded using the semi-quantitative Brunt score (grade 0 = 0–5%; grade 1 = 5–33%; grade 2 = 33–66%; grade 3 >66% of fatty droplets in a variable numbers of high-power fields). This score is subject to inter- and intra-observer variability, which may affect reproducibility and accuracy of results. Digital automated quantification of the whole liver tissue slide, in contrast to random area selection, has the potential to overcome this.
Aims and Methods: We aim to develop and validate a steatosis quantification algorithm for automated digital analysis of whole slide images. For the training and validation cohort, hematoxylin-eosin stained liver tissue slides from patients with or without NAFLD are included and digitally scanned at 20x magnification. Steatotic areas are manually annotated in representative biopsies from each steatosis grade. Next, thresholds for size and roundness parameters are identified by logistic regression to discriminate steatosis from surrounding liver tissue. The resulting algorithm produces a steatosis proportionate area (SPA; ratio of steatotic area to total tissue area described as percentage) which will be correlated to the steatosis grade. The software is implemented as a Java plugin in FIJI, in which digital whole slide images can be processed automatically with use of the Pathomation extension.
Results: Liver tissue specimens of 61 NAFLD patients and 18 controls were included. The area under the curve of correctly classified steatosis by the algorithm was 0.970 (95% CI 0.968–0.973), $p < .001$. Accuracy of the algorithm was 91.9%, with a classification error of 8.1%.
The median SPA per steatosis grade was: grade 0 1.41% (IQR 1.03–1.80%); grade 1 4.99% (IQR 2.97–9.31%); grade 2 13.65% (IQR 10.90–16.10%), and grade 3 16.34% (IQR 14.48–20.54%). SPA correlated significantly with steatosis grade (Rs = .845, CI:.749-.902, $p < .001$). In post-hoc analyses, SPA increased significantly with each individual steatosis grade, except between grade 2 and 3. Median fat droplet size increased with steatosis grade (grade 0 108 um^2 (IQR 94–124); grade 1 170 um^2 (IQR 158–233); grade 2 249 um^2 (218–309); grade 3 226 um^2 (207–321), $p < .001$). Number of fat droplets (median 169.8 (IQR 136.1–304.2)) did not increase with steatosis grade.
Conclusion: We have developed a novel digital analysis algorithm that accurately quantifies steatosis in whole liver slides. SPA percentages were in all cases lower than the percentage range resembled by the steatosis grade. This underlines the variability, typically associated with visual examination. Automated analyses of whole slide images benefits from objective and labor-free analysis. This algorithm can be incorporated when quantification of steatosis is warranted, such as in clinical trials studying efficacy of new therapeutic interventions in NAFLD.
Disclosure: Nothing to disclose

P1262 FATTY LIVER PROMOTES GAMMA-GLUTAMYL TRANSPEPTIDASE ACTIVITY-INDUCED ARTERIAL PLAQUE FORMATION

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Introduction: Recent studies have provided evidence for a pivotal role of gamma-glutamyl transpeptidase (GGT) activity in arterial plaque formation. Furthermore, many studies have suggested a positive association of fatty liver disease with carotid atherosclerosis, a well-known risk factor for cardiovascular disease (CVD). In a previous cross-sectional study, we reported a strong relationship between the combination of fatty liver and an elevated serum GGT level and the presence of carotid plaque (*J Atheroscler Thromb*. 2015; 22(10): 1051–60). The aim of the current longitudinal study was to determine whether this combination can indeed cause carotid plaque formation.
Aims and Methods: This study included subjects who had no evidence of carotid plaque at baseline and received an annual health checkup more than 7 years. Exclusion criteria were as follows: a history of CVD; hepatitis B or C virus infection; heavy drinking (more than 60 g per day of alcohol); medications capable of influencing the course of atherosclerosis in the past and during the follow-up period, including antihypertensive agents, antidyslipidemic agents,

antidiabetic agents, and antiplatelet/anticoagulant agents. We performed ultrasound examinations for assessing fatty liver and carotid plaque. Carotid plaque was defined as an intima-media thickness greater than 1.5 mm in any portion of the carotid arteries. We calculated cumulative incidence rates of carotid plaque formation by the Kaplan-Meier method and investigated predictors for carotid plaque formation using the Cox proportional hazards model.
Results: A total of 599 subjects had received a health checkup more than 7 years until the end of 2016. After excluding subjects according to the above criteria, we enrolled 107 subjects (median age, 49 years; 76 male and 31 female). At baseline, fatty liver and serum GGT levels ≥ 50 U/L (the median value as the cut-off) were observed in 15 and 38 subjects, respectively. During a median follow-up period of 13.3 years (range, 7.2 to 15.5 years), carotid plaques emerged in 34 subjects (24 male and 10 female); the cumulative incidence rates were 10%, 23%, and 40% at 5, 10, and 15 years, respectively. There was no significant difference in the incidence rates of carotid plaque emergence between subjects with and without fatty liver, while the rates were significantly higher in subjects with a serum GGT level ≥ 50 U/L than in those with GGT levels < 50 U/L (p = 0.02). Surprisingly, when combining fatty liver and serum GGT levels, subjects with both fatty liver and a serum GGT level ≥ 50 U/L had the highest incidence rates (62.5% at 10 years; n = 8), followed by those only with a serum GGT level ≥ 50 U/L (34.3% at 10 years; n = 30), those without the conditions (14.5% at 10 years; n = 64), and those only with fatty liver (0% at 10 years; n = 5) (p = 0.017). Univariate analysis revealed that variables with p < 0.1 were smoking, HDL cholesterol, triglyceride, and the combination of fatty liver and a serum GGT level ≥ 50 U/L. In multivariate analysis, this combination was the only significant predictor for carotid plaque formation (age- and sex-adjusted hazard ratio 4.4; 95% confidence interval 1.5–13.0; p = 0.007)
Conclusion: Our results suggest that the presence of fatty liver may promote GGT activity-induced arterial plaque formation. Checking the combination of fatty liver and an elevated serum GGT level can help identify subjects who are at high risk of future CVD.
Disclosure: Nothing to disclose

P1263 THE ASSOCIATION BETWEEN NONALCOHOLIC FATTY LIVER DISEASE AND MILD COGNITIVE IMPAIRMENT IN THE ELDERLY

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Introduction: Up to now, more and more researchers have found that metabolic syndrome (MS) and its elements are closely related to cognitive impairment. Since nonalcoholic fatty liver disease (NAFLD) was regarded as an element of MS in liver and they share a lot of similarities in pathogenesis, it is fair to hypothesize that NAFLD is also related to cognitive impairment. However, the correlation between NAFLD and cognitive impairment in the elderly and the underlying mechanisms had not been revealed. Considering the elderly is the major population affected by cognitive impairment, and we lack effective treatment for serious cognitive impairment as dementia, MCI may be a good period to prevent serious cognitive impairment.
Aims and Methods: We aimed to investigate the association between NAFLD and MCI and the possible underlying mechanisms in the elderly.
A total of 392 elderly objects (60 years), with and without NAFLD were enrolled in this study and were subdivided into NAFLD group (n = 191) and non-NAFLD group (n = 201). Their clinical data including medical history, medications, blood pressure, body mass index (BMI), liver function, kidney parameters, glucose metabolism parameters, serum lipid profile, NAFLD fibrosis score and carotid plaques were collected, and logistic regression analysis was used to investigate the association between NAFLD and MCI.
Results: Detection rate of MCI in NAFLD group is significantly higher than that in non-NAFLD group (19.9% vs 10.4%, 2 = 6.837, P = 0.009); and NAFLD is an independent risk factor (OR = 2.625, 95% confidence interval (CI) 1.250–5.512, P = 0.011) for MCI after adjusting confounding variables such as age, gender, education, cardiovascular disease and its risk factors. In addition, female (OR = 2.775, 95%CI 1.363–5.651, P = 0.005), unstable plaques of carotid (OR = 2.736, 95%CI 1.131–6.620, P = 0.026), history of stroke (OR = 4.122, 95%CI 1.374–12.363, P = 0.011), serum albumin (OR = 0.908, 95%CI 0.840–0.982, P = 0.015), fast serum glucose (OR = 1.268, 95%CI 1.076–1.493, P = 0.004), serum AST/ALT ratio (OR = 2.984, 95%CI 1.370–6.500, P = 0.006) were also independently associated with MCI in the elderly. Among them, female, unstable plaques of carotid, a history of stroke, higher levels of fasting serum glucose and AST/ALT ratio were independent risk factors for MCI in the elderly.
Conclusion: NAFLD is independently associated with MCI in the elderly.
Disclosure: Nothing to disclose

P1264 NONINVASIVE FIBROSIS SCORES (APRI, FIB 4 INDEX, BARD)-USEFUL TOOLS FOR EVALUATING FATTY LIVER DISEASE

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Introduction: Several noninvasive fibrosis assessment tests were developed in order to replace liver biopsy.
Aims and Methods: Our goal was to assess the correlation between APRI, FIB 4 Index and BARD score with transient elastography (TE) in diabetic patients with fatty liver disease.
We conducted a prospective study from October 2016- December 2017 which included 413 diabetic patients out of which 353 had liver steatosis (mean age 61 ± 8.5 years, 55.8% females, 44.2% males) evaluated both by serum markers (TGO, TGP, platelets) as well as by TE (Fibroscan, Echosense,Paris, France, with incorporated CAP function). Based on specific formulas we calculated APRI, FIB 4 index and BARD score. We excluded all patients without liver steatosis at ultrasound. Liver stiffness measurement was considered reliable only if 10 valid values were obtained, with an IQR < 30% and a success rate > 60%. For differentiation between different stages of liver fibrosis, the following cut-off values were used (1): F2-F3: 7–10.2kPa, F4≥10.3 kPa. We considered mild steatosis if CAP = 230–275dB/m, moderate steatosis-CAP = 275–300 dB/m and severe steatosis-CAP > 300 dB/m (recommended by the manufacturer).
Results: Severe steatosis according to CAP measurements prevailed: 68.7% of patients, whereas the distribution between mild and moderate steatosis was similar 17% vs 14.1% (p > 0.05). The patients' distribution regarding the different stages of fibrosis was the following: F0-F1–202 patients (57.2%), F2-F3 -78 patients (22.2%), F4-73 patients (20.6%).
Out of the 353 patients, 27.1% of them were overweight (BMI 25–29.9 kg/m2), whereas 64% patients were obese (BMI≥30 kg/m2).
We found a weak, but significant correlation between liver stiffness assessed by TE and liver stiffness predicted by APRI (Pearson r = 0.24, p = 0.001). Considering an APRI score < 2 to rule out liver cirrhosis, 349 patients had APRI < 2, among which 259 patients (74.2%) had also LSM < 10.3 kPa.
Regarding FIB 4 score, we found out that 95.3% of patients had FIB4 < 2.6 thus ruling out advanced liver fibrosis (as compared to 79.3% patients (280) with LSM < 10.3kPa). The correlation between them was very weak, but statistically significant (r = 0.15, p = 0.005).
16.4% (58) of patients had a BARD score < 2, having a strong negative predictive value for advanced hepatic fibrosis. Among them, only 1.7% had LSM≥10.3 kPa.
Conclusion: An APRI score < 2, FIB 4 score < 2.6 and BARD score < 2 can rule out advanced fibrosis quite accurately. These simple scores can be used as first line tests to rule out patients without advanced fibrosis in diabetic patients with fatty liver disease.
Disclosure: Speaker Fee: General Electrics; Philips

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P1265 ENHANCED LIVER FIBROSIS (ELF) SCORE FOR NONINVASIVE DIAGNOSIS OF NONALCOHOLIC STEATOHEPATITIS (NASH) WITH ADVANCED FIBROSIS

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Introduction: The Enhanced Liver Fibrosis (ELF) test is a noninvasive fibrosis panel composed of hyaluronic acid (HA), procollagen-3 N-terminal peptide (P3NP), and tissue inhibitor of metalloproteinase-1 (TIMP1). Nonalcoholic steatohepatitis (NASH) with advanced fibrosis (F3) or cirrhosis (F4) shows increased liver-related mortality. Noninvasive tests are needed to identify patients with these advanced stages of NASH who require lifestyle intervention and/or are eligible for enrolment in clinical trials.
Aims and Methods: Aim of the present study was to determine the diagnostic accuracy of ELF score for prediction of NASH with advanced fibrosis/cirrhosis. We enrolled consecutive patients with NAFLD admitted to two Austrian outpatient liver clinics who underwent liver biopsy. Histological NASH was defined as presence of steatosis > 5%, hepatocellular ballooning and lobular inflammation. Fibrosis was staged according to the clinical research network (CRN) score. Serum samples obtained at the time of liver biopsy were used to perform ELF test (Siemens Health Care, Vienna, Austria). The predictive value of ELF score for diagnosis of fibrosis stage was assessed by receiver operating characteristic (ROC) analysis and compared to that of NAFLD fibrosis score (NFS) and FIB-4, two simple fibrosis tests based on routine clinical and laboratory parameters.
Results: Our study cohort contained 188 patients with NAFLD. On liver histology, NASH was present in 111 patients (59%), advanced fibrosis stage (F3-4) in 49 patients (26%), and both features in 38 patients (20%). ELF score was significantly higher in patients with NASH plus fibrosis stage F3-4 compared to the rest of the cohort (11.0 ± 1.8 vs. 8.8 ± 1.3, p < 0.001). ROC analysis revealed superior diagnostic accuracy of ELF score (AUROC 0.87 [CI 0.79–0.95]) vs. FIB-4 (AUROC 0.81 [CI 0.71–0.92]) or NFS (AUROC 0.77 [CI 0.67–0.88]) for prediction of NASH with fibrosis stage F3-4. An ELF score of ≥9.5 was identified by Youden index as the best cut-off for diagnosis of NASH with fibrosis stage F3-4 (sensitivity 86%, specificity 80%, PPV 51%, NPV 96%).
Conclusion: Based on our findings, ELF score shows high accuracy for noninvasive diagnosis of NASH with advanced fibrosis among patients with NAFLD. An ELF score < 9.5 was found to reliably rule out NASH with fibrosis stage

F3-4 and thus may be very useful in assessing eligibility of NAFLD patients for clinical trials with drugs in development for treatment of NASH.
Disclosure: Nothing to disclose

P1266 THE ROLE OF CXCL10 FOR PREDICTING THE CARDIOVASCULAR RISK AND THE OCCURRENCE OF METABOLIC SYNDROME IN LIVER TRANSPLANT RECIPIENTS

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Introduction: Patients who have undergone liver transplantation often develop metabolic syndrome (MetS) and de-novo non-alcoholic fatty liver disease (NAFLD).
Aims and Methods: Our aim was to evaluate the cardiovascular risk in these patients using CXCL10, a serum biomarker whose expression levels have been associated with inflammatory diseases. CXCL10 was chosen considering that early changes of immune biomolecules in peripheral blood, reflecting immune status, could be candidate biomarkers able to diagnose or predict cardiovascular complications.
60 liver transplant recipients were assessed for clinical and biological features, performing abdominal ultrasound and transient elastography (TE) with controlled attenuation parameter (CAP), calculated non-invasive scoring systems for advanced fibrosis and NAFLD (APRI, FIB-4, NAFLD score). The cardiovascular risk was assessed using the Framingham risk score and the presence of metabolic syndrome.
Results: The main indication for liver transplantation was HCV (69% of patients) and the mean age 56 years. The paired t-test showed a significant association of CXCL-10 with the presence of the metabolic syndrome ($p < 0.001$) and also with the non-invasive scores for advanced fibrosis and NAFLD. The metabolic syndrome was present in 51% of patients. 23% of patients had a Framingham risk score higher than 12 (10% mortality in 10 years) and 13% a score higher than 17 (30% mortality in 10 years). The multivariate analysis indicated as independent prediction factors for higher values of the Framingham score the serum levels of ferritin ($p = 0.03$) and urea ($p = 0.02$). The Spearman rank correlation test showed a significant association between the serum levels of CXCL10 and ferritin ($p = 0.04$), urea ($p = 0.003$), but also with uric acid ($p = 0.04$), an already established risk factor for cardiovascular mortality.
Conclusion: Serum levels of CXCL10 could have an important role in assessing the cardiovascular risk in liver transplant recipients, especially when features of the metabolic syndrome are present. Our study is ongoing, aiming to establish the role of biomarkers, including CXCL10 in cardiovascular related mortality in these patients.
Disclosure: Nothing to disclose

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P1267 UDCA IMPROVED INSULIN SENSITIVITY AND METABOLIC PARAMETERS IN NASH PATIENTS

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Introduction: Nonalcoholic steatohepatitis (NASH) is a prevalent liver disease associated with increased morbidity and mortality. Ursodeoxycholic acid (UDCA) may have antioxidant, anti-inflammatory, and antifibrotic properties and may reduce liver injury in NASH.
In the pathogenesis of fatty liver disease are the main hypercholesterolemia and impaired glucose tolerance. Studies in recent years have suggested an improvement in cholesterol on UDCA therapy, which could potentially be due to a direct effect on cholesterol or an improvement in the course of the disease. UDCA is a potent modulator of GLP1, which are all important regulators of lipidand glucose metabolism.
To date, no studies have assessed the efficacy of UDCA in treatment of insulin resistance in patients with NASH.
Aims and Methods: We conducted a 6-month randomized controlled multicenter trial to evaluate the efficacy of UDCA (10–15 mg/kg per day) in 228 patients with NASH and insulin resistance. The comparison group of 76 patients used only low-fat hypoglycemic diet (LFHD). The primary study end point was reduction in glucose and insulin levels from baseline in patients treated with UDCA. Secondary study end points were the proportion of patients with HOMA-IR normalization, relative reduction in the scores of serum markers of fibrosis and hepatic inflammation, and safety and tolerability.
Results: UDCA significantly reduced mean ALT levels at 58.4% from baseline after 3 months compared with 12.6% with diet ($p < 0.001$). At the end of the trial, ALT levels normalized in 84.5% of patients treated with UDCA. The median GGT reduction was 62.1% vs 9.6%. UDCA significantly reduced the FibroTest serum fibrosis marker ($p < 0.001$) compared with diet. Patients treated with UDCA experienced significant reductions in serum glucose, glycosylated hemoglobin, and serum insulin levels. Serum glucose improved in 16.3% vs 4.5%, glycosylated hemoglobin improved in 8.4% vs 3.8%, and serum insulin level improved in 18.5% vs 6.2%. UDCA also significantly improved markers of glycemic control and reduce insulin resistance in 21%. There were no safety issues in this population. Treatment with UDCA was safe, improved cholesterol and glucose levels, atherogenicity index, HOMA-IR and selected metabolic parameters.
Conclusion: This study demonstrates that UDCA, 10–15 mg/kg per day, is safe and well-tolerated in patients with NASH. Treatment with UDCA resulted in a strong and sustained reduction of ALT levels, suggesting that the numerous hepatoprotective actions of this molecule.
UDCA treatment resulted in an improvement of hypercholesterolemia and insulin resistance in patients with NASH. UDCA resulted in beneficial effects on glycemic control and insulin sensitivity.
Disclosure: Nothing to disclose

P1268 NEW MARKERS FOR STEATOSIS ASSESSMENT IN NAFDL – THE IMPORTANCE OF METABOLOMICS

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Introduction: Due to the increasing prevalence of NAFLD and the difficulties to select patients who need closer surveillance for fatty liver, various serum surogate markers were proposed. The evaluation of steatosis severity is important for the correlation with metabolic features and for the impact on followup and prognosis. We used the metabolomic approach for determining new diagnostic markers through specific high performance liquid chromatography coupled with mass spectrometry (HPLC-MS) and principal component analysis (PCA). As reference, we used the morphological analysis, which was estimated using SteatoTest (R) (Biopredictive, Paris, France) for the steatosis grading and NASHTest (R) (Biopredictive) for the confirmation and exclusion of steatohepatitis.
Aims and Methods: We aimed to determine new metabolomic markers the diagnosis and assessment of steatosis severity and to find new diagnostic markers for NASH. We used the metabolomic approach for determining new diagnostic markers through specific high performance liquid chromatography coupled with mass spectrometry (HPLC-MS) and principal component analysis (PCA). As reference, we used the morphological analysis, which was estimated using SteatoTest (R) (Biopredictive, Paris, France) for the steatosis grading and NASHTest (R) (Biopredictive) for the confirmation and exclusion of steatohepatitis.
Results: We included in the study 30 patients with NAFLD and 10 controls. Seven patients (23.3%) had NASH as confirmed by NASHTest. A significant association was found between vitamin D (25(OH)D3) levels and steatosis grades evaluated through SteatoTest ($p = 0.013$). Vitamin D was also useful for the exclusion of steatosis in three patients that were firstly enrolled in the NAFDL group based on ultrasound ($p < 0.001$). Other markers were also found to be associated with steatosis: androstenon ($p = 0.002$), phenyl lactic acid ($p = 0.001$) and hexacedenoic choline ($p = 0.03$). Of these markers, androstenon and hexadecenoic choline were significantly associated with the presence of NASH ($p = 0.013$ and 0.042 respectively). The asscociation of phenyl lactic acid with NASH did not reach the statistic significance ($p = 0.07$).
Conclusion: In conclusion, our pilot data suggest that new metabolomics markers can be used for the diagnosis of steatosis and for the rapid assessment of steatosis severity and steatohepatitis in NAFLD.
Disclosure: Nothing to disclose

P1269 HEPATOMETABOLIC SYNDROME. NEW CRITERIAS FOR THE DEFINITION OF MS

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Introduction: Metabolic syndrome (MS) is a set of metabolic and cardiovascular risk factors that have the capacity to predict a better cardiovascular and type 2 diabetes mellitus (T2DM) risk development than its individual components. Non-alcoholic fatty liver disease (NAFLD) is considered to be the hepatic manifestation of metabolic syndrome (MS). A definition that includes NAFLD among the mandatory criteria for defining MS is still missing. In patients with NAFLD, cardiovascular disease is the primary cause of death. Classical cardiovascular risk scores underestimates the cardiovascular risk in patients with MS.
Aims and Methods: Our aim was to identify objective criteria in order to include NAFLD as a mandatory criteria for the definition of MS. We included 4 groups of patients: NAFLD with MS patients, NAFLD without MS patients, MS patients and controls. MS was diagnosed with the presence of any three out of the five criteria (abdominal obesity, hypertriglyceridemia, hipo-HDL-cholesterolemia, hypertension, impaired fasting glucose or T2DM). NAFLD diagnosis was established based on clinical examination and ultrasonography. Diagnosis of non-alcoholic steatohepatitis (NASH) was based on Fibromax determination. For the cardiovascular risk (CVR) assesment, ultrasound measurement of carotidian intimate-media thickness (CIMT-in cm, normal value = 0.07cm) was used. Anthropometric parameters and usual paraclinical parameters were recorded.
Results: The CIMT values were higher than normal, except the control group (NAFLD + MS 0.134 +/−0.099, MS 0.149 +/−0.086, NAFLD 0.076 +/−0.051, controls 0.061 +/−0.023), with statistical difference between NAFLD + SM vs NAFLD patients ($p = 0.002$), but no statistical difference between NAFLD+SM vs SM patients ($p = 0.21$).
In patients with NAFLD, the presence of NASH implied higher values of CIMT, statistically significant (0.09 vs 0.06, $p = 0.025$).
Of the histological changes of NAFLD, there was a correlation between the presence of fibrosis and the CIMT values ($\rho = 0.595$, $p = 0.004$).
The presence of T2DM nor impaired fasting glucose did not correlate statistically significantly with higher CIMT values in all the four groups of patients included in the study ($p = 0.159$, $p = 0.345$, $p = 0.450$, $p = 0.261$).
Of the classical metabolic risk factors, in patients with NAFLD, with and without MS, there was a statistically significatnt correlation between CIMT values and abdominal circumference ($\rho = 0.284$, $p = 0.005$), body mass index ($\rho = 0.227$, $p = 0.027$), hypertension ($\rho = 0.446$, $p < 0.001$), and between the presence of hypertension and CIMT values in patients with NAFLD and MS ($\rho = 0.497$, $p < 0.001$).
Conclusion: The patients with NAFLD are a particular set of patients regarding cardiovascular risk. Taking into account the particularities of the patients with metabolic risk factors for cardiovascular diseases development, we propose a new definition for MS. The current MS ordinances to be marked with 1 point (including impaired fasting glucose), except for the presence of T2DM, which is to be marked with 2 points, NAFLD – 1 point, and NASH – 2 points. The diagnosis of MS is set when there are at least 4 points (10 possible). Of course, it is mandatory for this new model to be validated in further studies.
Disclosure: Nothing to disclose

P1270 CLINICAL IMPACT OF COMORBIDITIES IN AN ITALIAN NAFLD COHORT

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Introduction: Non- Alcoholic fatty liver disease (NAFLD) is a common disease associated to several clinical conditions. Prevalence of comorbidities associated to NAFLD has not been deeply evaluated in epidemiological studies so far.
The aim of this study is to assess the prevalence of common chronic diseases in a cohort of consecutive NAFLD subjects referred to a tertiary center. Moreover, assuming their possible impact on liver disease, the association between comorbidities and liver fibrosis (non-invasively assessed) has been evaluated.
Aims and Methods: From January 2016 to January 2017 we prospectively recruited subjects with clinical suspicious of NAFLD/NASH because hypertransaminasemia or ultrasound evidence of steatosis referred to the Outpatient Liver Unit of Fondazione Policlinico Gemelli in Rome. Patients with chronic liver disease related to viruses (HBV, HCV), alcohol or autoimmune disease were excluded. Medical comorbidities, anthropometric measurements, and laboratory tests were obtained during assessment. The Charlson Comorbidity Index (CCI) was used for the stratification of patients based on comorbidity.[1] Multimorbidity was defined as CCI≥2. Fibrosis-4 score (FIB-4) was used for non-invasive evaluation of fibrosis. Significative fibrosis was considered as FIB-4 > 3.25 (or >2.0 in patient >65 years old).[2]
Results: We enrolled 398 consecutive patients (males 55.7%, age 56.9 ± 13.8 y). 207 patients (52%) fit the diagnostic criteria for Metabolic syndrome, 115 (28.9%) have type 2 diabetes mellitus and 207 (52%) have arterial hypertension. In our cohort of NAFLD patients the most common comorbidities included in CCI is diabetes mellitus followed by non-metastatic tumors (7.5%). The most common coexistent chronic conditions, excluding those included in CCI, were gastroesophageal reflux (14.5%), hypothyroidism (10.8%), cholelithiasis (6%) and sigmoidal diverticulosis (5.8%).
Multimorbidity (CCI≥2) was present in 252 patients (63.3%). In Multimorbid patients was present a higher prevalence of metabolic syndrome (68.3% vs 28.6%) and diabetes (43.6 % vs 3.4%) and a higher severity of fibrosis (FIB-4 2.0 ± 3.8 vs 0.9 ± 0.4) when compared with patients without Multimorbidity.
Conclusion: Our study highlights the great prevalence of comorbidities in NAFLD patients, especially in those affected by metabolic syndrome or diabetes. Thus, a multidisciplinary clinical assessment of NAFLD patient, especially in those with significant fibrosis, is advisable.
Disclosure: Nothing to disclose

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P1271 N-3 POLYUNSATURATED FATTY ACIDS IN NAFLD (A DOUBLE-BLIND RANDOMISED PLACEBO-CONTROLLED STUDY)

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Introduction: Non-alcoholic fatty liver disease (NAFLD) represents the most common chronic liver disease in western countries with a global prevalence of 25% in adults. It encompasses a wide spectrum of liver damage ranging from benign simple steatosis, to non-alcoholic alcoholic steatohepatitis (NASH), liver fibrosis and cirrhosis. The detailed pathogenic mechanisms involved in the development of NAFLD remain unclear. There is no established pharmacological treatment of NAFLD. Weight reduction and lifestyle modification with increased physical activity stay the only effective therapeutic measures, but they are difficult to achieve and sustain. It has been reported that n-3 polyunsaturated fatty acids (PUFA) are able to ameliorate hepatic steatosis and insulin resistance, whereas a diet deficient in PUFA with a high n-6/n-3 ratio could induce fatty liver. Up to date published papers using PUFA have yielded contradictory results.
Aims and Methods: The aim of the study was to assess the effects of administration of PUFA in development of NAFLD in patients during one year follow-up. We have examined 60 patients with metabolic syndrome and NAFLD in different stage of disease (simple steatosis/NASH (n = 55)/liver cirrhosis (n = 5)). Patients were randomized into two groups: 30 used PUFA in daily dose 1.8 g of eicosapentaenoic acid and 1.36 g of docosahexaenoic acid in four divided doses; 30 patients used placebo in the same scheme. During one year follow-up were patients periodically examined – anthropometry (weight, waist circumference, BMI), biochemistry (liver enzymes, glucose metabolism etc.), blood count, abdominal ultrasound, liver stiffness measurement using ARFI®, nuclear magnetic resonance spectroscopy (MRS; at the start and end of follow-up). After one year follow-up results were evaluated and statistically processed.
Results: Of the 60 patients enrolled in the study were 45 men and 15 women, the mean age was 51.9 ± 12.2 years, the weight was 97.1 ± 15.2 kg and the mean BMI was 31.25 ± 4.25. There was no significant difference in any of these parameters among the monitored groups (PUFA versus placebo) at the beginning of the study. Similarly, between both groups there was no significant difference in other key parameters – ALT, GGT, or the percentage of fat in the liver tissue determined by MRS. After one year follow-up, no changes in anthropometric data (weight, waist circumference, or BMI) were observed in the patients enrolled in the study. On the other hand, there was a significant decrease in GGT activity in the PUFA group (2.27 ± 2.71 vs. 1.43 ± 1.55 ukat/L, $P = 0.0397$), without any change in the placebo group (2.31 ± 3.37 vs. 2.03 ± 2.8 ukat/L, $P = 0.064$). Other observed biochemical parameters (ALT, AST, ALP, and bilirubin) remained unchanged in both groups. During the follow-up liver elastography did not change in either group, as well as percentage of fat in hepatic tissue measured by MRS in both groups (PUFA 13.44 ± 7.7%, placebo 13.24 ± 9.1%).
Conclusion: We observed significant decrease in GGT serum activity after 12 months of PUFA administration, the total amount of liver fat remained unchanged. We conclude that PUFA could represent a potential agent in preventing the development of NAFLD in patients with metabolic syndrome.
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P1272 HIGH-DENSITY LIPOPROTEIN LEVELS AND URIC ACID LEVELS MAY BE USEFUL TO DISTINGUISH ALCOHOLIC FATTY LIVER AND NONALCOHOLIC FATTY LIVER

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Introduction: Fatty liver is classified as alcoholic and nonalcoholic according to the amount of alcohol consumed. In some cases, however, both drinking and overnutrition are involved in the development of fatty liver. Furthermore, epidemiological studies have demonstrated that light to moderate alcohol consumption appears to protect against fatty liver. The relation between alcohol and fatty liver possibly varies in each patient, depending on several cofactors. To make recommendation to modify patients' lifestyle, it may be not appropriate to distinguish alcoholic fatty liver and nonalcoholic fatty liver by a simple quantitative threshold of alcohol intake.

Aims and Methods: To answer whether they should drink or stop drinking, we aimed to distinguish alcohol-induced fatty liver and nutrition-induced fatty liver among drinkers. We obtained clinical and laboratory data from 8.879 Japanese subjects who underwent ultrasonography as a part of systematic health checkups at Junpukai Health Maintenance Center between 2006 and 2010, excluding individuals with the concurrent liver disease, any missing components of data, or missing follow-up study. The amount of alcohol consumed was stratified into following 5 groups: <70 g/week, 70–140 g/week, 140–280 g/week, 280–420 g/week, and >420 g/week. We hypothesized that abstinence or cutting down on alcohol intake would be required for remission of the alcohol-induced fatty liver and that remission of fatty liver without cutting down on alcohol consumption would indicate nutrition-induced fatty liver. Among patients who had remission of fatty liver, we compared those with cutting down on alcohol consumption (group A) and those without (group N) to elucidate the difference between them.

Results: In 8879 examinees, 31% had fatty liver and 60% reported habitual drinking at baseline. The prevalence of fatty liver in drinkers was significantly lower than that in non-drinkers (40% vs. 49%, $P < 0.001$ in men; 11% vs. 15%, $P < 0.001$ in women). During the observation period, the remission of fatty liver was observed in 345 out of 1.756 drinkers with fatty liver at baseline (20%). While the median amount of alcohol consumed had decreased from 154 g/week to 132 g/week in group A ($n = 80$), it increased from 132 g/week to 154 g/week in group N ($n = 265$). In comparison between group A and group N, significant differences were found in high-density lipoprotein levels (60 mg/dl vs. 55 mg/dl as median, $P = 0.025$) and in uric acid levels (6.4 mg/dl vs. 6.2 mg/dl, $P = 0.025$). When cases were stratified by the amount of alcohol consumed at baseline, the difference in HDL levels remained significant in cases with alcohol intake of >420 g/week (81 mg/dl vs. 56 mg/dl, $P = 0.029$). Among those without medication for dyslipidemia or hyperuricemia ($n = 316$), receiver operating characteristic analysis indicated that each optimal cut point for high-density lipoprotein level and uric acid level to distinguish group A and group N is 63 mg/dl ($AUC = 0.570$) and 7.0 mg/dl ($AUC = 0.587$), respectively. In cases with high-density lipoprotein levels >63 mg/dl and uric acid levels >7.0 mg/dl, group A accounted for 80%.

Conclusion: High-density lipoprotein levels and uric acid levels are possibly useful to judge whether the fatty liver was induced by alcohol consumption or by overnutrition. Abstinence or cutting down on alcohol intake may resolve fatty liver in patients with high-density lipoprotein levels >63 mg/dl and uric acid levels >7.0 mg/dl.

Disclosure: Nothing to disclose

P1273 GENDER DIFFERENCES IMPACT THE PD-1 AND PD-L1 EXPRESSION ON PERIPHERAL T AND B CELLS IN PATIENTS WITH ALCOHOLIC LIVER DISEASE

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Introduction: Exposure to excessive alcohol consumption, its breakdown metabolites and gut-derived endotoxins dysregulates immune signaling. As a result the non-resolving inflammatory response and damage within the gastrointestinal tract and other organs may occur. The programed cell death 1 (PD-1) receptor and its ligand PD-L1 play a critical role in inhibition of self-reactive and inflammatory effector cells and the protection against immune-mediated tissue damage.

Aims and Methods: Evaluation of the PD-1/PDL-1 expression on peripheral T and B lymphocytes, its correlation with markers of inflammation and the severity of liver dysfunction in the course of alcoholic liver disease (ALD).

Fifty six inpatients with ALD (38 males, 18 females, aged 49.23 ± 10.66) were prospectively enrolled and assigned to subgroups based on their: 1/ gender, 2/ severity of liver dysfunction (Child-Pugh, MELD scores, mDF), 3/ presence of ALD complications, and followed for 30 days. Twenty five age- and gender-matched healthy volunteers, who consumed no more than 10 g alcohol per day, served as the control group. Flow cytometric analysis of the PD-1/PD-L1 expression on peripheral lymphocyte subsets were performed.

Results: The general expression of PD-1 and PDL-1 on T and B cells did not differ between the ALD and control group. Although, when the groups were analyzed based on their gender, significantly higher expression of PD1 and PD-L1 on CD19+ B cells in ALD females comparing to controls was observed. ALD females with severe alcoholic hepatitis (AH) and $mDF > 32$ or $MELD > 20$ showed significantly higher expression of PD-1 on CD19+ B cells and PD-L1 on all studied T and B subsets. The same pattern of the PD-1/PD-L1 expression was found when ALD females were compared with ALD males including the subgroups with $mDF > 32$ and $MELD > 20$. No correlations of PD-1+/PD-L1+ expression with mDF, CTP and MELD scores, nor with complications of ALD were observed, but significant correlations of CD19+ PD-L1+ frequencies with all conventional markers of inflammation (i.e. white blood cell and neutrophil counts, C-reactive protein and neutrophil-to-lymphocyte ratio) were found.

Conclusion: Gender-related differences in the PD-1/PD-L1expression on peripheral T and B cells may account for the different susceptibility to ethanol-related liver damage in males and females. Upregulation of PD-1/PD-L1 expression paralleled the severity of AH and liver dysfunction in females with ALD.

Disclosure: Nothing to disclose

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P1274 SYSTEMIC UPREGULATION OF SELECTED CCL AND CXCL CHEMOKINES IN THE COURSE OF ALCOHOLIC LIVER DISEASE

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Introduction: Excessive inflammatory response in the course of alcoholic liver disease /ALD/ may induce a massive loss of hepatocytes leading to irreversible liver damage and progressive fibrosis. Chemokines are immune messengers implicated in pro-inflammatory signaling by recruiting selected subsets of leukocytes to the site of inflammation.

Aims and Methods: We aimed to explore the systemic blood expression of selected CCL and CXCL chemokines in patients with ethanol-related liver dysfunction and their accuracy in the noninvasive assessment of ALD liver failure and outcome.

Sixty-three inpatients with ALD /45 males, 18 females, aged 48.63 ± 11.38/ were prospectively recruited and followed for 30 days. Twenty five age-, sex- and ethnicity-matched healthy volunteers served as the control group. Selected CCL (CCL2/MCP1; CCL17/TARC; CCL20/MIP-3a) and CXCL (CXCL9/MIG, CXCL10/IP-10, CXCL16) chemokine concentrations were quantified in blood samples using immunoenzymatic ELISAs. Correlation coefficients between plasma chemokine levels and (i) indicators of systemic inflammation (neutrophil-to-lymphocyte ratio, C-reactive protein, white blood cell and neutrophile counts, modified Glasgow Prognostic Score (mGPS), (ii) liver dysfunction severity scores (Child-Turcotte-Pugh, MELD scores, mDF) and (iii) complications of liver disease were calculated. The receiver operating curves (ROC) for studied chemokines were constructed and their areas under the curve (AUCs) were checked in order to assess their accuracy in predicting the degree of liver failure and the development of ALD complications. Multivariable logistic regression was applied in order to select independent predictors of advanced liver dysfunction.

Results: Significant systemic upregulation of both CCL and CXCL chemokines was observed in patients with ALD. Only CCL17 (TARC) concentrations were markedly decreased indicating that Th2-type immune reactions are attenuated in ALD. This was in line with increased CCL2 and CXCL10, which polarize towards Th1 response. None of studied chemokines correlated with aminotransferase activity, but CCL20, CXCL9, CXCL10, CXCL16 showed positive correlations with the alkaline phosphatase level. CCL20 and CXCL16 correlated with standard indicators of inflammation. Patients with advanced liver dysfunction (MELD > 20, mDF > 32, Child B and C class) presented with significantly higher CCL20 and the six non-survivors with significantly higher CXCL10 concentrations.
Conclusion: Our findings emphasize the importance of both major chemokine subfamilies in the pathogenesis of ALD, therefore they represent a promising area of the potential therapeutic intervention. The high blood CCL20 concentration seems to be the disease severity indicator, while CXCL10 the predictor of the poor prognosis in ALD.
Disclosure: Nothing to disclose

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P1275 CALCULATION OF LILLE MODEL BETWEEN DAY 3 AND 4 CAN ACCURATELY PREDICT CORTICOSTEROID RESPONSE: A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction: Patients with severe alcoholic hepatitis (SAH) should be treated with corticosteroids (CT). Response do CT is assessed at 1 week using the Lille Model score (LM). Adverse effects of CT specially the risk of infection raise concerns amongst practitioners. A recent study demonstrated that LM calculated at day 4 is as accurate as LM calculated at day 7.[1] This finding needs further validation.
Aims and Methods: To access the accuracy of the LM calculated between day 3 and 4 in predicting CT response compared with the standard day 7.
Single-center retrospective study that included all patients admitted between January 2012 and December 2017 with a diagnosis of SAH defined by clinical and laboratory evidence and a Maddrey Discriminant Function (DF) $\geq$ 32. Response to CT treatment was determined by calculation of the LM score between day 3 and 4 and then at day 7 according to the cutoff >0.45. Statistical analysis was performed with SPSS v.24 Agreement between LM3-4 and LM7 was assessed by the Cohen's kappa (κ). Receiver operating characteristics (ROC) curves were used to compare accuracy between LM3-4 and LM7 in predicting 30-day mortality.
Results: 49 patients with SAH were included in the study. 81.6% were male and the mean age was 51.16 ($\pm$8.73) years. Median DF was 71.7 (40–195.2). 30 patients were treated with corticosteroids (CT). 16 patients had their LM score calculated at day 3, 12 at day 4 and 26 at day 7. Median LM3-4 and LM7 for patients who received CT was 0.45 (0.10–0.97) and 0.37 (0.10–0.98) respectively ($\rho = 0.067$). A substantial agreement was found between the two scores in predicting CT response ($\kappa = 0.92$, $\rho < 0.0005$). 30-day mortality was 40.8% (n = 20). There were no significant differences between LM3-4 and LM7 in predicting 30-day mortality (AUC 0.750 vs. 0.735 $\rho = 0.615$, respectively).
Conclusion: Until the development of newer and safer alternatives for SAH limiting corticosteroid therapy may benefit patients. Further prospective studies are needed to validate these findings.
Disclosure: Nothing to disclose

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P1276 SIGNIFICANCE OF CIRCULATING MEDIATORS RELEASED FROM ACTIVATED NEUTROPHILS IN PATIENTS WITH ALCOHOLIC LIVER DISEASE

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Introduction: Neutrophils are the first-line effectors of human innate immune system. Inflammatory dysregulation and neutrophil infiltration are hallmarks of alcoholic liver disease (ALD). Given their destructive potential, extracellularly released neutrophil enzymes should be carefully controlled to avoid damage to host tissues.
Aims and Methods: Assessment of the systemic profile of neutrophil-derived mediators i.e. neutrophil elastase (NE), myeloperoxidase (MPO), as well as alpha1-antitrypsin (A1AT)- a potent inhibitor of neutrophil proteases, with emphasis on their potential relevance in the course of ALD.
Sixty-two patients with ALD /47 males, 15 females, aged 49.2 $\pm$ 9.9/ were prospectively recruited and assigned to subgroups based on their 1/ gender, 2/ severity of liver dysfunction (Child-Pugh, MELD scores, mDF) 3/ presence of ALD complications, and followed for 30 days. Twenty four age-, sex- and ethnicity-matched healthy volunteers served as the control group. Selected plasma markers of neutrophil activation were quantified using immunoenzymatic ELISAs. Correlation coefficients between their blood concentrations and (i) indicators of systemic inflammation (the neutrophil-to-lymphocyte ratio, C-reactive protein, white blood cell and neutrophil counts), (ii) liver dysfunction severity scores (Child-Pugh, MELD, mDF), and (iii) ALD complications were calculated. The receiver operating curves (ROC) for studied molecules were constructed and their areas under the curve (AUCs) checked in order to assess their accuracy in predicting the degree of liver failure and the developmant of ALD complications.
Results: Concentrations of MPO and NE were significantly increased in the blood of patients with ALD in comparison with controls, but the A1AT level was not different. ALD females presented with higher MPO levels in comparison with ALD males. There were no gender-related differences in NE levels in ALD group. NE, but not MPO, correlated with MELD and mDF scores. MPO, but not NE, correlated with standard markers of inflammation. ALD subgroups with mDF > 32, Child class C and hepatic encephalopathy presented with significantly higher NE, but not MPO levels.
Conclusion: Our results support the value of MPO and NE in the ALD assessment. MPO seems to be an inflammatory marker, while NE the disease severity indicator. The higher systemic NE/A1AT ratio in the course of ALD may facilitate the expansion of the inflammatory cascade. Gender-related differences in neutrophils' activation in ALD may impact the different susceptibility to toxic liver injury in males and females.
Disclosure: Nothing to disclose

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P1277 EVALUATION OF CYTOSTATIC-INDUCED LIVER INJURY RISK IN PATIENTS WITH ACUTE MYELOID LEUKEMIA

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Introduction: Chemotherapy (CHT) for acute myeloid leukemia (AML) is accompanied by the risk of hepatotoxic reactions, severity of which influences patients' further management and leads to the need of drugs dose reduction. The main

negative prognostic factor, which does not depend on tumor morphology and patient's state, is an absence of adherence to the dosage and administration regimens of cytostatic agents. Timely performed diagnostics of hepatotoxic reactions, induced by cytostatic agents, and their prophylaxis play the main role.
Aims and Methods: – to study the frequency and character of hepatotoxic reactions in patients with AML depending on morphologic variant according to the FAB classification and prescribed CHT scheme.
A total of 63 patients with firstly diagnosed AML and normal liver function tests were examined, 29 (46%) of them were females and 34 (54%) – males. ECOG performance status was I-II, Karnofsky index was 60–80%. Patients were divided into groups: I (n = 27) – patients with AML M_0, M_1, M_2 according to FAB-criteria; II (n = 36) – patients with AML M_4, M_5 according to FAB-criteria. Patients were receiving the 1-st remission induction course. Activity of serum alanine and asparagine aminotransferases, alkaline phosphatase, concentration of total bilirubin were assessed before the CHT course, on 7-th, 14-th, and 28-th days of treatment.
Results: Conduction of the 1-st remission induction course in AML patients with M_0-M_2 variants was accompanied by the I grade hepatotoxicity on the 7-th and 14-th days in 2 (7.4%) patients, and in AML patients with M_4-M_5 variants – in 11 (30.5%) patients, in 8 (22.2%) out of them the grade I of severity was detected, in 3 (83%) – grade II. Hepatotoxic reactions in 2 (7.4%) patients with AML M_0, M_1 and M_2 variants of the group I were characterized as cytolytic. Among the patients of the group II with AML M_4 and M_5 variants the next types of hepatotoxic reactions were registered: in 2 (5.5%) – cytolytic, in 4 (11.1%) – cholestatic, and in 5 (13.9%) – mixed.
Hepatic function state was restored until 28-th day in all groups of comparison, where liver tests disturbances were observed on the 7-th and 14-th days.
Conclusion: M_4-M_5 variants of AML are associated with an increased risk of hepatotoxic reactions onset, that is determined by hemoblastosis morphology and higher toxicity of CHT regimens with etoposide inclusion.
Disclosure: Nothing to disclose

P1278 SAFETY ASSESSMENT IN THE HERBAL FIELD: COMMON PITFALLS

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Introduction: While safety of herbal products is recently gaining increased attention (1), safety assessments in this field often suffer from methodological weaknesses, as limitations of available data are often not sufficiently taken into account in the assessment. This applies both to data on quality, as to non-clinical as well as clinical and post marketing surveillance data.
Aims and Methods: To address this issue, a systematic data base search for reviews in this field, combined with hand searching in text books, was conducted. Sources of bias were classified according to data types involved.
Results: Depending from the data involved, different sources of bias were identified:
1. Data on quality: Often the great differences of the composition of herbal products prepared from the same plant, but from e.g. different plant parts or by different manufacturing processes are neglected, so leading to flaws by the transfer of data from products with a less favourable safety profile to safe products and vice versa, as e.g. in Kava and St. John's wort (2, 3).
2. Nonclinical data: Common pitfalls are the transfer of data from in vitro studies to the clinical setting, without taking into account the influence of ADME. Often also effects from sublethal high-dose settings are used without sufficiently taking into account dose dependency or, e.g. in carcinogenicity studies on ginkgo, methodological ambiguities (4).
3. Data from clinical studies and post marketing surveillance: While the lack of differentiation between negative studies and failed studies leads to wrong conclusions on inefficacy (5), the evaluation of safety using NIS data and spontaneous reports from pharmacovigilance data bases is often seriously flawed by neglecting background incidences of concomitant diagnoses as e.g. in case of hepatotoxicity (6), by protopathic bias, and by the clinical and academic settings influencing the awareness and views of authors of case reports (7).
Conclusion: A higher awareness of common pitfalls in the assessment of safety data on herbal products is needed, especially in case of hepatotoxic risks, if we want to avoid that methodological artefacts and misperceptions of the generalizability of data continue to influence our view of the safety of herbal products and their regulatory environment, both by neglecting risks, as, more abundant, by exaggerating non-existing risks.
Disclosure: OK is employee of Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany. KN and KK have received Speaker honoraries from Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany

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P1279 PREVALENCE AND PREDICTIVE FACTORS OF CIRRHOTIC CARDIOMYOPATHY IN A COHORT OF CIRRHOTIC PATIENTS

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Introduction: Cirrhotic cardiomyopathy (CCM) is a relatively new concept that currently appears as a particular clinical entity, characterized by impaired contractile response to stress, diastolic dysfunction and electrophysiological abnormalities in the absence of a known cardiac disease. Data on the epidemiology and natural history of CCM is still lacking.
Aims and Methods: We aimed to determine the prevalence of CCM and investigate its predictive factors in patients with liver cirrhosis.
This cross-sectional study was conducted on all cirrhotic patients (N = 109) who were admitted in our department from September 2016 to May 2017. Patients with structural or ischemic heart disease, hypertension, chronic alcoholism, severe anemia (Hemoglobin < 7 g/dl) or recent bleeding (< 1 month) were excluded (N = 33). Resting ECG was done in all patients. QTc interval of > 0.44 sec was considered as prolonged. A detailed two-dimensional echocardiography was also performed in all patients. CCM was considered present when diastolic and/or systolic dysfunction was diagnosed at rest, together with supporting criteria such as electrophysiological abnormalities, based on the criteria of the Montreal 2005 consensus. A stepwise Cox regression model was fitted to determine factors associated with the diagnosis of CCM. All statistical analysis were performed using the SPSS 21.0 version.
Results: A total of 76 patients were included in this study, out of which 45 (59%) were males and 31 (41%) were female. The mean age was 54 years (±11.8). The most common etiology was hepatitis B (38.2%). Median Child Pugh and MELD scores were 7 [5–12] and 11 [7–33], respectively. Twenty-five patients (32.9%) had ascites. Diastolic dysfunction was noted in 39 patients (51.3%) while 4 patients (5.3) showed evidence of systolic dysfunction. A prolonged QT interval was found in 33 patients (43.5%). CCM was then diagnosed in 43 patients (53.9%). In multivariate analysis, 3 independent predictive factors were identified: age > 50 years (OR 1.05; CI 95% :1.003–1.103; $p < 0.039$), female gender (OR 3.006; CI 95%: 1.029–8.778; $p = 0.044$) and Child Pugh score ≥9 (OR 4.363; CI 95%: 1.328–14.331; $p = 0.015$).
Conclusion: Cirrhotic cardiomyopathy is a frequent complication of cirrhosis. Given its association with the severity of liver disease, we recommend cardiac assessment in all Child Pugh B and C cirrhotic patients.
Disclosure: Nothing to disclose

P1280 ASSESSMENT OF CARDIAC DYSFUNCTION IN CIRRHOSIS USING TISSUE-DOPPLER AND SPECKLE TRACKING ECHOCARDIOGRAPHY

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Introduction: Cardiac dysfunction in cirrhosis, labeled "Cirrhotic cardiomyopathy" (CCM) includes a variety of structural myocardial changes, systolic and diastolic dysfunction and electrophysiological changes. Its diagnosis is based mostly on conventional echocardiography which is frequently unable to detect abnormalities at rest and identifies only the late stages of cardiac dysfunction.
Aims and Methods: We aimed to evaluate cardiac function in cirrhotic patients using newer methods: Tissue Doppler imaging (TDI) and Speckle Tracking Echocardiography (STE) and to compare it with previously proposed definition criteria of CCM.
We prospectively evaluated consecutive patients with a diagnosis of cirrhosis based on clinical, laboratory, ultrasonographic, endoscopic and/or histologic criteria. Patients with a history of any cardiovascular disease, chronic alcoholism, severe anemia (Hemoglobin < 7 g/dl), recent bleeding (< 1 month) and those who were technically unsuitable for STE and TDI analysis were excluded. A single experienced operator performed the echocardiograms. Left ventricle ejection fraction (LVEF) and LV diastolic function were assessed as recently recommended by the American and European societies of echocardiography. STE allowed the measurement of global longitudinal strain (GLS); systolic dysfunction was defined as a GLS value < -18%.
Results: Out of 109 cirrhotic patients, 76 were eligible for the study (median age 54 ± 11.8 years, males 59%). The most frequent underlying disease was Hepatitis B infection (38.2%) followed by cryptogenic cirrhosis (22.3%). Regarding the Child Pugh score, 45% of the cirrhotic patients were stratified in the Child score

B, and 43% were categorized in the Child score A. On conventional echocardiography, systolic dysfunction (LVEF < 55%) was found in 4 patients (5.3%). On STE, an altered GLS was found in 10 patients (13.1%). Based on mitral-flow pattern, diastolic dysfunction was present in 39 patients (51.3%). Using a TDI based definition, the prevalence of diastolic dysfunction was 32.9%. The agreement between the two definitions of diastolic dysfunction was moderate (kappa = 0.448, P = 0.001).
Conclusion: Patients with cirrhosis have both systolic and diastolic cardiac dysfunction at rest. Newer echocardiographic techniques may identify patients with functional impairment more accurately than conventional methods.
Disclosure: Nothing to disclose

P1281 ENDOSCOPIC VARICEAL LIGATION FOLLOWED BY ARGON PLASMA COAGULATION AGAINST ENDOSCOPIC VARICEAL LIGATION ALONE: RESULTS OF 5.5-YEAR FOLLOW UP

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Introduction: Our group had started a randomised controlled trial in April 2012 to study the effect of argon plasma coagulation (APC) after esophageal varices eradication using endoscopic variceal ligation (EVL) on recurrence of esophageal varices after previous bleeding episode. Recurrence of esophageal varices during 2.5 years was 21% in the APC group against 68% in the EVL only group. (P = 0.003). No one in the APC group needed rebanding while 63.2% of the EVL only group underwent rebanding (P < 0.001). These results were published.(1)
Aims and Methods: To continue the follow up of both groups to determine the ability of Argon plasma coagulation to maintain its efficacy in prevention of esophageal varices recurrence over a longer period (5.5 years). Endoscopic follow up intervals in the APC group were increased to be every 12 months, while in the EVL only group they became every 6 months if there were no recurrent varices and every 3 months if there were small recurrent varices without risk signs.
Results: In the APC group 35.3% of cases experienced recurrence of esophageal varices during the 5.5-year follow up against 93.8% of cases in the EVL only group (P < 0.001). Still no one from the APC group needed rebanding as all recurrent varices were small and without risk signs.
Conclusion: APC after esophageal varices eradication using EVL can decrease the risk of esophageal varices recurrence and the need for rebanding over long period with the possibility of decrease in endoscopic follow up intervals. This also can decrease the burden on endoscopic units especially in countries where liver diseases are endemic.
Disclosure: Nothing to disclose

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P1282 GLOMERULAR FILTRATION RATE BASED ON SERUM CREATININE IN DECOMPENSATED LIVER CIRRHOSIS – COMPARATIVE STUDY WITH THE "ROYAL FREE HOSPITAL" FORMULA

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Introduction: Renal dysfunction is a marker of poor prognosis in liver cirrhosis. Serum creatinine tends to overestimate the true value of the glomerular filtration rate (GFR) in these patients.
The equations commonly used to calculate GFR are the MDRD-4, MDRD-6, and CKD-EPI equations. These equations are commonly used in clinical practice due to their easy access. However, these equations are not validated in patients with cirrhosis. Recently, a new equation was developed and validated specifically for cirrhosis: "Royal Free Hospital Glomerular Filtration Rate" (RFH).
Aims and Methods: We propose to evaluate the relationship between GFR based on commonly used equations in clinical practice and the equation already validated in decompensated cirrhosis.
A retrospective analysis of the GRF values based on different formulas was performed in cases of decompensated liver cirrhosis admitted to a tertiary center during a 7-year period. Renal dysfunction was considered clinically significant for GFR lower than 30 mL/min/m^2, being that this GFR values generally imply modification of therapeutic strategies in clinical practice.
Results: A total of 418 cases were evaluated [78.7% men (n = 329), mean age 66.25 ± 11.79 years]. The median serum creatinine was 0.91 mg/dL (IQR 0.7–1.36 mg/dL). Death occurred within the first 100 days after admission in 20.1% of the patients.
At admission, the GFR was less than 30 mL/min/m^2 in 15.3% (MDRD-4), 19.6% (MDRD-6), 16% (CKD-EPI) and 21.5% (RFH) of the cases.
The GFR measured by the RFH formula showed a strong correlation with the GFR measured by the other equations (MDRD-4: r = 0.97, p < 0.001; MDRD-6: r = 0.98, p < 0.001; pCKD-EPI r = 0.95, p < 0.001).
Active infection and ascites were associated with the lowest mean value of GFR measured in all formulas (Active disease, MDRD-4 p = 0.008; MDRD-6 p = 0.003; CKD-EPI p < 0.001; RFH p = 0.007; Ascites: MDRD-4 p = 0.001; MDRD-6 p = 0.001; CKD-EPI p = 0.001; RFH p = 0.001).
The data concerning early mortality (<100 days) showed that average survival was significantly lower for GFR <30mL/min/m^2 calculated by RFH (GFR > 30, mean 47.2 ± 28.2 mL/min/m^2; GFR < 30, mean 32.8 ± 28.4, mL/min/m^2, p = 0.040), but not when the GRF was estimated by CKD-EPI (GFR > 30, mean 46.01 ± 29.04 mL/min/m^2; GFR < 30, mean 30.53 ± 24.91, mL/min/m^2; p = 0.06), MDRD-4 (GFR > 30, mean 45.59 ± 29.05 mL/min/m^2; GFR < 30, mean 31.57 ± 25.51 mL/min/m^2; p = 0.097) and MDRD-6 (GFR > 30, mean 46.73 ± 28.42 mL/min/m^2; GFR < 30, mean 32.10 ± 27.95 mL/min/m^2; p = 0.05) equations.
Conclusion: In this study, the new RFH formula had a strong correlation with the other creatinine-based estimated glomerular filtration rate equations. This supports that the most common formulas can still be used in the clinical management of patients with cirrhosis.
However, a GFR under the value of 30mL/min/m^2 estimated by the RFH formula (but not with other formulas) was related with a lower survival at 100 days.
Disclosure: Nothing to disclose

P1283 THE IMPACT OF BETA-BLOCKERS IN ADVANCED CIRRHOSIS

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Introduction: The non-selective Beta-Blockers (BBs) are widely used in the prevention of variceal hemorrhage (VH). Their benefit has been demonstrated. However, are they safe in advanced cirrhosis? The aim of this study was to study the complications observed in patients under BBs in advanced cirrhosis.
Aims and Methods: We conducted a retrospective study that collects all Child-Pugh C cirrhotic patients followed in the Gastroenterology Department of Habib Thameur Hospital over a period of 45 months. These patients were divided into 2 groups according to whether they received BBs (Group 1; G1) or did not (group 2;G2). Complications of cirrhosis were then compared in both groups.
Results: Ninety patients were included. The mean age at diagnosis was 56. The sex ratio (M/F) was 0.6. Most of cirrhosis were due to viral hepatitis C (30%) followed by viral hepatitis B (23%). The most frequent circumstance of discovery of cirrhosis was an oedemato-ascitic decompensation (79%). Endoscopic signs of portal hypertension were observed in 95% of patients. First group included 68 patients (75.6%): 37 patients were under BBs in primary prevention of VH while 31 patients received the treatment in secondary prevention. In the 2nd group (24.4%), BBs were not indicated in 15 patients; 4 patients had a contraindication such as asthma (N = 1), atrio-ventricular block (N = 2) and severe heart failure (N = 2). Three patients stopped BBs for poor tolerance.
At least one complication was observed in all the patients of G2 (100%) against 94% of patients of G2. The spontaneous bacterial peritonitis was noted in 25% of the patients under BBs against 13% of the patients without BBs (p = 0.49). Hepatic encephalopathy occured in 36.7% of patients of G1 against 54.4% of patients of G2 (p = 0.21). Hepatorenal syndrome was observed in 26.5% of patients under BBs against 22.7% of patients of G2 (p = 0.48). It was type 2 in all cases. BBs did not reduce the occurrence of hepatocellular carcinoma (G1 = 26.6%, G2 = 13.6; p = 0.53).
However, BBs significantly decreased the occurrence of decompensation by ascites (95% in G2 Vs 75% in G1, p = 0.019). In addition, they significantly improved the median survival time (72 months in G1 Vs 18.8 months in G2, p < 0.0001).
Conclusion: According to our results, BBs do not generate more complications and are even protective since they significantly reduced the frequency of decompensation by ascites and improved survival. They should be pursued in the advanced stages of cirrhosis.
Disclosure: Nothing to disclose

P1284 ACUTE-ON-CHRONIC LIVER FAILURE SCORE IN ACUTE DECOMPENSATED CIRRHOSIS: MEASUREMENT AND PROGNOSTIC VALUE

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Introduction: Prognostic value of acute-on-chronic liver failure (ACLF) definiton of the North American Consortium for the Study of End-Stage Liver Disease (NACSELD) in predicting 30-day survival was confirmed in a large recent study.
Aims and Methods: The aim of this work was to analyze the NACSELD-ACLF score performance to predict intrahospital mortality in patients with decompensated cirrhosis.
We retrospectively enrolled patients with decompensated cirrhosis (April to December 2017). Organ failure assessment were performed upon admission.

NACSELD-ACLF were analyzed in terms of prediction of 30-day using either a Chi-square test or Fisher's Exact test. Backwards elimination multi-variable logistic regression analyzing 30-day mortality was performed on all patients.
Results: Eighty-two patients were included with a sex-ratio at 0.9 and a mean age of 60 ± 9 years (23–74). The main comorbidities were diabetes mellitus (25%) and hypertension (20%). Hepatitis C was the most common etiology of cirrhosis (42%). Child-Pugh score was mainly C (63%) and 13 ± 3. Main MELD score was 10 ± 6. Bacterial infection was the main cause of decompensating (27%). 30-day mortality was 16%. In comparison with the surviving group, deceased patients had similar demographic characteristics. NACSELD-ACLF was ≥ 2 in 15% of patients. Patients who met criteria for NACSELD-ACLF had an overall 20% 30-day survival vs 85% in patients without NACSELD-ACLF ($p < 0.001$). RR was 22 (95% IC :5.47–91.15).
Conclusion: NACSELD-ACLF might predict 30-day mortality in cirrhotics in decompensation with a good sensitivity and specificity. However, it concerns only 15% of patients admitted for acute decompensation of cirrhosis which makes it a very restrictive score.
Disclosure: Nothing to disclose

P1285 THE NEW RECOMMENDED CRITERIA FOR SEPSIS ARE INAPPROPRIATE FOR PATIENTS WITH DECOMPENSATED CIRRHOSIS

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Introduction: The new criteria of sepsis published in 2016, based on the SOFA (*Sequential Organ Failure Assessment*) score is very difficult to apply in patients with advanced cirrhosis. On the other hand the modified SOFA score for decompensated cirrhosis *(Chronic Liver Failure – Sequential Organ Failure Assessment* - CLIF-SOFA), do not have a specific focus on infection and sepsis. Early diagnosis of sepsis is crucial in patients with decompensated cirrhosis. Recent studies have shown a good performance of presepsin and resistin as early diagnostic tools for sepsis but their performances in patients with cirrhosis is not known.
Aims and Methods: The aims of the study were: 1.) to identify the most accurate definition for sepsis in cirrhosis using the 28-day mortality as endpoint; 2.) to compare the diagnostic performances of procalcitonin, presepsin and resistin as early sepsis markers in patients with decompensated cirrhosis.
114 consecutive patients with decompensated cirrhosis were enrolled. Complete infectious workup and determination of procalcitonin, presepsin and resistin levels was done at admission. SOFA, CLIF-SOFA, CLIF-OF (*Chronic Liver Failure – Organ Failure)* scores and ACLF (*Acute on Chronic Liver Failure*) grade were calculated. In infected patients, for sepsis diagnosis we used the following definitions: the presence of SIRS (*Systemic Inflammatory Response Syndrome*), a SOFA score ≥2, CLIF-SOFA≥ 8 with an ACLF grade ≥1 and a CLIF-OF subscore of 3 points. Data regarding 28-day mortality were registered, and the accuracy for sepsis definition was calculated using 28-day mortality as endpoint. Statistical analysis was performed using SPSS software.
Results: The most accurate definition for sepsis diagnosis was a CLIF-SOFA score≥8 with an ACLF grade≥1 (accuracy 74%), while a SOFA score ≥2 in the presence of infection had significant lower accuracy, only 64% ($p < 0.0001$). The classic definition using the presence of SIRS and the CLIF-OF subscore = 3 in infected patients, had both a 72% accuracy for the diagnosis of sepsis, without statistically significant difference compared with the first definition ($p = 0.7$). The AUROC for sepsis diagnosis (defined as CLIF-SOFA≥8 with ACLF≥1) was 0.82 for presepsin (95% CI: 0.74–0.90, $p < 0.0001$, accuracy of 80%, cutoff 1444.5 pg/ml), 0.72 for PCT (95% CI: 0.60–0.83, $p < 0.0001$, accuracy of 77%, cutoff 0.99 ng/ml), 0.70 for resistin (95% CI: 0.56–0.83, $p = 0.006$, accuracy of 70%, cutoff 20.3 ng/ml).
Conclusion: The present definition for sepsis (SOFA score ≥2 in context of infection) is not appropriate for decompensated cirrhosis. The most accurate definition for sepsis diagnosis in these patients is a CLIF-SOFA score ≥8 points with an ACLF grade of at least 1. Presepsin is the most accurate tool for early diagnosis of sepsis in patients with decompensated cirrhosis.
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P1286 LIMITED DIAGNOSTIC PERFORMANCE OF CONTROLLED ATTENUATION PARAMETER FOR ASSESSING HEPATIC STEATOSIS IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE AND PORTAL HYPERTENSION

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Introduction: Transient elastography (TE) assesses liver stiffness as a measure of liver fibrosis but is influenced by hepatic perfusion pressure. TE-based controlled attenuation parameter (CAP) is a non-invasive marker for hepatic steatosis. However, the diagnostic performance of CAP has yet to be investigated in patients with advanced chronic liver disease (ACLD)/portal hypertension (PH; hepatic venous pressure gradient (HVPG) ≥6 mmHg).
Aims and Methods: Eighty-eight patients with liver stiffness values ≥10 kPa and/or HVPG ≥6 mmHg undergoing simultaneous liver biopsy, CAP and HVPG measurement were included in this retrospective analysis. Steatosis (S) was histologically graded according to the Brunt classification.
Results: Sixty-four (72.7%) Child-Pugh A, 16 (18.2%) Child-Pugh B and 8 (9.1%) Child-Pugh C patients with a mean MELD Score of 11 (SD ± 4) points were included. The underlying causes of liver disease were viral hepatitis in 22 (25.0%), non-alcoholic fatty liver disease in 12 (13.6%) and alcoholic liver disease in 11 (12.5%) patients. Twenty-two (25.0%) patients had other etiologies, while the cause was cryptogenic in 21 (23.9%). Median HVPG was 16 (IQR:10–19) mmHg, median liver stiffness was 27.4 (IQR:16.2–48.9) kPa and mean CAP value was 221 (SD ± 75) dB/m.
According to histology, 47 (53.4%) patients had no steatosis (S0), 28 (31.8%) had S1, 11 (12.5%) had S2, and 2 (2.3%) had S3. CAP was significantly different between patients with any hepatic steatosis (S1/2/3; 252(SD ± 70) dB/m) and without (S0; 202(SD ± 72) dB/m; $p = 0.002$). The AUROC of CAP for diagnosing any hepatic steatosis (S1/S2/S3 vs. S0) was 0.692 (95% confidence interval (95%CI): 0.582–0.802) in the overall cohort, 0.667 (95%CI: 0.552–0.783) in patients with PH, 0.629 (95%CI: 0.497–0.761) in the subgroup with clinically significant portal hypertension (CSPH, HVPG≥10mmHg; n = 69). Among patients with cirrhosis diagnosed by histology (n = 56), the AUROC was 0.607 (95%CI: 0.459–0.756). Applying the previously defined cut-off of 248 dB/m, sensitivity and specificity of CAP for diagnosing any steatosis (S1/S2/S3 vs. S0) were 48.8% and 76.6% with a positive predictive value (PPV) and a negative predictive value (NPV) of 64.5% and 63.2% in the overall cohort.
CAP correlated with the percentage of steatotic hepatocytes (Spearman's $\rho = 0.402$, $p = < 0.001$) and liver stiffness ($\rho = 0.225$; $p = 0.035$). HVPG neither correlated with percentage of steatotic hepatocytes ($\rho = 0.055$; $p = 0.654$), histological steatosis grade ($\rho = 0.026$; $p = 0.829$), nor with CAP values ($\rho = 0.054$; $p = 0.653$).
Conclusion: The diagnostic performance of CAP for assessing hepatic steatosis seems to be limited in patients with ACLD/PH, especially in patients with CSPH or cirrhosis based on histology.
Disclosure: Nothing to disclose

P1287 THE VALUE OF ULTRASOUND-BASED ELASTOGRAPHIC METHODS FOR RULING OUT THE PRESENCE OF ESOPHAGEAL VARICES IN LIVER CIRRHOTIC PATIENTS

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Introduction: Ultrasound-based elastographic methods are non-invasive techniques for the evaluation of liver stiffness that might have also a place in the assessment of portal hypertension.
Aims and Methods: The aim of this study was to evaluate the value of 5 ultrasound-based elastographic methods for rule out the presence of esophageal varices in patients known with liver cirrhosis.
The study included 69 consecutive subjects diagnosed with liver cirrhosis (patients known with history of chronic liver disease with clinical, biological, ultrasound, endoscopical or histological signs of liver cirrhosis), in whom liver stiffness (LS) was evaluated in the same session by means of 5 elastographic methods: Transient Elastography (TE)-FibroScan, EchoSens; Point shear wave elastography techniques: Virtual Touch Tissue Quantification (VTQ)-Acuson S2000, Siemens and ElastPQ technique-Affinity, Philips; 2D Shear Waves Elastography-Aixplorer, Supersonic Imagine (2D SWE.SSI) and the LogiqE9, General Electric (2D-SWE.GE). Reliable LS measurements were defined as follows: for TE, ElastPQ, VTQ and 2D-SWE.GE- the median value of 10 measurements and for 2D-SWE.SSI the mean value of 3 measurements acquired in a homogenous area.
Results: In 50 patients out of 69, all 5 elastographic methods had valid measurements and were included in the final analysis. 19/50 patients from the study group had varices, while 31/50 did not have varices.

The best cut-off values for "rule out" esophageal varices for the 5 different techniques are presented in the following table:

Method	Cut-off	Se	Sp	PPV	NPV	LR-	LR+	AUROC
TE (1)	≤21.5 kPa	85.7%	73.9%	66.7%	89.5%	0.45	1.2	0.67
VTQ (2)	≤1.88 m/s	90%	23.3%	43.9%	77.8%	0.48	1.1	0.57
ElastPQ (3)	≤10.4 kPa	95%	13.3%	42.2%	80%	0.38	1.1	0.66
2D-SWE.SSI (4)	≤13.2 kPa	95%	23.3%	45.2%	87.5%	0.24	1.24	0.58
2D-SWE.GE (5)	≤12.2 kPa	95%	53.3%	51.7%	76.2%	0.48	1.61	0.68
NPV $p > 0.05$ for 1 vs. 2 vs. 3 vs. 4 vs.5								

[The best cut-off values for "rule out" esophageal varices for the 5 different elastography techniques]

Conclusion: Ultrasound based elastographic methods seem to have the same performance for rule out the presence of esophageal varices in patients with liver cirrhosis.

Disclosure: Speaker fee from General Electric; Philips

P1288 TRANSJUGULAR LIVER BIOPSY PERFORMED BY HEPATOLOGISTS TRAINED IN HEPATIC VENOUS PRESSURE GRADIENT MEASUREMENTS IS SAFE AND PROVIDES IMPORTANT DIAGNOSTIC AND PROGNOSTIC INFORMATION

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Introduction: Liver biopsy provides important diagnostic and prognostic information in patients with (unknown) liver disease. Transjugular liver biopsy (TJLBX) represents an alternative to percutaneous liver biopsy, especially in patients with impaired coagulation. Here we describe our experience with TJLBX performed by hepatologists being experienced in HVPG measurements.

Aims and Methods: 445 TJLBX (16G Menghini aspiration needle) of 399 adult patients at the Vienna Hepatic Hemodynamic Laboratory (01/2004–12/2016) were retrospectively included. Safety and diagnostic value of TJLBX were assessed.

Results: Mean age was 51 (SD ± 13) years, 273 (61.3%) were male, 156/399 (39.1%) had decompensated cirrhosis, and 36/399 (9.0%) patients had undergone liver transplantation. A mean number of 6.2 portal tracts (SD ± 4.8; median: 5 [IQR: 2–9]) was obtained, median sample length was 6mm (IQR: 5–10mm).

Among patients with an unknown cause of acute liver failure (n = 11; 2.5%) or unknown etiology of liver disease (n = 151; 33.9%), a diagnosis could be established in eleven (100%) and 126 (83.4%) individuals, respectively.

Complications occurred in 28 patients (6.3%) including 22 (4.9%) with minor complications (subclinical capsule perforation [n = 12], puncture site bleeding [n = 4], benign tachyarrhythmia [n = 2], hypotension [n = 2], abdominal pain [n = 2]). Major complications occurred in six patients (1.3%) including renal biopsy (n = 2), pneumothorax (n = 2), ventricular fibrillation (n = 1) and mediastinal hematoma (n = 1). No deaths due to TJLBX were observed.

Neither the presence of ascites (n = 151, 39%) nor of coagulopathy (platelets < 50G/L and/or prothrombin time index < 50%; n = 82, 18.4%) was associated with a higher risk of complications: 6.6% complications (1.3% major complications) in ascites, 4.8% complications (0% major complications) in patients with coagulopathy.

Conclusion: TJLBX performed by hepatologists experienced in HVPG measurements is safe – even in patients with ascites or coagulopathy. TJLBX has sufficient diagnostic value for histological evaluation of liver disease.

Disclosure: Nothing to disclose

P1289 DIAGNOSTIC ACCURRACY OF BAVENO VI CRITERIA FOR SCREENING OF VARICES IN PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE – A META-ANALYSIS

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Introduction: The Baveno VI criteria based on platelet count $>150x10^9$cells/L and liver stiffness measurement (LSM) <20kPa, have been proposed for identification of compensated advanced chronic liver disease (cACLD) patients who could safely avoid screening endoscopy. However, evidence are inconsistent. We performed a systematic review and meta-analysis to assess the diagnostic accuracy of Baveno VI criteria for diagnosis of any size varices and varices needing treatment in patients with cACLD.

Aims and Methods: We systematically searched MEDLINE, EMBASE, Cochrane Library and grey literature sources through April 2018. We included diagnostic studies that assessed the accuracy of Baveno VI criteria for any varices or high risk varices (HRVs), as defined by the authors, in patients with cACLD. We evaluated studies that utilized upper endoscopy as reference standard. We evaluated study quality by using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool.

Results: We included 27 studies with 5091 participants. Fourteen studies (2916 patients) provided data for varices of any size and 17 studies (3742 patients) evaluated the criteria for HRVs. All studies were cross-sectional with sample size ranging from 32 to 774 patients. Time interval between liver stiffness measurement and endoscopy was usually 6 to 12 months. The median prevalence of varices of any size was 0.38 (range 0.15–0.72) and the median prevalence of HRVs was 0.10 (ranged from 0.04 to 0.20). Most of the studies were retrospective and deemed at unclear risk of bias. Pooled sensitivity of Baveno VI criteria for diagnosis of any varices was 88% (95% CI 82 to 92), specificity 43% (95% CI 32 to 55), positive likelihood ratio (LR+) 1.5 (95% CI 1.3 to 1.8), negative likelihood ratio (LR-) 0.27(95% CI 0.22 to 0.34). Pooled sensitivity for HRVs was 98% (95% CI 93 to 99), specificity 27% (95% CI 22 to 33), positive likelihood ratio (LR+) 1.3 (95% CI 1.2 to 1.4), negative likelihood ratio (LR-) 0.09(95% CI 0.03 to 0.27).

Conclusion: The Baveno VI recommendations can adequately rule out the presence of clinically significant varices in cACLD patients. They could be used as a triage test since they can identify low risk patients who could safely avoid screening endoscopy.

Disclosure: Nothing to disclose

P1290 ABILITY OF MELD SCORE AND PLATELET COUNT FOR RULING-OUT HIGH-RISK VARICES IN COMPENSATED LIVER CIRRHOSIS PATIENTS

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Introduction: Portal hypertension is a major pathophysiological alteration in liver cirrhosis. Upper gastrointestinal (GI) endoscopy is generally required in these patients since their management is defined by the presence and type of esophageal varices. Since Baveno VI, the use of fibroscan and platelets count is recommended to avoid endoscopy in some low-risk patients. Recently, new evidence about the usefulness of MELD score and platelets count to avoid endoscopy mainly in patients with HCV-related cirrhosis has been published.

Aims and Methods: We aimed at assessing the accuracy of MELD and platelets count to rule out high-risk varices in a population of mainly alcohol-related cirrhosis.

A retrospective analysis of patients with compensated cirrhosis of any etiology under follow-up at our Liver Unit was performed. Patients with Child-Pugh score 5 or 6 (A), upper endoscopy indicated for evaluation of portal hypertension over the last 5 years, and blood analysis done ≤3 months before or after endoscopy, were included. Patients with previous variceal bleeding, history of endoscopic variceal ligation, splenectomy, liver transplantation or esophageal or gastric surgery were excluded. High-risk varices were defined as large varices or varices with red spots. Results are shown as mean and percentages and analyzed by chi-square test and Student-t test. Accuracy of MELD and platelet count for predicting high-risk varices was calculated.

Results: 115 patients were included (80.3% male), with a median age of 57 years (range 17–81). The main aetiology was alcohol (72.1%), followed by virus (12.1%) and steatohepatitis (6.8%). Upper GI endoscopy excluded the presence of varices in 60% of patients. 32 patients (27.8%) had small varices without red spots (low-risk), whereas high-risk varices were detected in 14 patients (12.1%). Patients with low-risk and high-risk varices were similar in terms of gender, age, aetiology and MELD score (7.57 vs 8.71; $p = 0.063$). Platelet count was significantly lower in patients with high-risk varices (86.071 vs 134.039/μL; $p < 0.01$). High-risk varices were never present in patients with a MELD score of 6 and a platelet count ≥100.000/μL (n = 36). Only one out of 62 patients (1.61%) with MELD ≤8 and platelets ≥100.000/μL had high-risk varices. A negative predictive value of 90.4% for high-risk varices was obtained in patients with MELD ≤8 and platelets >150.000/μL

Conclusion: A MELD≤8 together with a platelet count ≥150.000/μL allows avoiding upper GI endoscopy for esophageal varices screening in patients with liver cirrhosis.

Disclosure: Nothing to disclose

P1291 NON-ALCOHOLIC FATTY LIVER DISEASE AFTER LIVER TRANSPLANTATION IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS AND CRYPTOGENIC CIRRHOSIS: THE IMPACT OF PRE-TRANSPLANT GRAFT STEATOSIS

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Introduction: Non- alcoholic fatty liver disease (NAFLD) is a growing disease worldwide and is an increasing cause of liver transplantation when progresses to non-alcoholic steatohepatitis (NASH) and cirrhosis. NAFLD may also complicates liver transplant recipients especially in patients who have undergone liver transplantation for NASH and cryptogenic cirrhosis.

Aims and Methods: This study aimed to investigate prevalence and risk factors of fatty liver disease after liver transplantation in patients with NASH and cryptogenic cirrhosis. In a cross-sectional study liver transplant data of all patients who had undergone liver transplantation between 2013 and 2017 at Shiraz Organ Transplant Center, Shiraz, Iran were reviewed. Fatty liver was diagnosed by ultrasound. Data regarding post-transplant diabetes mellitus (DM), hyperlipidemia, height, weight, body mass index (BMI), laboratory data and allograft steatosis were recorded. Patients were treated with tacrolimus based immunosuppressive regimen. Obesity was defined as BMI$>$ 30 kg/m2. To investigate the impact of macrovesicular steatosis of graft on development of fatty liver after liver transplantation, recipients were grouped as those with $\leq$ 15% graft steatosis and those with $>$15% graft steatosis. Data were analyzed using the Student's t-test, and Chi-square test. Logistic regression analysis was used to calculate the influence of independent variables on development of fatty liver.

Results: 267 patients were included in the study (72 patients with NASH and 195 with cryptogenic cirrhosis). In a mean follow up of 14.7 months, 56.9% of NASH patients and 26.9% of cryptogenic patients developed fatty liver after liver transplantation (OR = 3.59; 95% CI: 1.94- 6.62, P $<$ 0.001). There was no statistically significant difference in development of fatty liver between patients with $>$15% pre-transplant graft steatosis and patients with $\leq$ 15% pre-transplant graft steatosis (OR = 1.07; 95% CI: 0.49–1.73, P = 0.817). In univariate analysis, post-transplant DM, hyperlipidemia, obesity, age, serum fasting blood sugar, triglyceride and cholesterol were associated with NAFLD after liver transplantation (P $<$ 0.05). In regression analysis, post-transplant DM was an independent predictor of development of NAFLD after liver transplantation (OR = 2.29; 95% CI: 1.01–5.18, P = 0.045). Post-transplant DM (OR = 5.58; 95% CI: 3.03- 10.29, P $<$ 0.001), hyperlipidemia (OR = 4.17; 95% CI: 2.23- 7.80, P $<$ 0.001) and obesity (OR = 4.65; 95% CI: 2.17- 9.94, P $<$ 0.001) were more prevalent in patients with NASH compared to patients with cryptogenic liver cirrhosis.

Conclusion: NAFLD and components of metabolic syndrome are prevalent after liver transplantation in patients with NASH and cryptogenic cirrhosis. Post-transplant DM is an independent predictor of hepatic steatosis after liver transplantation. These patients should be followed for metabolic complications after liver transplantation.

	OR (Odds ratio)	95% CI (confidence interval)	P- value
Post-transplant DM	2.29	1-01-5.18	0.045
Hyperlipidemia	2.06	0.92–4-61	0.077
Obesity	2.52	0.73–8.75	0.144
Age	1.01	0.95–1.03	0.644
BMI	1.02	0.90–1.15	0.686

[Regression analysis of risk factors for development of fatty liver after liver transplantation]

Disclosure: Nothing to disclose

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P1292 GADOXETIC ACID ENHANCED MRI DISTINGUISHES ADVANCED CHRONIC LIVER DISEASE PATIENTS WITH IMPROVING LIVER FUNCTION AFTER SUSTAINED VIROLOGIC RESPONSE AND PATIENTS WITH PERSISTENT LIVER DAMAGE

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Introduction: There is an unmet need for non-invasive markers to facilitate individualized surveillance strategies after hepatitis C virus (HCV) eradication.

Aims and Methods: We evaluated changes in relative liver enhancement (RLE; indicating hepatic fibrosis and inflammation) obtained by gadoxetic acid enhanced MRI (GA-MRI) in the hepatobiliary phase, as well as the changes in splenic volume (SV; indicating portal hypertension) as indicators of liver function in patients before and after SVR to IFN-free therapy. In addition, we assessed their predictive value for (further) hepatic decompensation during follow-up (FU).

We enrolled 31 consecutive HCV patients with advanced chronic liver disease who underwent GA-MRI before and after successful IFN-free treatment and were followed for the development of (further) hepatic decompensation. (Further) hepatic decompensation was defined by variceal (re-) bleeding, incident ascites/worsening of ascites (requirement of paracentesis), incident hepatic encephalopathy (HE)/worsening of HE (admission for grade 3/4 HE).

Fourteen untreated chronic HCV patients with paired GA-MRI served as a control group.

Results: RLE increased significantly by 66%(95%CI:20%-94%; $P < 0.001$) from pre- to post-treatment. SV decreased by -16%(95CI:-28%–8%; $P < 0.001$). However, SV increased in 5 out of 31 patients (16%), the identical patients who showed a decrease in RLE ('GA-MRI non-response'). There was an inverse correlation of moderate strength between the changes in RLE and SV ($\rho = -0.608$; $P < 0.001$).

In contrast, in the untreated control group, we observed a decrease in RLE by -11%(95%CI:-25%–3%; $P = 0.019$) and an increase in SV by 23%(95%CI:7%-43%; $P = 0.004$) (both $P < 0.001$ vs. treated patients).

During a median post-treatment FU of 25.2(IQR:16.9) months, 6 patients developed (further) hepatic decompensation, with variceal bleeding (n = 1), ascites (n = 2), or HE (n = 3) being the first events. Two patients underwent liver transplantation and one patient died after developing further hepatic decompensation. Interestingly, GA-MRI non-response was associated with a substantially increased risk of (further) hepatic decompensation at 2 years (80%vs.8%; $P < 0.001$).

Conclusion: This is the first study demonstrating that GA-MRI might be able to distinguish between individuals with improving liver function (i.e. regression of liver fibrosis and portal hypertension) and those with persistent liver damage despite HCV eradication. Thus, it might have important prognostic implications. If confirmed by larger studies, GA-MRI might facilitate individualized post-SVR surveillance.

Disclosure: M.M. has served as a speaker and/or consultant for AbbVie, Bristol-Myers Squibb, Gilead, Janssen, and W. L. Gore & Associates.

P1293 THE CLINICAL DIFFERENCES BETWEEN CRYPTOGENIC CIRRHOSIS WITH CIRRHOSIS SECONDARY TO NON-ALCOHOLIC STEATOHEPATITIS AND AUTOIMMUNE HEPATITIS

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Introduction: It has been suggested that majority of patients with diagnosis of cryptogenic cirrhosis (CC) have been evolved from non-alcoholic steatoheptitis (NASH) and autoimmune hepatitis (AIH) and some experts use CC and NASH cirrhosis synonymously. However, it seems that demographic, risk factors and disease course are different in cryptogenic cirrhosis compared to patients with NASH and AIH related cirrhosis.

Aims and Methods: This study aimed to investigate differences in clinical characteristics between patients with CC and patients with cirrhosis due to NASH and AIH based on the hypothesis that patients currently diagnosed as CC may not be evolved from NASH or AIH and have really an unidentified liver disease. Pre- transplant data of patients with liver cirrhosis referred to Shiraz Liver Transplant Center, Shiraz, Iran between January 2000 and December 2017 were reviewed. Demographic data and clinical characteristics of patients including body mass index (BMI), history of diabetes mellitus (DM), hypertension (HTN), hyperlipidemia, hepatocellular carcinoma (HCC), portal vein thrombosis (PVT), and were recorded. CC was defined as cirrhosis when causes of chronic liver diseases were thoroughly searched and excluded. NASH cirrhosis was diagnosed if patient had liver biopsy compatible with NASH and AIH was diagnosed based on serological and/or biopsy findings of patients before liver transplantation. Data were analyzed using student t- test or chi- square test using SPSS software.

Results: 1044 patients were included in the study (72 patients with NASH, 526 with CC and 446 patients with cirrhosis due to AIH. 37 patients (51.4%) with NASH and 115 patients with CC (21.9%) had DM before liver transplantation (OR = 3.77; 95% CI: 2.27–6.28, P $<$ 0.001). 34 patients with NASH (47.3%) and 61 patients with CC (11.6%) were obese (BMI$>$30 kg/m2) (OR = 6.24; 95% CI: 3.62–10.75, P $<$ 0.001). DM was diagnosed in 47 cirrhosis patients with AIH (10.5%) compared to the 115 patients with CC (21.9%) (OR = 2.37; 95% CI: 1.64–3.42, P $<$ 0.001). Obesity was detected in 61 patients with CC (11.6%) and 30 patients (7.2%) with cirrhosis due to AIH (OR = 1.99; 95% CI: 1.26–3.16, P = 0.004). 304 patients (68.2%) with AIH were female compared to 176 patients (33.5%) with CC (OR = 4.25; 95% CI: 3.25–5.57, P $<$ 0.001). 57 patients (79.2%) with NASH cirrhosis were male compared to 350 patients (66.5%) with CC (P = 0.031). Patients with NASH cirrhosis were older and had higher mean BMI when compared to the patients with AIH and CC (P $<$ 0.001) (Table). There was also significant difference in trend of incidence of NASH, AIH and

CC. NASH was significantly increasing as a cause of liver cirrhosis requiring liver transplantation while trend of CC and AIH is stable ($P < 0.05$).
Conclusion: Clinical characteristics of patients with cryptogenic cirrhosis are totally different from NASH cirrhosis and patients with cirrhosis due to AIH. Therefore, cryptogenic cirrhosis may not be simply consider equal to cirrhosis secondary to NASH or AIH. Further studies are needed to discover true nature of cryptogenic cirrhosis.

	Cryptogenic cirrhosis	NASH	P-Value	AIH	P-Value
Age (years)	43.06 ± 13.45	54 ± 7.8	<0.001	33.86 ± 11.52	<0.001
BMI	25.80 ± 6.9	31.73 ± 10.5	<0.001	23.80 ± 4.10	0.020

[[Age and BMI in patients with cryptogenic cirrhosis compared to patients with NASH and AIH related cirrhosis]]
Disclosure: Nothing to disclose

Reference

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P1294 HCV ERADICATION: A GAME-CHANGER IN THE RELATIONSHIP BETWEEN LIVER STIFFNESS AND PORTAL PRESSURE IN COMPENSATED ADVANCED LIVER DISEASE

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Introduction: Eradication of HCV infection with direct acting antiviral (DAA) therapy in patients with compensated advanced chronic liver disease (cACLD) is an important step further in the management of these patients, but brings new questions regarding the reliability and the accuracy of noninvasive tests in the post-HCV settings. Recent data reported that liver stiffness (LSM) rapidly decreases especially during first 4 weeks of DAA, with no notable changes at EOT or SVR12 (1). Data from the Peg-IFN era showed that baseline HVPG (hepatic-vein portal gradient), irrespective of achieving SVR, is the sole predictor of long-term decompensation and mortality (2).
Aims and Methods: Knowing that LSM is a very good predictor of clinically significant portal hypertension (CSPH) (3.4), we aimed to investigate whether obtaining SVR diminishes the accuracy of LSM to estimate CSPH, and, as a consequence, if LSM could still be used to diagnose CSPH and to predict long-term outcome in cACLD patients that achieved HCV eradication.
Consecutive HCV cirrhotic patients evaluated for DAA therapy were included. Baseline LSM and HVPG measurement were performed in the same day. LSM was further assessed at EOT and when estimating SVR12, while HVPG was reassessed only at SVR12. Descriptive, correlation and accuracy statistic tests were performed using SPSS.21software.
Results: Of the 69 HCV+ cACLD patients (mean age 59.2(±8.2) years; 63.8% females) treated with DAA, 55 already finalized the therapy and achieved SVR. LSM decreased from 23.15(6.4–62.7) kPa at baseline to 18.7(7.3–47.2) kPa at EOT ($p = 0.015$) and remained unchanged at SVR12 [19.8(5.9–55.1) kPa; $p = 0.37$]. HVPG dropped from 12.5(3–27) mmHg at baseline to 9(3–27) mmHg at SVR12, $p = 0.013$. The proportion of patients with CSPH decreased from 74.2% at baseline to 46.7% at SVR12 (chi-square = 13.48; $p < 0.001$). Interestingly, the correlation between LSM and HVPG increased at SVR12 ($r = 0.839$; $p < 0.001$) as compared to baseline ($r = 0.698$; $p < 0.001$). Furthermore, the performance of LSM to detect CSPH was better after obtaining viral clearance [AUROC of 0.88(95%CI: 0.82–1.00) vs. 0.82(95%CI: 0.70–0.94) and diagnostic accuracy of 80% vs 57.6%] and the best cut-off values (calculated using the Youden index) were different: 12 kPa at SVR12 vs, 20.5 kPa at baseline. The baseline LSM cut-off value (20.5 kPa) has a 91% PPV, it could be used to rule-in CSPH. while the SVR12 cut-off (12 kPa) has a 100% NPV, being more suitable to rule-out CSPH, especially in the absence of HCV infection.
Conclusion: In conclusion, the HCV clearance due to DAA therapy induces a reduction in LSM and HVPG, mainly because of eliminating the inflammatory component of hepatic resistance. As a consequence, in the absence of HCV infection, LSM and HVPG are better correlated and LSM is a better noninvasive tool to rule-out CSPH.
Disclosure: Nothing to disclose

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P1295 NEW IFN-FREE TREATMENT IMPROVES METABOLIC PROFILE IN HCV-RELATED LIVER TRANSPLANT RECIPIENTS

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Introduction: The new direct antiviral agents (DAAs) provide a safe and efficacious treatment for liver transplant recipients with recurrent HCV infection.
Aims and Methods: The aim of this study is to evaluate the impact of HCV eradication on the metabolic factors in liver transplant recipients.
Retrospective single-centre study on HCV-related liver transplant recipients treated with IFN-free DAAs including both treatment naive and treatment-experienced patients. DAA impacts on the metabolic profile assessed at baseline and SVR >24 weeks.
Results: In total, 91 liver transplant recipients with recurrent HCV infection received IFN-free DAA treatment, 62 patients had IFN-based treatment failure and 29 were treatment-naïve, of whom 87(96%) achieved SVR. Eradication of recurrent HCV infection was associated with reduction in the treatment of diabetes and hypertension by 38% and 22% from the baseline respectively.
HbA1c levels declined from mean 35.5 ± 4.3mmol/mol to 33.3 ± 3.6 mmol/mol beyond 24 weeks post-treatment. [p 0.03]. Total cholesterol levels increased from 3.8 ± 0.9 mmol/L to 4.9 ± 0.9 mmol/L beyond 24 weeks post-treatment. [$p < 0.0001$] reflecting a significant increase in serum LDL levels [2.0 ± 0.8 to 2.9 ± 0.8; $p = < 0.0001$]. Estimated eGFR (ml/min) levels increased from 64.9 ± 20 ml/min to 69.6 ± 20 ml/min beyond 24 weeks post-treatment. [$p = 0.0004$]. Glucose, lipid profile and eGFR changes were independent of weight changes and immunosuppression dosage and trough levels.
Conclusion: Eradication of recurrent HCV infection by DAA therapy has beneficial impact on glucose metabolism and renal profile and reverses the hypolipidemic effect of HCV in liver transplant recipients. These extrahepatic effects of DAA therapy need to be validated by larger prospective studies.
Disclosure: Nothing to disclose

P1296 NS5A AND NS5B RESISTANCE-ASSOCIATED SUBSTITUTIONS ARE ASSOCIATED WITH VIROLOGIC FAILURE IN HEPATITIS C VIRUS GENOTYPE 1 PATIENTS TREATED WITH SOFOSBUVIR AND LEDIPASVIR

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Introduction: In July, 2015, sofosbuvir (SOF) (an NS5B inhibitor) and ledipasvir (LDV) (an NS5A inhibitor) combination therapy were authorized for the treatment of chronic hepatitis or compensated cirrhosis in patients with HCV genotype 1 in Japan. An open-label phase 3 clinical trial in Japan showed that an SVR was achieved by 100% of patients. However, in the real world, some patients experience virologic failure.
Aims and Methods: We aimed to reveal the factors associated with virologic failure in patients treated with SOF/LDV, and to identify the baseline NS5A and NS5B resistance-associated substitutions (RASs). Four hundred ninety-three patients with Hepatitis C Virus (HCV) genotype 1b infection were treated with SOF/LDV; 31 had a history of interferon (IFN)-free treatment with daclatasvir and asunaprevir. The effect of baseline RASs on the response to SOF/LDV therapy was analyzed. We investigated the viral genome sequence by direct sequencing.
Results: The age of the patients ranged from 26 to 90 years (mean, 68 years). There were 295 female patients (60%) and 105 (21%) patients with cirrhosis. Sixty-three patients (13%) had previously been treated for hepatocellular carcinoma (HCC). Overall, a sustained virologic response at 12 weeks (SVR12) was achieved in 476 patients (96.6%). The SVR12 rates in the patients with IFN-free treatment-naïve and retreatment were 97.6% and 80.6%, respectively. HCV eradication was not achieved in 17 patients, 11 (including 5 with IFN-free retreatment) of whom had virologic failure. Eight patients had coexisting NS5A RASs of Q24, L28 and/or R30, L31, or Y93 and one patient had coexisting NS5A RASs of P32L and A92K. Interestingly, 10 and 8 patients had NS5B A218S and C316N RAS respectively. No patients had NS5B L159, S282, L320 or V321 RASs at the baseline. In particular, the patients who had NS5B C316

RAS also had coexisting A218 RAS. In addition, no patients acquired these RASs. According to a multivariate analysis, coexisting NS5A RASs, NS5A P32 RAS, NS5B A218 and/or C316 RASs, and γ-glutamyltranspeptidase were associated with virologic failure. In the naïve patients, all patients without NS5B A218 and/or C316 RAS achieved an SVR12. Notably, the SVR12 rates of patients with coexisting NS5A and NS5B RASs were significantly lower (83.3%).
Conclusion: Although SOF/LDV therapy resulted in a high SVR12 rate, coexisting NS5A and NS5B RASs were associated with virologic failure. These results might indicate that the coexisting baseline RASs influence the therapeutic effects of SOF/LDV.
Disclosure: Nothing to disclose

P1297 SAFETY AND EFFICACY OF SOFOSBUVIR-BASED REGIMENS IN TREATING HEPATITIS C VIRUS IN EGYPTIAN PATIENTS: REAL-WORLD STUDY: SINGLE-CENTER EXPERIENCE

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Introduction: Hepatitis C virus (HCV) is the main leading cause of liver disease in Egypt. A new era of HCV treatment has been started with the evolution of direct acting antiviral agents which are expected to change epidemiology of the disease. Sofosbuvir (SOF)-based therapy was introduced by the Egyptian ministry of health through a national HCV treatment program in 2014 in an attempt to decrease disease burden.
Aims and Methods: To evaluate efficacy and safety of Sofosbuvir-based regimens in HCV Egyptian patients with compensated liver disease. In the period between February 2015 and December 2016, 758 chronic HCV patients with compensated liver disease were randomized into 4 groups according to treatment regimen applied for each group; group 1 received SOF, PEG-IFN plus ribavirin (RBV) for 12 weeks, group 2 received SOF plus RBV for 24 weeks, group 3 received SOF and Simeprevir (SIM) with or without RBV for 12–24 weeks according to the state of fibrosis and treatment status, group 4 SOF and Daclatasvir with or without RBV for 12–24 weeks according to the state of fibrosis and treatment status. Patients with Child-Pugh score more than 8, impaired kidney functions or hepatocellular carcinoma (HCC) whether active or recently treated with less than 4 weeks elapsed after successful treatment have been ruled out. SVR12 was the end point used to assess treatment efficacy. All adverse events have been reported in each group.
Results: Seven hundred out of 758 patients fulfilled the inclusion criteria; group 1 included 159 patients, group 2 included 138 patients, group 3 included 201 patients and group 4 included 202 patients. The mean age was 49.4 ± 9.2, 54.6 ± 9.3, 49.5 ± 11.4 and 50.3 ± 10.8 years in the 4 groups respectively. The overall SVR was 90.9% in group 1, 81.5% in group 2, 95% in group 3 and 98% in group 4. SVR in patients with liver cirrhosis was 90.56, 79.16, 95 and 96% in the 4 groups respectively. In treatment experienced patients, SVR was 86.8% in group 1, 78.3% in group 2, 100% in group 3 and 86.7% in group 4. The overall SVR and SVR among patients with liver cirrhosis was significantly higher in group 4 ($p < 0.001$) while SVR in treatment experienced patients was significantly higher in group 3 ($p < 0.001$). The rate of adverse events was 55.97, 59.42, 40.79 and 9.4% in the 4 groups respectively with significantly lower rate in group 4 ($p < 0.001$). The most reported adverse events were flu-like illness (15.1%) and anemia (12.6%) in group 1, anemia (18.8%) and hyperbilirubinemia (18.1%) in group 2, hyperbilirubinemia (11.9%) and fatigue (6.5%) in group 3, hyperbilirubinemia (5.9%) and anemia (3.5%) in group 4.
Conclusion: Sofosbuvir plus daclatasvir with or without ribavirin is the safest and most effective SOF-based regimen in treatment of HCV Egyptian patients with compensated liver disease.
Disclosure: Nothing to disclose

P1298 RIGHT TIMING FOR TRANSIENT ELASTOGRAPHY LEADS TO THE RIGHT FOLLOW-UP AFTER HCV TREATMENT

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Introduction: The improvement of liver fibrosis assessed using transient elastography (TE) by FibroScan® is leading to new insights in the concepts of fibrosis regression.
The possibility of using new direct antiviral agents (DAA) in cirrhotic patients, previous excluded from PegInterferon treatment for risk of hepatic failure, has permitted to verify the hypothesis of fibrosis regression in these patients. TE should be interpreted taking into account the inflammatory profile associated with hepatitis.
Aims and Methods: To establish the stiffness variations in a court of HCV patients before and after antiviral treatment to assess the correct follow up in patients with high stiffness value.
We enrolled 246 consecutive patients treated with DAA for chronic hepatitis C. TE and blood tests were performed before therapy and during follow-up.
Results: Each patient underwent TE before therapy; 60 of them performed TE at 24th week after end of treatment (EOT) and also at 24th month after EOT. Before therapy, 91 of 246 patients (37%) had stiffness >12 kPa (suggestive of advanced fibrosis stage); all 91 had a Child-Pugh score A5 but only 49 (56%) had APRI score suggestive of cirrhosis. Regardless of DAA-schedule, all 246 patients reached SVR. At follow-up only 3 patients presented stiffness >12 kPa (5%) and they were the same patients who maintained APRI score >1. Respect to the basal stiffness, after therapy all patients showed a significant decrease at 24th week after EOT (mean 14.9 kPa vs 9.5 kPa, $P = 0.0009$). This decay was unchanged at 24th month after EOT (mean 9.5 kPa vs 8 kPa, P = NS).
Conclusion: The sudden improvement of liver stiffness assessed by TE within the 24th week after EOT could be related to the "switch-off" of necro-inflammatory activity achieved by antiviral therapy. Follow-up should be established regarding APRI score and TE performed at 24th week after EOT instead of the pretreatment values.
Disclosure: Nothing to disclose

P1299 HEPATITIS C VIRUS INFECTION: AN INSULAR REALITY

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Introduction: Hepatitis C virus (HCV) infection is a public health problem on a global scale. In Portugal, it is estimated that the prevalence of seropositivity is between 1–1.5%, and there are no studies regarding this reality in Madeira archipelago. The World Health Organization has proposed an ambitious goal of eradicating the disease 2030.
Aims and Methods: Identification of the areas with the highest prevalence and the caracterization of HCV infection in Madeira archipelago. Retrospective study was made based on the population with HCV seropositivity from 2012 to 2017. Data from the patients were analyzed together with the 2011 Census, for the study of the distribution of 11 municipalities and 54 civil parishes. The data were analyzed using Excell software and SPSS.
Results: We evaluated 3741 tests involving 1759 patients. 88% male (n = 1548), with a mean age of 36 ± 10.86 years. The prevalence in the archipelago and in the island of Madeira was 0.61%, in the island of Porto Santo was 0.5%. The prevalence in varying between 0.12 and 1.05%, and there was a more marked asymmetry at the level of parishes (0–2.03%) When adjusted for the masculine gender, 17 parishes, belonging to 5 municipalities, present more than 1% (0–3.7%). Drug-addicted patients were the largest at-risk group with 48% (n = 844) of the total and inmates with 13% (n = 234). 41% (n = 727) of the patients had loss of follow-up.
Conclusion: The patients identified in this study with HCV-HCV seropositivity allowed to estimate a prevalence of 0.61% in Madeira archipelago.
Our data showed some geographical heterogeneity, which reinforces the importance of a "targeted" population strategy to eradicate infection in the most prevalent areas, as envisaged in the "micro elimination or eradication" strategy.
Disclosure: Nothing to disclose

P1300 FIBROSCAN VS. FIBROMAX IN PATIENTS WITH HCV COMPENSATED LIVER CIRRHOSIS

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Introduction: The severity of liver disease should be assessed prior to therapy. Identifying patients with cirrhosis is of particular importance, not only for treatment, but also for prognosis. Noninvasive evaluation of liver fibrosis can be

performed using biological tests, such as the FibroMax, or by using ultrasound based elastographic methods, such as Transient Elastography (TE).
Aims and Methods: The aim of the present study was to evaluate the accuracy of these tests (FibroMax and Transient Elastography) for predicting HCV liver cirrhosis (LC), in viremic naive or treatment-experienced patients, with compensated liver disease.
The study prospectively included 460 consecutive patients previously diagnosed with compensated HCV LC based on clinical, biologic, ultrasonographic, endoscopic (esophageal varices), liver biopsy or/and laparoscopic criteria, who were considered for interferon-free treatment (Viekirax/Exviera). Liver fibrosis was assessed during a two weeks period by means of TE (using M or XL probe) and by FibroMax. For TE, reliable measurements were defined as median value of 10 liver stiffness measurements, with a SR≥60% and an IQR < 30%. For diagnosing cirrhosis by means of TE we used a cut-off value 12 kPa (1) and for FibroMax a value of 0.75.
Results: Out of the 460 patients, reliable measurements by TE were obtained in 453 (98.4%). According to the FibroMax cut-off, 77% (349/460) patients were correctly classified, while according to TE cut-off – 94.2% (427/453) patients ($p < 0.0001$). Out of the 453 cirrhotics, 1.5% were misclassified by TE as having significant fibrosis (F2) and 4.3% with severe fibrosis (F3). When we evaluated the performance of FibroMax, 8.1% of the 460 patients with LC were misclassified as having F1, 2.2% as having F2.10.8% as having F3 and 1.9% as having F3/F4.
Conclusion: The accuracy of FibroMax for predicting HCV liver cirrhosis in viremic naive or treatment-experienced patients, with compensated liver disease was significantly lower than of TE (77% vs. 94.2%; $p < 0.0001$).
Disclosure: Nothing to disclose

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P1301 RECURRENCE RATE OF HEPATOCELLULAR CARCINOMA (HCC) IN PATIENTS WITH HCC AND VIRUS C COMPENSATED CIRRHOSIS TREATED WITH OMBITASVIR, PARITAPREVIR/ R+DASABUVIR+RIBAVIRIN

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Introduction: Patients with HCV-associated cirrhosis and hepatocellular carcinoma (HCC) maintain a high rate of HCC recurrence even after subsequent DAA therapy resulting in sustained viral response. Further research is needed in order to establish the impact of DAA therapy on the recurrence rates and survival in these patients.
Aims and Methods: From a national prospective cohort enrolling 5861 Romanian patients with virus C compensated liver cirrhosis who received reimbursed DAA with Paritaprevir/ Ombitasvir /r, Dasabuvir and Ribavirin (OBV/PTV/r + DSV + RBV) for 12 weeks during december 2015- august 2016, we analyzed 22 patients with a history of treated HCC. Most of them were treated by resection (8/22), followed by radiofrequency ablation (RFA) 6/22 and transarterial chemoembolisation (TACE) 8/22. DAA treatment was administered on the condition that the absence of tumor relapse was confirmed 6 months after the last session of therapy. A control group was defined including an equal number of HCC patients treated by surgery/RFA/TACE with matching age, gender and Barcelona Clinic Liver Cancer (BCLC) staging. All the patients were screened for tumor recurrence every 3–4 months with dynamic CT scan and/or MRI. They were divided in 4 groups: DAA- resection+ RFA (patients with HCC treated through resection or RFA who received DAA therapy), Control- resection+ RFA, DAA- TACE (patients with HCC treated through TACE who received DAA therapy), Control- TACE. Data were obtained from the Romanian National health Agency. Ordinal and scale variables with non-normal distribution were summarized as mean (±standard deviation), and compared by t-student test, while categorical variables were summarized as number (%) and compared by Fisher exact test.
Results: Results are depicted in table 1

Parameter	DAA-RESECTION +RFA (14)	CONTROL-RESECTION +RFA (14)	p-value
Sex M	7/14 (50%)	6/14 (42.3%)	0.7
Mean age (±SD) *	62.8 ± 7	64.4 ± 8.2	0.59
Follow-up (mean ± SD) **	46.7 +/− 20.1	33.7+/− 27	0.16
SVR 12 (per protocol)	12/14 (85.7%)	NA	NA
Recurrence rate	3/14 (21.4%)	12/14 (85.7%)	0.001
Survival without recurrence	45.1+/− 12.5	18.1 +/−16.2	0.005
Parameter	DAA-TACE (8)	CONTROL-TACE (8)	p-value

(continued)

Continued

Parameter	DAA-RESECTION +RFA (14)	CONTROL-RESECTION +RFA (14)	p-value
Sex M	2/8 (25%)	2/8 (25%)	1
Mean age (±SD) *	67.9 +/− 7.2	64.9 +/− 8.3	0.453
Follow-up (mean ± SD) **	40.4+/−12.9	16.5+/− 9.2	0.001
SVR 12 (per protocol)	7/8 (87.5%)	NA	NA
Recurrence rate	3/8 (37.5%)	8/8 (100%)	0.007
Survival without recurrence **	37.3 +/− 7.3	14.3 +/− 8.1	0.003

[Table1. Main characteristics, SVR 12, recurrence rate and survival without recurrence of the 4 groups, SVR 12 where applicable]
Two female patients died of acute liver insufficiency (9.5%) one after completing 12 weeks of treatment, and the other in week 7 of DAA therapy (in the DAA-resection+ RFA group). One male patient from the DAA-TACE group had a viral relapse 12 weeks after EOT.
Conclusion: SVR rate per protocol analysis in patients with treated HCC and compensated liver cirrhosis that received DAA with OBV/PTV/r + DSV + RBV was 86.4% Although a recruitment bias may be involved, recurrence rate in patients with HCC treated by resection and RFA that received DAA therapy was 21% compared with 86% in the control group. In those with HCC treated by TACE on DAA therapy the recurrence rate was 37.5% vs 100% in the control group. This favorable impact of DAA therapy on the recurrence rate of HCC was reflected into an improved survival without recurrence in both groups.
Disclosure: Nothing to disclose

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P1302 LONG-TERM FOLLOW-UP OF CHRONIC HEPATITIS C PATIENTS: WILL SUSTAINED VIROLOGICAL RESPONSE BE ENOUGH TO PREVENT CIRRHOSIS IN THE LONG TERM?

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Introduction: Cirrhosis development is an important stage in the natural history of chronic hepatitis C(CHC), because it heralds significant morbidity and mortality and higher health care costs related to complications of end-stage liver disease. Treatment response has been proven to be the determinant factor for the development of cirrhosis. It has also been shown that disease progression can be predicted by AST/ALT, Fibrosis-4 (FIB-4) and AST/Platelet ratio index (APRI) scores (1.2,3). In the present study, we aimed to evaluate the impact of sustained virological response (SVR) and some other predictive factors on development of cirrhosis secondary to chronic hepatitis C.
Aims and Methods: 100 patients with CHC, who were followed at least for 1 year between 2000–2015 in Uludag University, School of Medicine Hospital were reviewed and cirrhosis development was investigated. AST/ALT ratio, APRI (AST (IU/L)/Platelet) and FIB-4 ((Age (year) × AST(IU/L))/(Platelet × (sqr (ALT) (IU/L)) scores were calculated. SVR was defined as aviremia 24 weeks after completion of therapy. Annual rates and the cumulative incidences of cirrhosis for 3-5-10 years were estimated.
Results: The median follow-up period was 5.9 (1–14.4) years. The 10 year cumulative incidence of cirrhosis was significantly lower in the treated group compared to untreated group (19.5% and 44.4%, $p = 0.025$). In the treated group; cirrhosis wasn't observed in the cases with SVR ($p < 0.001$). Univariate analysis revealed that female gender ($p = 0.041$), age ≤ 40 ($p = 0.05$), platelet count >150,000 ($p < 0.001$), low AST/ALT score ($p = 0.003$), low Fib-4 score ($p < 0.001$), low APRI score ($p < 0.001$), SVR ($p < 0.001$) resulted in statistically significant less cirrhosis. In cox regression analysis; SVR was found to be the only independent factor affecting development of cirrhosis (Hazard ratio, HR = 0.279; $p = 0.04$).
Conclusion: Although there are useful parameters in predicting the development of cirrhosis in CHC patients, SVR is the only independent factor to prevent cirrhosis. Elimination of cirrhosis with higher SVR rates with currently used new direct-acting antiviral agents will be probably shown in the future long-term studies.
Disclosure: Nothing to disclose

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P1303 DIAGNOSTIC PERFORMANCE EVALUATION OF RAPID DIAGNOSTIC ORIENTATION TEST IN THE DETECTION OF HEPATITIS C

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Introduction: Hepatitis C is an infectious disease of viral origin with primarily blood transmission. It is a real public health problem. Screening for hepatitis C is very interesting for preventing the spread of the infection, improving access to care and reducing the risk of chronic liver complications. The rapid diagnostic tests (RDTs) represent an interesting alternative to enzyme immunoassay.
Aims and Methods: The aim of this study is to prospectively evaluate the diagnostic performance of CE-marked RDTs (Toyo® tests) which detects the anti-hepatitis C virus (HCV) antibodies in capillary whole blood and to study their sensitivity and specificity as well as their predictive values.
This is a prospective comparative study done in the Hepato-Gastroenterology service of Oujda's Mohammed VI university hospital, over a period from March 2017 to July 2017 and collected all the patients hospitalized during this period. We analyzed 150 blood samples tested for HCV by RDTs.
Results: One hundred and fifty patients were included. The average age of our patients was 47.74 years old with extremes: 17 years-98 years. There are 79 men and 71 women with a sex ratio H/F: 1.11. The risk factors for contamination by hepatotropic viruses were found in 71.33% (Non-medical care: 82.24%, tattooing: 32.71%, transfusion: 28.03%, cupping therapy: 18.70%, unprotected sex: 4.67%). The viral serology of hepatitis C (anti-HCV antibodies) was positive in 13 cases, or 8.66%. RDTs were positive in 10 cases (6.66%), as well as polymerase chain reaction (PCR). The sensitivity of the RDTs to viral serology was 76.92%, while its specificity was 100%. The positive predictive value was 100% and the negative predictive value was 97.8%. The same results were found by calculating the specificity, sensitivity and predictive values of PCR in relation to viral serology.
Conclusion: Based on this work, we found that the positivity of RDTs allows the establishment of the hepatitis C diagnosis for 100 per cent. However, the use of a serological assay remains necessary when the test is negative. While our study involved a small number of patients, it is a rough sketch for a work with a larger sample to thoroughly assess the efficiency of HCV RDTs and to estimate the real impact of their use in reducing the diagnosis of the infection at an advanced stage and facilitate access to rapid therapeutic management.
Disclosure: Nothing to disclose

P1304 PREDICTIVE FACTORS OF RESPONSE TO URSODESOXYCHOLIC ACID IN PRIMARY BILIARY CHOLANGITIS

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Introduction: Primary biliary cholangitis (PBC) is an autoimmune chronic cholestatic disease. Its treatment is based on ursodesoxycholic acid (UDCA) which purpose is to normalize liver tests and delay progression to cirrhosis.
Aims and Methods: The aim of this study was to determine the factors influencing the response to UDCA in PBC.
We investigated all the PBC patients admitted in our department in the period between January 1996 and December 2014. Only patients with treated with UDCA and followed for at least one year. The definition of response to UDCA was based on Paris II criteria[1].
Results: Thirty patients were included in our study among 75 having a PBC. Their mean age was 51.3 years [31–73] and the sex ratio was 0.07 (2M/28F). Discovery of the disease was fortuitous in 26% of patients. The mean levels of aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transferase, alkaline phosphatase, total bilirubin, albumin and IgM were respectively 1.97 ULN [1–6 ULN], 2.85 ULN [1–15 ULN], 7.4 ULN [1–30 ULN], 3.09 ULN [1–8 ULN], 2.22 ULN [1–14 ULN], 36 g/l [25.2–46.8g/l] and 2.44 g/l [1.06–11.4 g/l]. serological tests showed positive antimitochondrial antibodies (AMA) in 83% of cases, their mean level was 1/2737, in addition, antinuclear antibodies (ANA) were positive in 70% of cases and smooth muscle antibodies in 6 patients only. A second autoimmune disease was associated to PBC in 63% of cases (N = 19). Three patients had cirrhosis at diagnosis, the rest had a liver biopsy (N = 27), showing a PBC scheuer's stage $\geq$ 2 in 60% of cases with a fibrosis score $\geq$ 2 in 37%.
All patients were treated by UDCA at the dose of 14 mg/kg/day. Response to UDCA therapy at one year of follow-up was adequate in 63% of cases. we compared the groups of patients with and without response to UDCA, no differences were found according to age, sex, absence of symptoms, pretherapeutic levels of serum transaminase activity, ALP and GGT, levels of AMA and ANA, positivity of AML, histological liver steatosis, Bile duct loss and ductular reaction, stage according to scheuer's classification, fibrosis, coexistence of other autoimmune diseases, and delay in starting UDCA therapy. However, biochemical response was inversely correlated o pretherapeutic level of total bilirubin ($p = 0.023$).
Conclusion: According to our study, an elevated pretherapeutic of total bilirubin (superior to 2 ULN) is a predictive factor to the absence of a biochemical response to UDCA therapy in PBC.
Disclosure: Nothing to disclose

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P1305 COMBINATION THERAPY OF FENOFIBRATE AND URSODEOXYCHOLIC ACID IMPROVES THE PROGNOSIS IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS WITH INCOMPLETE RESPONSE TO URSODEOXYCHOLIC ACID

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Introduction: Most patients with Primary Biliary Cholangitis (PBC) respond to ursodeoxycholic acid (UDCA) therapy. For those who do not respond to UDCA, therapeutic alternatives are scarce. Fibrates have been suggested as second-line agents in patients who do not achieve adequate biochemical response to UDCA monotherapy. The objective of this study is to evaluate the role of fibrates as second-line therapy in PBC.
Aims and Methods: PBC was diagnosed according to accepted criteria and staged according to the Ludwig classification. The absence of response to UDCA therapy was assessed using the GLOBE score. Liver function tests, renal function and the UK-PBC score were assessed at 6 and 12 months after fibrate onset and at the date of the last follow-up visit. Patients receiving fibrate were compared with a control group of patients not responding to UDCA who did not receive fibrates.
Results: Thirty-nine patients were included (fibrates group n = 13; control group n = 26). Patients in both groups did not differ in terms of age, gender or follow-up time. Side effects were observed in two patients (arthralgias and myalgias), leading to the suspension of the fibrate in one patient. There was a significant decrease in alkaline phosphatase levels at 6 and 12 months and at the end of the follow-up in the group that received fibrates compared to the control group ($p < 0.05$). Transaminase and IgM levels also decreased significantly, while bilirubin and albumin levels remained unchanged in the group receiving fibrates. A higher proportion of patients in the fibrate group achieved POISE response criteria compared to the control group at all time points studied ($p < 0.05$).
Conclusion: Combination therapy of fibrate and UDCA is safe and induces significant biochemical and prognostic scores improvement in patients with PBC and incomplete response to UDCA.
Disclosure: Nothing to disclose

P1306 PREDICTIVE FACTORS OF URSODESOXYCHOLIC ACID IN PRIMARY BILIARY CHOLANGITIS

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Introduction: Primary biliary cholangitis (PBC) is a cholestatic chronic liver disease characterized by a progressive destruction of small intrahepatic bile ducts. Ursodesoxycholic acid (UDCA) have benefit in slowing down the liver disease progression. However, some (30 -40%) patients experience treatment failure.
The aim of our study was to evaluate the prognostic factors of UDCA failure in patients with PBC.
Aims and Methods: We retrospectively collected the medical files of patients with PBC who received UDCA from January 2005 to December 2016. Non-reponse to treatment was evaluated with Paris criteria.
Results: Seventy- one patients were included in our study. There were 66 females (93%) and 5 (7%) males. Ages ranged from 23 to 81 years (median 55.23). All patients were treated with UDCA (13–15 mg/Kg/ day) associated with corticosteroids and azathioprine in overlap syndromes (28.1%). The average of follow-up time was 64 months (range 3–64 months).
Complete response was observed in 34 (48%) patients. Partial response or non-response were seen in 34 (52%) patients.
Predictive factors of treatment failure were: high serum bilirubin level $>$50 µmole/L ($p = 0.039$), advanced cirrhosis ($p = 0.026$), overlap syndrome ($p = 0.046$) and interface hepatitis ($p = 0.006$). Gender, age and association with other autoimmune diseases were not identified as prognostic factors. The evolution into an advanced cirrhosis was significantly observed in patients who failed UDCA ($p = 0.038$). Interestingly, 2 cases of hepatocellular carcinoma were diagnosed in patients with UDCA failure.
Conclusion: UDCA has a crucial role in PBC treatment. It may slow down the progression into advanced liver disease. However, high serum bilirubin level,

advanced cirrhosis, overlap syndrome and interface hepatitis predicted poor outcome.
Disclosure: Nothing to disclose

P1307 LIPIDOMICS ANALYSES IN SERUM IDENTIFIED CANDIDATE BIOMARKERS FOR DISEASE PROGRESSION AND DEVELOPMENT OF PRIMARY SCLEROSING CHOLANGITIS AND BILIARY DYSPLASIA

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic, usually progressive, stricturing disease of the biliary tree that may eventually lead to cirrhosis and cholangiocarcinoma (CCA). The etiopathogenesis is heterogeneous, involving both genetic and environmental factors. Early diagnosis and better tools for monitoring disease progression and detection of biliary dysplasia poses a major medical challenge. Novel serum biomarkers enabling a more precise diagnostic and prognostic of both PSC and biliary dysplasia are urgently needed.
Aims and Methods: This study aimed identifying a set of serum lipids that would serve as biomarkers for detection and prognosis of PSC and biliary dysplasia. After informed consent, serum samples (n = 185) were drawn from participants (n = 175) distributed across four experimental groups representing different disease stages: non-advanced PSC (n = 67), advanced PSC (n = 73), biliary dysplasia (n = 34), and healthy controls (n = 11). These samples were subsequently analyzed using a novel lipid-screening platform (Lipidyzer^{TM}, Sciex) to determine the concentration of 1134 lipids species across 13 lipid classes.
Results: Model-based analyses (Generalized Estimating Equations) pinpointed a set of triglycerides as significantly altered in PSC patients respect to healthy controls, after correction for type-I error: TAG48:5-FA18:3 (triglycerides with 48 carbons and 5 double bonds, including alpha-linolenic acidin its composition; p-value: 5.2710^{-7}), TAG50:5-FA18:1 (triglycerides with 50 carbons and 5 double bonds, including oleic acid in its composition, p-value: 3.5110^{-5}), and TAG54:3-FA20:1 (triglycerides with 50 carbons and 5 double bonds, including 11Z-eicosenoic acidin its composition, p-value: 1.7010^{-6}). In addition to the above mentioned, one more lipid was pinpointed when comparing all affected patients (PSC and dysplasia) to healthy controls: TAG56:2-FA20:0 (triglycerides with 50 carbons and 5 double bonds, including arachidic acid in its composition, p-value: 7.2610^{-5}). Finally, a set of triglycerides were detected when comparing patients with biliary dysplasia respect to those with PSC: TAG54:5-FA22:4 (triglycerides with 54 carbons and 5 double bonds, including arachidonic acid in its composition; p-value: 8.4510^{-5}), TAG54:6-FA22:5 (triglycerides with 54 carbons and 6 double bonds, including 7,10,13,16,19-docosapentaenoic acid in its composition; p-value: 1.3610^{-4}), TAG54:7-FA16:1 (triglycerides with 54 carbons and 7 double bonds, including cis-9-palmitoleic acid in its composition; p-value: 5.9110^{-5}), and TAG56:4-FA22:4 (triglycerides with 56 carbons and 4 double bonds, including adrenic acid in its composition; p-value: 1.6010^{-5}).
Conclusion: From the extensive lipid panel initially screened, this study was capable of detecting a set of 4 triglycerides as candidate serum biomarkers that allowed differentiating between persons affected with PSC or biliary dysplasia from the healthy controls. Importantly, 4 additional triglycerides allowed discriminating between PSC and biliary dysplasia patients.
Disclosure: Nothing to disclose

P1308 A STUDY ON PRURITUS IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS (PBC) BASED ON A SURVEY

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Introduction: Pruritus of the skin is a clinical symptom characteristic of primary biliary cholangitis (PBC), but the frequency and severity has not been studied enough in detail. The purpose of this study is to document the actual state of pruritus in PBC patients.
Aims and Methods: The subjects were 49 patients who were diagnosed with PBC at our department. By means of a questionnaire, we evaluated the patients regarding pruritus, and classified them into 5 stages (0: none, 1: slight, 2: mild, 3: moderate, 4: intense), using Shiratori's criteria on the severity of pruritus, and compared them by age, duration from diagnosis, values of total bilirubin (mg/dl), albumin (g/ml), prothrombin time (%), platelet count, values of type 4 collagen 7S (ng/ml), and hyaluronic acid (ng/ml).
Results: The patients were 3 men and 46 women, with an average age of 67.8. Pruritus evaluated in 5 stages (0/1/2/3/4) were present during the day in (12/13/17/6/1) patients, and during the night in (14/12/18/3/2) patients. The rate of patients feeling pruritus during the day was 75.5%, and during the night, 71.4%, accounting for a high percentage. There was no relation between pruritus and age or duration from diagnosis with PBC, for both day time and night time. There was no correlation between pruritus and the value of total bilirubin(daytime: 0.6/0.5/0.7/0.5/0.8, night time: 0.6/0.6/0.5/1.4/0.5), the value of albumin(-day time: 4.2/4.1/3.9/4.0/4.1, night time: 4.2/4.0/4.0/3.4/4.1), the prothrombin time(daytime: 99/99/96/100/100, night time: 99/98/99/82/100), platelet count(day time: 20.4/17.3/20.2/18.2/15.2, night time: 21.4/17.1/19.2/17.5/17.7), type 4 collagen 7S(day time: 4.2/4.0/4.0/3.8/3.5, night time: 4.0/4.2/4.0/4.2/3.5), or hyaluronic acid(day time: 109.3/100.9/88.1/62.0/31.3, night time: 98.3/107.5/80.1/106.4/49).
Conclusion: The liver lesions of the patients in this study were mostly not advanced, but the rate of those feeling pruritus was high. There was no significant correlation between pruritus and age, duration of disease, or indicators of liver reserve. It has become clear that in PBC, pruritus manifests in the early stage.
Among PBC patients there are many who have pruritus regardless of the degree of advancement, but at the present point, there is no other way to confirm it than by history taking. Identification of a useful biomarker for confirming pruritus will be needed.
Disclosure: Nothing to disclose

P1310 UGT2B28 GENOMIC VARIATION IS ASSOCIATED WITH THE ONSET AGE OF ALCOHOLISM-ASSOCIATED HEPATOCELLULAR CARCINOMA

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Introduction: Early hepatocellular carcinoma (HCC) is often absent of pathognomonic symptoms, and thus many patients have untreatable disease when first diagnosed. Single-nucleotide-polymorphisms (SNPs) on the *UDP glucuronosyltransferase gamily 2 member B28 (UGT2B28)* gene have been proved associated with hepatitis B virus e-antigen clearance in response to peginterferon therapy, prostate cancer progression and colorectal cancer risk. The gene product, UGT2B28, is an enzyme associated with sex hormone metabolism, an important factor in HCC progression, whereas its clinical role in HCC has never been studied. Here, we aimed to investigate this issue and to explore the possible application of our findings in diagnosis of HCC.
Aims and Methods: A cohort of 382 patients with HCC having received curative resection was retrospectively recruited. We evaluated the correlation between *UGT2B28*-rs2132039 genotypes and clinicopathological factors.
Results: Among these patients, 52.6% patients had rs2132039-CT genotype, and the others had rs2132039-TT genotype. Intriguingly, none had rs2132039-CC genotype. Univariate analysis revealed that "CT" genotype was associated with age (OR, 1.021; 95% CI, 1.006–1.036; P = 0.005), ascites (OR, 3.223; 95% CI, 1.264–8.215; P = 0.014) and hepatitis C (OR, 1.839; 95% CI, 1.148–2.945; P = 0.011). Multivariate analysis showed that these three factors were independent of each other. Subgroup analysis discovered that "CT" genotype was most significantly associated with age in alcoholism-related HCC patients (OR, 1.079; 95% CI, 1.035–1.125; P < 0.001). The average ages at diagnosis (onset ages) of alcoholism-related HCC were 59.3 ± 10.7 and 49.6 ± 12.2 years (a 10-year difference) for "CT" and "TT" genotypes, respectively.
Conclusion: Alcoholic patients with *UGT2B28*-rs2132039-TT genotype had a 10-year earlier onset of HCC, compared to the "CT" genotype. Intensive ultrasound surveillance for HCC should start before 50 years of age in alcoholic patients with "TT" genotype.
Disclosure: Nothing to disclose

P1311 METHYLATION OF MULTIPLE TUMOR SUPPRESSOR GENES(RUNT-RELATED TRANSCRIPTION FACTOR 3 (RUNX3), RAS ASSOCIATION DOMAIN FAMILY1 ISOFORM A(RASSF1A) AND E-CADHERIN) IN HCV-RELATED LIVER CIRRHOSIS AND HEPATOCELLULAR CARCINOMA IN EGYPTIAN PATIENTS

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Introduction: Recognition of circulating DNA can be useful for the diagnosis of many cancers, including the hepatocellular carcinoma (HCC). The pathogenesis of HCC involving different genetic and epigenetic alterations. HCV viral proteins may participate in epigenetic regulation of hepatic cancer and induce HCC-specific epigenetic changes. HCV infection was related to aberrant methylation on multiple genes. Runt-related transcription factor 3 (RUNX3), Ras association domain family1 isoform A(RASSF1A) and E-Cadherin genes are tumor suppressor genes which could be inactivated by hypermethylation in many tumors including HCC, causing a decrease of gene expression.

Aims and Methods: In this study, the methylation of RUNX3, RASSF1A, and E-Cadherin genes were studied in the serum of patients with HCV related liver cirrhosis and patients with HCC as diagnostic biomarkers for HCC. DNA was extracted from the peripheral blood of 53 healthy volunteers, 207 HCV related liver cirrhosis (LC) patients and 193 HCC patients. Routine laboratory investigations, assessment of serum AFP and detection of circulating hypermethylated RASSF1A, RUNX3 and E-Cadherin genes by methylation-specific PCR were done for all participants.
Results: A significant hypermethylated RASSF1A gene was found in HCC group when compared to both LC and healthy groups (OR = 9.9675), (OR = 5.6802) respectively. As regard gene RUNX3 a significant hypermethylation was found in HCC group when compared to both LC and healthy groups (OR = 3.2380), (OR = 6.5732) respectively. As regard E- Cadherin gene a significant hypermethylation was found in HCC group when compared to both LC and healthy groups (OR = 6.4459), (OR = 4.7850) respectively with p-value <0.0005. whereas there was no significant hypermethylation was found between LC and healthy group as regard the 3 tumour suppressor genes ($P > 0.05$). No significant association was found between methylation of the 3 genes with neither the size nor the staging of HCC ($P > 0.05$). Furthermore no Association was found between the methylation and Child Turcotte Pugh scoring system ($P > 0.05$). A significant association was found only between AFP value (>200 nl) and hyper methylated E-Cadherin in HCC group ($p = 0.036$) while no significant association was found as regard RASSF1A and RUNX 3 genes in HCC group ($p = 0.902$, $p = 0.496$) respectively. When ROC curve was applied to assess the diagnostic performance of hyper methylated RASSF1A, E-Cadherin and RUNX 3 genes in discrimination between HCC and LC it was found that at cut of levels of >0.389, >0.14 and >0.23 respectively the sensitivity was 46.36%,83.96% and 76.19% respectively and specificity was 86.7%,59.46% and 58.6% respectively.
Conclusion: The presence of hypermethylated RASSF1A, RUNX3, and e Cadherin in serum may be useful biomarkers for HCC early prediction in patients of LC with HCV.
Disclosure: Nothing to disclose

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P1312 THE ANTI-INFLAMMATORY RECEPTOR TREM2 HALTS THE GENERATION OF HCC IN MICE THROUGH THE INHIBITION OF LIVER INFLAMMATION AND HEPATOCYTE PROLIFERATIVE RESPONSES

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Introduction: Hepatocellular carcinoma (HCC) is the most prevalent primary liver tumour and the third most common cause of cancer-related death. Even though a number of interventional treatment methods are currently in use, this tumour remains highly chemo-resistant and shows a poor prognosis. HCC slowly unfolds on a background of chronic liver injury, where inflammation and liver regeneration processes are involved. Toll-like receptor (TLR) derived signalling in non-parenchymal liver cells accelerates carcinogenesis by modulating inflammatory responses. Therefore, regulation of pro-inflammatory signals arises as a promising therapeutic strategy for HCC. The triggering receptor expressed on myeloid cells 2 (TREM2) acts as an anti-inflammatory receptor, as it inhibits TLR-derived signalling in various tissues, yet its role in HCC is still unknown.
Aims and Methods: This study aims to unravel the role of TREM2 in HCC development and progression. For that, TREM2 mRNA expression was analysed in liver tissue samples from patients with HCC compared to control individuals and in murine models of HCC and liver regeneration. To study the role of TREM2 in HCC development and progression, *wild type* (WT) and *Trem2*$^{-/-}$ mice were treated with the hepatocarcinogen diethylnitrosamine (DEN) and analysed at different time-points during disease development. The early molecular mechanisms triggered in response to DEN were analysed in WT and *Trem2*$^{-/-}$ mice in acute phases (6, 24, 72h). To evaluate the role of TREM2 in liver regeneration a ~70% partial hepatectomy (PHx) model was performed in WT and *Trem2*$^{-/-}$ mice, and animals were sacrificed at 1, 6, 36, 72 hours and 5 days post-surgery.
Results: *TREM2* mRNA expression is significantly upregulated in human HCC samples compared to control livers and correlates with markers of inflammation. Similarly, *Trem2* mRNA expression is also elevated in murine HCC and in a liver regeneration model compared to control livers. *Trem2*$^{-/-}$ mice show augmented tumour number and bigger tumours after DEN. This was accompanied by an increase in the expression of liver damage and hepatocyte proliferation markers. *Trem2*$^{-/-}$ mice exhibited exacerbated liver damage and ROS in acute phases in response to DEN. Regarding liver regeneration following PHx, PCNA expression and BrDU incorporation indicated an increased hepatocyte proliferation in the *Trem2*$^{-/-}$ mice. The expression of pro-inflammatory genes was also elevated in these mice. Interestingly, the results observed in the HCC model could be rescued with an anti-inflammatory diet (BHA).
Conclusion: TREM2 is upregulated in human and murine HCC and in murine liver regeneration. This anti-inflammatory receptor inhibits proliferation and HCC tumour generation in mice through the inhibition of liver inflammation and ROS. TREM2 arises as a novel therapeutic strategy for HCC.
Disclosure: Nothing to disclose

P1313 MUSASHI 2 CONTRIBUTES TO THE MAINTENANCE OF STEMNESS OF CD44V6+ LIVER CANCER STEM CELLS VIA NOTCH SIGNALING PATHWAY

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Introduction: Liver cancer stem cells (LCSC) drive hepatocellular carcinoma (HCC) recurrence and metastasis. Notch signaling pathway play crucial roles in the maintenance of stemness characteristics. Musashi 2 (Msi2), a member of conserved gene family of RNA binding protein, was highly expressed in HCC tissues correlating with poor prognosis of HCC patients. We hypothesize that Msi2 contributes to the maintenance of stemness of CD44V6+ liver cancer stem cells through activation of Notch signaling pathway via LFNG gene.
Aims and Methods: CD44v6+/− cells were isolated from human hepatoma cell lines (SNU398 and MHCC-97H) using microbeads sorting. Stem-like properties, such as self-renew and metastasis ability were analyzed in vitro and in vivo (xenograft tumor model in mice). In order to investigate the role of Msi2 gene in CD44v6+ LCSCs, we downregulated Msi2 with lentiviral particles (Lenti-ShRNA Msi2) in CD44v6+ cells, upregulated Msi2 with Lenti Msi2 in CD44v6- cells, and analyzed stem-like characteristic. Furthermore, we detected the mRNA and protein levels of Notch signaling pathway in the system above. The roles of Notch signaling pathway in the CD44v6+ LCSCs was verified by inhibiting with lentivirus or γ-secretase inhibitor (RO4929097). To explore the mechanism of Msi2 gene and Notch signaling pathway, RT^2 Profiler PCR Array was carried out after Msi2 gene was downregulated in CD44v6+ liver cancer cells, and CO-IP was used to verify the direct binding of Msi2 and LFNG gene in Notch pathway.
Results: In our study, CD44V6 could be one of the surface makers of liver cancer stem cells. CD44V6+ cells expressed more Msi2, compared with CD44V6- cells. We demonstrated that downregulating Msi2 in CD44V6+ CSCs could decrease the ability of self-renewal, invasion and migration, proliferation, tumorigenicity and the expression of stemness-associated genes. Meanwhile, upregulating Msi2 in CD44V6- cells increased the ability of self-renewal, invasion and migration, chemotherapy resistant and tumorgenicity. In CD44v6+ cells, the key molecules of Notch signaling pathway down-regulated after Msi2 gene was down-regulated, while in the CD44v6- cells the key molecules up-regulated after increasing Msi2 gene. Furthermore, the self-renewal ability and tumorigenicity of CD44v6+ cells was obviously decreased after inhibiting notch signaling pathway. Last but not the least, according to the result of RT^2 Profiler PCR Array, Msi2 contributes to the maintenance of stemness of CD44V6+ liver cancer stem cells via activation of Notch signaling pathway by binding to LFNG.
Conclusion: Msi2 play an important role in the maintenance of stemness of CD44V6+ liver CSCs. Msi2 contributes to the maintenance of stemness of CD44V6+ liver cancer stem cells through activation of Notch signaling pathway via binding directly to LFNG. Our study provided a new insight to the recurrence and metastasis of HCC and potential molecular targets for targeted therapy for liver cancer.

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Disclosure: Nothing to disclose

P1314 MICRORNA-195 INCREASES APOPTOSIS IN HEPATOCELLULAR CARCINOMA BY TARGETING THE KEY CELL CYCLE REGULATOR WEE1

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Introduction: MicroRNA-195 (miR-195) plays an important role in many types of tumors. However, the roles of WEE1 in cancer and miRNAs that directly regulate WEE1 have not been elucidated. The purpose of this experiment is to assess

the effects of miR-195 on inhibiting WEE1 and to clarify the regulating mechanism of miR-195 in pancreatic cancer.
Aims and Methods: Real-time fluorescence quantitative PCR was used to detect the expression of miR-195 in HCC tissues and adjacent normal tissues from 36 cases. We also detected the expression level of miR-195 in eight human hepatoma cell lines including HepG2, Huh7, PLC/PRF/5, SMMC-7721, SK-HEP-1, MHCC97-H, MHCC97-L and Hep3B, as well as in human normal liver cell lines L02 and Chang liver. The effect of miR-195 and siWEE1 on cell viability was evaluated using cck-8 assays, apoptosis levels were determined using FACS analysis of Annexin V/PI stained cells, and target protein expression was determined using western blot. To investigate the potential anti-tumor activity of miR-195 in vivo,we constructed Tumorigenesis assay in nude mice.
Results: We found that miR-195 was downregulated in HCC cell lines and tissues. We also found that over-expression of miR-195 could suppress the proliferation and increase the apoptosis of HCC cell line. Knockdown of WEE1 by RNAi in HCC cells, similar to miR-195 overexpression, decreased liver cancer cell growth and induced apoptosis. In a mouse model, therapeutic administration of miR-195 mimics could significantly suppress the growth of hepatoma xenografts in nude mice.
Conclusion: MicroRNA-195 increases apoptosis in hepatocellular carcinoma by targeting the key cell cycle regulator WEE1. This finding suggests a potential novel strategy for therapeutic interventions of this disease.
Disclosure: Nothing to disclose

P1315 THE RELATION BETWEEN MICRO-RNA GENE POLYMORPHISMS AND DEVELOPMENT OF HEPATOCELLULAR CARCINOMA IN EGYPTIAN PATIENTS

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Introduction: The development and progression of hepatocellular carcinoma (HCC) is a multistage process involving the deregulation of genes that are crucial to cellular processes. Multiple risk factors are correlated with HCC. MicroRNA is differentially expressed in development of different types of malignancies, including hepatic malignancy. Single nucleotide polymorphisms (SNPs) are the most common sequence variation in human genome. SNPs in miRNAs may affect transcription, processing or target recognition and result in malignant diseases.
Aims and Methods: We aimed to determine the association between micro-RNA gene polymorphisms and development of HCC in Egyptian Patients.
This study included 200 individual who were matched in age and sex. Tumor staging was done using BCLC staging system. Quantification and genotyping of Micro-RNA were performed.
Results: Among the 200 patients, 2 groups were described: group I included 90 HCC patients with a male majority (72.2%) and 110 controls in group II. Diabetes and hypertension were detected as risk factors. Three microRNA SNPs were assayed. There was a significant association between rs10061133 miR-499b and the risk of HCC. The genotypes GG or G allele were associated significantly to an increased risk of HCC (GG: OR (95% CI) = 2.91 (1.23–4.22), p = 0.013; G allele: OR (95% CI) = 1.79 (1.12- 2.15), p = 0.026) compared with the genotype of AA or AG or A allele.
Conclusion: There is an association between the mi-RNA SNPs and the susceptibility to HCC, aiming to explore some roles and mechanisms of SNPs within miRNAs in the occurrence and development of HCC.
Disclosure: Nothing to disclose

P1316 PERIOSTIN PROMOTES TUMORIGENESIS BY ACTIVATING EPITHELIAL-MESENCHYMAL TRANSITION IN LIVER CANCER

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Introduction: Hepatocellular carcinoma (HCC) mostly arises from underlying chronic inflammatory liver disease. Periostin is one of the matricellular proteins and the association of periostin with inflammation or tumor invasiveness and prognosis has been reported. We investigated a role and mechanism of periostin in the development of liver cancer.
Aims and Methods: Hep3B cells, a human hepatocellular carcinoma cell line, were used. Cell growth was assessed using the MTS assay and epithelial-mesenchymal transition signaling was explored by immunoblot analysis. Male wild type or periostin -/- mice (C57BL/6, 8 weeks old) were injected with diethylnitrosamine (DEN, 100mg/kg at week 8) and tetrachloride (CCl4, 1mg/kg biweekly from week 10~50) intraperitoneally to induce liver inflammation, fibrosis and tumor. Anti-tumor effects were evaluated by number of tumors and histopathological examination.
Results: Cell proliferation did not show significant change in Hep 3B cells treated with recombinant periostin or periostin siRNA. Recombinant periostin (50nM) promoted cell migration and invasion in Hep3B cells. E-cadherin expression was decreased while N-cadherin expression was increased in recombinant periostin-treated Hep3B cells. Recombinant periostin also induced JNK expression and inhibition of JNK signaling restored N-caderin expression. Compared to wild type mice, the number of hepatic tumors was significantly lower in periostin -/- mice.
Conclusion: Periostin may play a role in the tumorigenesis through epithelial-mesenchymal transition and is suggested as a potential target for the treatment of liver cancer.
Disclosure: Nothing to disclose

P1317 TUMORSUPPRESSIVE MICRORNA EXPRESSION IN HEPATOCELLULAR CARCINOMA IS REGULATED BY P63 AND HCC THERAPEUTICS

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Introduction: Transcription factors of the p53 family (p53, p63, p73) respond to cellular stress signals by inducing a defined set of target genes. In tumors such as hepatocellular carcinoma (HCC) they exert tumorsuppressive functions. p63 is known as a tumor suppressor with an important role in the development of epithelia and in epithelial mesenchymal transition, a process that results in metastasis of primary cancer. However, the role of p63 in the development of HCC is yet unknown. microRNAs (miRNAs, miR) are small non coding RNA molecules that control gene expression by binding to target mRNAs and inhibit their translation. Expression profiles of miRNAs can be regulated by p53-family members. In previous studies we identified a set of p53-regulated miRNAs in HCC (miR34a, miR149, miR192 and miR194). It is known that miRNA 34a can be induced by p53 and – in turn – exerts its tumorsuppressive functions by stabilizing the robustness of p53 responses to genotoxic stress. p63 has been shown to influence miRNA levels in squamous cell carcinoma (SCC) and a number of other epithelial carcinomas, but little is known about the role of p63 in miRNA regulation in HCC.
Aims and Methods: The aim of this study was to evaluate whether miRNA profiles in HCC cells are regulated by p63. p53-deficient Hep3B cells were transfected with rAd-p63 or rAd-GFP. Expression of miR34a, mir145, miR149, miR192 and miR194 was determined by qPCR. To analyse effects of HCC-relevant therapeutics on p63-dependent microRNA regulation transfected Hep3B cells were treated with HCC-relevant local and systemic therapeutics (doxorubicin, sorafenib, bleomycin, tivantinib and regorafenib) for up to 72 hours in concentrations corresponding to the serum levels of patients undergoing therapy.
Results: Overexpression of p63 resulted in a moderate increase of miR34a (1.9-fold) and miR149 (1.96-fold) and a stronger induction of miR192 (3.85-fold) and miR194 (5.25 fold) after 24h. In untransfected cells, *in vitro* incubation with HCC-relevant therapeutics had no effect on expression levels of the analysed miRNAs. However, in combination with p63 overexpression miRNA was strongly induced by the used drugs. 72h *in vitro* incubation with doxorubicin resulted in an increase of p63-dependent expression of miR34a (2.64-fold), miR149 (2.63-fold), miR192 (2.11-fold) and miR194 (1.91-fold) compared to rAd-transfected controls. Bleomycin increased p63-dependent miR34a expression by 4.29-fold. Sorafenib had a moderate increasing effect on p63-dependent miR34a expression (2.44-fold). Treatment with Tivantinib increased p63-dependent expression of miR192 by 2.42 fold and miR194 by 3.6 fold. Regorafenib displayed a moderate effect on p63-dependent expression of miR34a (2.06 fold) and miR149 (1.64 fold) after 72h. Interestingly, in combination with p63 overexpression systemic drugs showed a stronger impact on miR192 and miR194, while local treatment predominantly increased levels of miR34a and miR149.
Conclusion: This study demonstrates for the first time a p63-dependent induction of tumorsuppressive miRNAs in HCC. Furthermore, these results indicate that p63 interacts with HCC-relevant therapeutics to control expression profiles of specific microRNAs in HCC. This finding provides further understanding of the complex regulatory network by which p53 family members exert their tumorsuppressive functions in HCC.
Disclosure: Nothing to disclose

P1318 P73 AND TIVANTINIB COOPERATE TO ORCHESTRATE EXPRESSION OF TUMORSUPPRESSIVE MICRORNAS IN HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocelluar carcinoma (HCC) is the third leading cause of cancer deaths worldwide. Like in many other tumor entities, the p53 family of tumor suppressor proteins plays an important role in this disease. p53 is the best analyzed member of this family and belongs to the most frequently mutated genes in human tumors. However, besides p53, the p53-family of transcription factors

comprises also p63 and p73 with their different splice variants. Although p63 and p73 share a variety of tasks with p53, such as regulating cellular stress responses, they can also exert independent functions. Depending on their splice variants – with transactivation domain (TA)/dominant negative (DN) – and the characteristics of the particular binding site p53 proteins activate or inhibit specific target genes directly *via* promotor-binding or indirectly, *e.g. via* regulation of microRNAs. microRNAs are small, non-coding RNA-molecules with a length of about 22 nucleotides, which play an important role in gene regulation. They can exert tumor suppressive or oncogenic functions and many of them are known to be induced or repressed by the p53-familiy in different cancer entities. For instance, microRNA 34a can be induced by p53 and – in turn – exerts its tumor-suppressive functions by stabilizing the robustness of p53 responses to genotoxic stress.

Aims and Methods: So far, little is known about p73-controlled microRNAs in HCC. The aim of this study was therefore to analyze regulation of microRNAs in HCC cell lines by TAp73 and DNp73 and effects of the HCC-relevant therapeutic drug tivantinib. p53-deficient Hep3B cells were transfected with adenoviral vectors rAd-TAp73, rAd-DNp73 or rAd-GFP to induce overexpression of p73 isoforms. Cells were stimulated with 5.4 μM of tivantinib or DMSO for up to 72 hours. Expression profiles of microRNA (miR) miR-34a, miR-145, miR-149, miR-192 and miR-194 were examined by qPCR.

Results: In non-transfected cells tivantinib treatment induced an increase of all mentioned tumor suppressive microRNAs by up to 3.6-fold compared to DMSO-treated controls after 48h. Overexpression of DNp73 did not substantially alter microRNA expression profiles in the presence or absence of tivantinib. In contrast, overexpression of TAp73 in the absence of tivantinib had strong inductive effects on the expression of miR-34a (5.0-fold) and miR-149 (8.1-fold) after 72 hours compared to GFP-transfected cells, whereas the expression levels of miR-192 and miR-194 remained unchanged. Notably, a combination of TAp73 overexpression and tivantinib treatment was most effective, resulting in further enhanced microRNA expression rates of miR-34a (9.4-fold) and miR-149 (14.9-fold) compared to rAd-GFP-transfected and DMSO-treated cells after 72h.

Conclusion: TAp73 is an important regulator of tumor suppressive microRNA expression in Hep3B cells. Combined effects of TAp73 overexpression and tivantinib treatment result in a strong induction of miR-34a and miR-149. In contrast, DNp73 did not influence these targets, highlighting the differencial target gene regulation by TA and DN-isoforms.

HCC systemic therapies are rare and characteristics and pathways of most of the used drugs are not well understood. In this study we now provide evidence for regulation of tumorsuppressive microRNAs by a combination of tivantinib and TAp73 overexpression, suggesting novel therapeutic and prognostic options for HCC therapy.

Disclosure: Nothing to disclose

P1319 ASSOCIATION BETWEEN XRCC1 GENE POLYMORPHISM AND HEPATOCELLULAR CARCINOMA IN EGYPTIAN PATIENTS

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Introduction: Several major risk factors for hepatocellular carcinoma (HCC) have been identified, including chronic infection of hepatitis B virus (HBV) and hepatitis C virus (HCV). Nevertheless, only a fraction of infected patients develops HCC during their lifetime suggesting that genetic factors might modulate HCC development. X-ray repair cross complementing group 1 (XRCC1) participates in the base excision repair pathway of DNA.

Aims and Methods: We aimed to investigate the association of X-ray repair cross complementing group 1 (XRCC1) gene polymorphism with HCC in Egyptian population.

This study was assessed on 40 patients with HCC and 20 cirrhotic patients on top of HCV and 40 age and gender-matched healthy subjects as control group. After collection of relevant clinical data and basic laboratory tests, c.1517G[C SNPof XRCC1 gene polymorphism was performed by (PCR-RFLP) technique.

Results: Our study revealed statistical difference in XRCC1 (CC, GC) genotypes with increased (C) allele frequency in patients with HCC in comparison with cirrhotic patients as well as control group. In addition, patients with CC, GC genotypes showed significant higher number and larger size of tumor foci and significantly higher Child Pugh grades. The multivariate analysis showed that the presence of c.1517G[C SNPof XRCC1 gene is an independent risk factor for the development of HCC in chronic HCV patients with 3.742 folds increased risk of HCC development.

Conclusion: XRCC1gene polymorphism could be associated with increased risk of HCC development in chronic HCV-infected Egyptian patients.

Disclosure: Nothing to disclose

P1320 0-HYDROXY PYRENE IN URINE AS A BIOLOGICAL MONITORING OF EXPOSURE TO POLYCYCLIC AROMATIC HYDROCARBONS MIGHT EXPLAIN WHY HEPATOCELLULAR CARCINOMA DEVELOPED AMONG SOME CASES OF CHRONIC ACTIVE VIRAL HEPATITIS

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Introduction: Polycyclic aromatic hydrocarbons (PAHs) are among the most carcinogenic, mutagenic and toxic contaminates. Their exposure and metabolism to DNA-reactive metabolites in the body are considered to contribute to the etiology of many types of the human cancers.

We aimed to find out if exposure to polycyclic aromatic hydrocarbons is a risk factor for development of hepatocellular carcinoma among the exposed cases of chronic active hepatitis B and/C.

Aims and Methods: A case-control study was conducted between the periods from the first of March 2015 to end of August 2017. The study was conducted in the outpatient clinic of the Department of Hepatology and Gastroentrology at Theodor Bilharz Research Institute (TBRI), Cairo, Egypt. The minimum sample size required for the present study was calculated using Epi info program, considering the following data: two sided Confidence level = 95%, Power of test = 80%, Ratio of control: cases = 1:1, Percent of control exposed = 21%, Percent of cases exposed = 42% and Odds ratio = 2.8. Estimated number of cases was (77 cases with HCC on top of chronic active hepatitis B and/C) and (77 controls without HCC but suffering chronic active hepatitis B and/C). All subjects of both groups were subjected to the selected interview medical sheet and to biological monitoring of urinary for 1-hydroxy pyrene as a biomarker for PAHs exposure.

Results: 73% of cases of HCC have been found with increased level of 1-hydroxy pyrene in urine with statistical significance difference when compared to the controls, there was significant positive association between exposure to PAHs and development of HCC among cases group (OR = 4.9). There was significant association among the cases group between smoking and abnormal high level of 1-hydroxy pyrene in urine (OR = 1.7). There was significant positive association between exposure to PAHs and development of HCC among males (OR = 1.6). There was a highly positive correlation between 1-hydroxy pyrene and Alfa Feto Protein (AFP) among positive cases of 1-hydroxy pyrene in cases group.

Conclusion: PAHs might be a risk factor for developing HCC among cases of chronic active hepatitis B and/C. 1-hydroxy pyrene in urine could be an early indicator of HCC among cases of chronic active hepatitis B and/C.

Disclosure: Nothing to disclose

P1321 DIAGNOSTIC PERFORMANCE OF ALPHA- FETOPROTEIN, ALPHA-FETOPROTEIN-L3, PROTEIN INDUCED BY VITAMIN K ABSENCE, GLYPICAN 3 AND ITS COMBINATIONS FOR HEPATOCELLULAR CARCINOMA IN PATIENTS ADMITTED IN A LARGE TRANSPLANT CENTER IN ROMANIA

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Introduction: Alpha-fetoprotein (AFP) is the most widely used serum biomarker for hepatocellular carcinoma (HCC), despite its limitations. Alpha-fetoprotein-L3 (AFP-L3), protein induced by vitamin K absence (PIVKA-II) and Glypican-3 (GPC-3) have been proposed as complementary biomarkers.

Aims and Methods: This study aimed to investigate the diagnostic performance of AFP, AFP-L3 PIVKA-II, and GPC-3 as single or in combination to seek the best biomarker or panel, and to investigate the clinical factors affecting their performance for hepatocellular carcinoma (HCC) diagnosis in patients admitted to a transplant center from Romania.

From March 2016 to October 2017 we prospectively included a number of 153 patients, 101 were with HCC and 52 control patients with liver cirrhosis. Serum levels of AFP, AFP-L3, PIVKA-II and GPC-3 were measured by ELISA and clinicopathological features were determined for all subjects. To compare the diagnostic value in distinguishing HCC from nonmalignant chronic liver disease, receiver operating characteristic (ROC) curves were performed for each biomarker and for every combination of two to four markers.

Results: Of the four biomarkers, AFP-L3 showed the highest area under the curve (0.85). The sensitivity and specificity for each single biomarker was 55.6% and 99% (AFP >18.9ng/mL), 86.1% and 58.3% (PIVKA-II >63 mAU/mL), 86.1% and 72.7% (AFP-L3 >13.5 ng/mL), and 77.8% and 75.0% (GPC-3 >466ng/mL), respectively. The area under the curve was 0.75 for PIVKA-II, 0.79 for AFP and 0.77 for GPC-3 for HCC diagnosis.

Among the combinations of two biomarkers, AFP >18.9ng/mL and AFP-L3 >13.5ng/mL showed the best diagnostic performance with an area under the curve of 0.93. Triple or quadruple combination did not improve the diagnostic performance further. The patient's age, etiology and tumor invasiveness of HCC affected the performance of each marker.

There was a moderate significant correlation between initial PIVKA-II value and maximum diameter of the tumoral nodule ($r = 0.50$, $p = 0.001$), but no correlation between AFP value and tumoral diameter.
Conclusion: AFP-L3 was the most useful single biomarker for HCC diagnosis, and the combined measurement of AFP and AFP-L3 could maximize the diagnostic yield. PIVKA-II has a better correlation with tumor size compared AFP. Clinical decision should be based on the consideration of different factors affecting the diagnostic performance of each biomarker. Efforts to seek novel HCC biomarkers should be continued.
Disclosure: Nothing to disclose

P1322 TALIN-1, OTHER THAN A POTENTIAL MARKER FOR HEPATOCELLULAR CARCINOMA DIAGNOSIS

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Introduction: Hepatocellular carcinoma (HCC) is a major cause of cancer mortality worldwide. The outcome of HCC depends mainly on its early detection. Alpha-fetoprotein (AFP) is the currently available marker for HCC diagnosis. Talin-1 was previously proposed as a potential novel biomarker for HCC diagnosis but with a limited and inconsistent data.
Aims and Methods: We aimed to study the possible role of Talin-1 in diagnosis and prognostic stratification of patients with hepatocellular carcinoma.
In this prospective study, we recruited 96 patients from Ain Shams University hospitals' clinics and inpatient department, then classified them into three groups; 1) Cirrhosis group: 40 patients with liver cirrhosis without HCC, 2) HCC group: 40 patients with liver cirrhosis and HCC as diagnosed by triphasic CT, 3) Control group: 16 healthy volunteers, with matched age and gender. Talin-1 was detected using enzyme linked immunosorbent assay (ELISA).
Results: The highest level of Talin-1 was observed among HCC group followed by cirrhosis then control groups (25 vs. 12 vs. 1.9 ng/ml; $p \leq 0.001$) respectively. *In cirrhosis and HCC groups*; we found a significant positive correlation between Talin-1 and ALT, AST, ALP, Bilirubin, INR, urea and AFP ($p \leq 0.001$), and a significant negative correlation between Talin-1 and albumin, creatinine, hemoglobin, WBCs and platelets ($p \leq 0.001$), and no significant differences were found regarding sex, anti HCV and HBsAg ($p > 0.05$). *In HCC group*; significant correlation was found between Talin-1 and each of multifocal HCC (29.5 vs. 23 ng/ml; $p = 0.013$), portal vein invasion (27 vs. 21 ng/ml; $p = 0.022$), and presence of ascites (27 vs. 20 ng/ml; $p = 0.001$), no significant correlation was detected with tumor size ($p = 0.605$). ROC curve analysis was used to test the performance of Talin-1 and AFP for cirrhosis diagnosis; Talin-1 at 6.2 ng/ml cutoff level had 90% sensitivity, 93.75% specificity and AUC = 0.980, while AFP at 2.5 ng/ml cutoff level had 92.50% sensitivity, 87.50% specificity and AUC = 0.969. By combining both markers, the sensitivity was 95% with 100% specificity. As regard discrimination between HCC and cirrhosis groups; Talin-1 at 14 ng/ml cutoff level had 100% sensitivity, 65% specificity and AUC = 0.858, while AFP at 15 ng/ml cutoff level had 100% sensitivity, 100% specificity and AUC = 1.000. After combining both markers, sensitivity and specificity were 100%.
Conclusion: Talin-1 is a potential marker for diagnosis and prognostic assessment of both cirrhosis and HCC. Measuring both serum Talin 1 and AFP levels enhance the diagnostic sensitivity in early detection of HCC. Further studies are needed to investigate the ultimate diagnostic and prognostic utility of serum Talin-1.
Disclosure: Nothing to disclose

P1323 RADIOEMBOLIZATION WITH YTTRIUM-90 MICROSPHERES FOR INTERMEDIATE-ADVANCED HEPATOCELLULAR CARCINOMA: A SINGLE CENTRE REAL-LIFE EXPERIENCE

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Introduction: Hepatocellular carcinoma (HCC) is a common cause of worldwide mortality. Sorafenib represents the elective treatment for advanced stage HCC according to the Barcelona Clinic of Liver Cancer classification. However, its tolerability is suboptimal due to adverse effects and liver function deterioration. In the last years, transarterial radioembolization (TARE) with Yttrium-90 microspheres has been proposed for both intermediate HCC poorly responsive to transarterial chemoembolization (TACE) and locally-advanced HCC with segmental or lobar portal vein thrombosis (PVT).
Aims and Methods: The study aim was to evaluate efficacy and safety of TARE in HCC patients. A secondary aim was to confirm the treatment utility in special situation, i.e. tumors complicated by PVT and bridge to liver transplant. From November 2015 to April 2018 20 consecutive patients (M = 19, F = 1, median age 71 [24–85] years) with HCC were selected for TARE by the multidisciplinary HCC board. TARE was performed using 90Y glass microspheres. Tumor response was assessed using computed tomography or magnetic resonance at 3 months evaluated according to modified Response Evaluation Criteria in Solid Tumor.
Results: Among 20 patients treated with TARE, 1 (5%) had early, 10 (50%) intermediate and 9 (45%) advanced stage HCC. HCCs were firstly diagnosed 18 (range 2–96) months before TARE. All patients except three underwent previous treatments for HCC (median number of treatments 2, range 0–6). Other baseline features were: aetiology: hepatitis virus in 7 (35%), alcohol in 7 (35%), multiple in 6 (30%); Child-Pugh class A in 17 (85%), B7 in 3 (15%); median MELD score 7.5 (IQR 6.5–8); pathologic type: unifocal in 7 (35%), multifocal in 13 (65%); PVT in 9 (45%); comorbidities in 17 (85%); performance status: 0 in 7 (35%), 1 in 13 (65%). Only one patient presented side effects: ascites easily controlled with medications. Imaging evaluation at 3 months was performed in 19 patients. Complete response occurred in 13 (65%), partial response in 3 (15%), while progression was seen only in 3 cases (15%). During a median clinical follow-up of 13 months 2 patients repeated TARE due to partial response, 4 underwent TACE and 1 radiofrequency thermoablation due to recurrence of HCC and 2 patients underwent liver transplantation after successful down-staging. Death occurred in 10 patients: 7 died of hepatic failure due to HCC progression, the remaining 3 died of hepatorenal syndrome, heart failure and gastrointestinal bleeding. Median progression free survival and overall survival were respectively 12 and 16 months. HCC patients with or without PVT had no difference in overall survival (median overall survival 14 months in patients with PVT and 25 months in patients without PVT, log-rank test $p = 0.33$).
Conclusion: TARE was a valid and safe treatment option in patients with intermediate-advanced HCC stages even in the presence of PVT. Good median survival and no severe adverse effects were seen in this group. TARE was a suitable procedure for elderly comorbid patients and also led to down-staging, potentially allowing liver transplantation.
Disclosure: Nothing to disclose

P1324 RISK OF AGGRESSIVE/ADVANCED HEPATOCELLULAR CARCINOMA DEVELOPMENT AFTER DIRECT ACTING ANTIVIRAL THERAPY IN PATIENTS WITH HCV-RELATED CIRRHOSIS

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Introduction: Hepatocellular carcinoma (HCC) represents a serious complication of HCV-related cirrhosis. Introduction of direct acting antiviral (DAA) agents achieved high sustained viral response (SVR) rates of 90–95%, however, various reports have showed different results regarding risk of HCC development after DAA treatment, moreover data on the risk of developing aggressive or advanced HCC in DAA-treated patients is still unknown and needs to be assessed.
Aims and Methods: Our aim was to compare the patterns of HCC developed after DAA treatment to HCC patterns in patients who did not receive DAA. Methods: we conducted a retrospective study on 137 patients presented to the HCC clinic at our institute over the period of 2 years. 88 patients were included in the study and 49 were excluded due to insufficient DAA treatment details. The patients were divided into 2 groups according to receiving DAA including "DAA-treated" group with patients who received DAA and "DAA-non-treated" group with those who didn't receive DAA. Dynamic contrast enhanced CT/MRI were used to classify HCCs according to their size, number and presence of tumor vascular invasion (TIV) into: I) Early/non-aggressive (NA-HCC) defined as either single lesion < 5 cm or ≤ 3 lesions all of which ≤ 3 cm in diameter and absence of tumor vascular invasion, and II) Advanced/aggressive patterns (A-HCC) defined as either single lesion > 5 cm, ≤ 3 lesions with any > 3 cm, or > 3 coexisting lesions (multicentric), or infiltrative HCC pattern ± presence of TIV.
Results: Our study included 69 males and 19 females, with a mean (±SD) age of 60.2(±8.48). The onset of HCC presentation in DAA-treated group had a median (IQR) value of 7(12.6) months after end of treatment. The DAA-treated group showed significantly higher frequencies of A-HCC patterns on presentation as compared to the DAA-non-treated group ($\chi^2 = 8.17$, $p = 0.004$), with a higher risk of presence of A-HCC patterns after DAA therapy (RR = 0.67, CI 95% = 0.15–1.42). The treated group also showed higher frequencies of presence of TIV as compared to the DAA-non-treated group ($\chi^2 = 7.016$, $p = 0.008$) with a significantly higher risk of presence of TIV after DAA therapy (RR = 3.18, CI 95% = 0.26–12.8). Among the DAA-treated group 27 achieved SVR and 16 were DAA relapsers, yet no significant correlation was found between DAA relapse and presence of A-HCC patterns ($p = 0.948$).

	Study group: n = 88 (100%)		p value
	DAA-non-treated n = 45 (51.1%)	DAA-treated n = 43 (48.9%)	
Gender			
Male	34 (75.6%)	35 (81.4%)	

(continued)

Continued

	Study group: n = 88 (100%)		p value
Female	11 (24.4%)	8 (18.6%)	
Early/low-aggression	25 (28.4%)	11 (12.5%)	**0.004 ($\chi2 = 8.172$)**
Advanced/Aggressive	20 (22.7%)	32 (36.4%)	
TIV	3 (3.4%)	12 (13.6%)	**0.008 ($\chi2 = 7.016$)**
Relapse after treatment		16	
SVR		27	
De novo lesion		41	
Recurrent lesion		2	

[Table (1): Descriptive data of the study group]

Conclusion: In our study we showed a higher relative risk of presence of advanced/aggressive patterns and/or TIV at time of HCC presentation following DAA treatment as compared to DAA-non-treated patients.

Disclosure: Nothing to disclose

P1326 PREDICTIVE FACTORS FOR COMPLETE RESPONSE AND RECURRENCE AFTER TRANSARTERIAL CHEMOEMBOLIZATION IN HEPATOCELLULAR CARCINOMA PATIENTS: A FIVE-YEAR EXPERIENCE

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Introduction: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide, with most of the patients beeing diagnosed at intermediate to advanced tumour stages, at which therapy options are limited. TACE is the most used palliative treatment modality in this setting.

Aims and Methods: To investigate the predictive factors for complete response (CR) and recurrence after CR in patients with hepatocellular carcinoma (HCC) treated with transarterial chemoembolization (TACE).

From January 2013 to December 2017 we enrolled 168 newly diagnosed patients with HCC who were treated with TACE as a first therapy. We analyzed the predictive factors for CR and the risk factors for local and distant recurrence after CR using Cox proportional hazard model.

Results: The mean age of the patients was 62.2 ± 7.9 years. There were 115 male patients (68.4%) and 53 females (31.5%). Eighty-eight patients had an α-feto-protein (AFP) level >20 ng/mL. The median maximal diameter of the tumors was 3.5 cm. The median follow up period was 27.6 months. Sixty-three patients (37.5%) achieved CR after TACE, and recurrence after CR was detected in 37 patients (58.7%). In univariate analysis elevated serum AFP (>20 ng/mL) level (hazard ratio [HR], 1.985; 95% confidence interval [CI], 1.0477 to 3.7570; $p = 0.0355$), tumor size (>5 cm) (HR, 3.558; 95% CI, 1.3478 to 9.3809; $p = 0.0104$), multinodularity (HR, 5.0682; 95% CI, 2.2703 to 11.3144; $p < 0.001$) were correlated with CR after TACE. In multivariate analyses, tumor size (≤ 5 cm) and single nodularity were predictive factors for CR, with hazard ratios (HRs) of 2.56 ($p = 0.0330$) and 2.87 ($p = 0.002$), respectively. From the total 63 patients with CR, 55 patients had tumor size ≤ 5 cm, and only 8 patients (12.69%) had a tumor size >5 cm. Fifty-one patients (80.9%) had a single nodule and 12 patients (19%) showed multiple nodules. In patients with recurrence after CR, in univariate analysis, multinodularity (HR, 8.226; 95% CI, 0.9353 to 72.3505; $p = 0.475$) and elevated serum AFP (>20 ng/ mL) level (HR, 2.995; 95% CI, 0.4557 to 14.9057; $p = 0.0541$) were associated with HCC recurrence. In multivariate analysis only multinodularity (HR, 3.835; 95% CI, 1.452 to 12.961; $p = 0.0325$) was associated with HCC recurrence after TACE-induced CR. Of the 63 patients with CR, 11 patients (17.4%) had multinodularity and 22 patients (34.9%) had elevated serum AFP (>20 ng/mL) level. The recurrence rate of multinodularity (11/12 patients) was higher than that of single nodularity (26/51 patients) (91.6% vs 50.9%; $p = 0.02$). The recurrence rate of patients with elevated serum AFP (>20 ng/mL) level (18/23 patients) was higher than that of patients with normal serum AFP (≤ 20 ng/mL) level (19/40 patients) (78.2% vs 47.5%; $p = 0.03$).

Conclusion: In patients treated with TACE as a initial therapy, tumor size (≤ 5 cm) and single nodularity were predictive factors for CR. Multinodularity was a predictive factors for recurrence after CR. After achieving CR the median time period to recurrence was 12 months.

Disclosure: Nothing to disclose

P1327 MONOFOCAL HEPATOCELLULAR CARCINOMA (HCC): SHOULD THE 5 CM CUT-OFF BE CONSIDERED AS FUNDAMENTAL? AN ANALYSIS OF THE ITA.LI.CA DATABASE

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Introduction: The Barcelona Clinic Liver Cancer (BCLC) algorithm, adopted by the EASL (European Association for the Study of the Liver) guidelines, predicts prognosis and suggests treatmernt options in HCC.

Aims and Methods: This study aimed at evaluating the 5 cm cut-off, as adopted in the Milan Criteria, to correctly stage and treat monofocal HCC. Firstly, 2615 patients with a diagnosis of Monofocal HCC were selected from the 6476 patients of the ITA.LI.CA database (2001–2014); following that,1623 Monofocal HCC, excluding the "Very early" subgroup, stratified by diameter (1345 small HCC, $>2/\leq 5$cm, and 278 large HCC, >5cm), were analysed. Among them, 1087 were "Early" Monofocal HCC. The Monofocal (overall) and the "early" HCCs were compared to 1048 BCLC B stage HCC and sub-grouped according to the adherence to the guidelines for resection. Statistics included chi-square, Kaplan-Meier (Log-rank) and Cox multivariate analysis.

Results: Overall median survival was 38 months (Confidence Interval – C.I. – 36–41), with 49 months (C.I.: 45–53) in small "EARLY" HCC and 31 in large "EARLY" HCC (C.I.: 25–44) ($p < 0.0001$). At multivariate analysis size and treatment were the most important indipendent predictors of survival for both Early and Monofocal HCC overall, while CHILD status, performance status and cancer-related events ($>$AFP, PVT, ascites) were the best independent prognostic factors in Monofocal, such as in the original BCLC classification. Resection was associated with the longest survival, regardless of diameter, both in the Monofocal HCC overall and in the subgroup of "Early" single node HCC, with the obvious exception of liver transplant. Among resected patients, the median survival of BCLC B HCC was 44 months (C.I.: 30–55), significantly shorter from the small EARLY HCC survival ($p < 0.0001$), but not from the large EARLY HCC survival ($p = 0.9389$, HR = 1.016 with C.I.: 0.680–1.518). Sameresults were obtained considering Monofocal HCC overall.

Conclusion: The 5 cm cut-off – according to the Milan criteria – stratifies Monofocal ("Early" or not) HCC in two categories different in features, survival, predictors and therapeutic choices. Single HCC >5 cm has a median survival comparable to BCLC B HCC. In Monofocal and "Early" monofocal HCC, surgery correlates with the longest survival; although the best survival is reached in small HCC, resection should be recommended also in the large tumours, due to the best survival achievable, even though these are characterized by much lower survival. Tumor burden has a heavier impact on survival than "adherence to the guidelines".

Disclosure: Nothing to disclose

P1328 ANALYSIS OF THE BILIARY BACTERIAL COMMUNITIES IN CHOLEDOCHOLITHIASIS PATIENTS WITHOUT RECENT ANTIBIOTICS TREATMENT BASED ON 16S RRNA AMPLICON SEQUENCING

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Introduction: Biliary bacteria play an important role in the pathogenesis of choledocholithiasis, but at present there are very few studies about the biliary microbiota. Our previous studies observed great bacterial community heterogeneity among patients and provided evidence for the potential source of biliary bacteria. However, the sample numbers of both studies were small due to the difficulty of sample collection. Besides, the medication history (i.e. the recent antibiotics treatment) might also lead to bias in the composition of bacterial communities. Thus, the biliary microbiota of a larger scale of choledocholithiasis patients, especially those with no recent antibiotics treatment, still needs further investigations.

Aims and Methods: This study aimed at the biliary microbiota of a larger scale of patients diagnosed with common bile duct stones. Bile samples from the common bile duct of primary choledocholithiasis patients were collected by ERCP. These patients had no other infections and did not receive antibiotics for at least one month before ERCP. They were divided into two groups: group NN, the first treatment ones, no recent antibiotics use with no endoscopic sphincterotomy (EST) history; group NE, the recurrent ones, no recent antibiotics use with a EST history. Eventually, group NN contained 33 patients and group NE contained 19 ones. 16S amplicon sequencing was employed to analyze the biliary microbiota. Predictive functional analysis was also performed.

Results: 1) At the phylum level, *Proteobacteria*, *Firmicutes*, *Bacteroidetes*, *Fusobacteria* and *Actinobacteria* were identified in both groups with a total relative abundance ≥ 0.87. At the genus level, the abundance of *Escherichia/Shigella* was the highest in both groups (NN = 0.27 and NE = 0.17), The average relative abundances of *Pseudomonas*, *Streptococcus*, *Enterococcus*, *Prevotella*, *Neisseria*, *Klebsiella*, *Fusobacterium*, *Granulicatella*, *Veillonella*, *Aeromonas*, *Bacteroides* and *Pyramidobacter* were greater than 0.01, which was consistent with our previous studies.

2) Analysis of similarity using Bray-curtis distance showed that the microbiota dissimilarity of intra-group was significantly lower than that of inter-group. The similarity of the bacterial communities between samples within group NN was

significantly higher than that within group NE ($P = 0.003$). Principal coordinate analysis (PCoA) results revealed that there were differences in the microbial composition between the two groups. Compared with group NN, the relative abundances of *Pseudomonas*, *Neisseria*, *Ochrobactrum*, *Actinomyces* and *Rothia* in NE group were decreased, while the abundances of *Pyramidobacter*, *Akkermansia* and *Porphyromonas* were increased (all $P < 0.05$). These bacteria were also confirmed by our previous studies.
3) The relative abundances of KEGG pathways in the biliary microbiota were predicted by PICRUSt. Compared with group NN, the abundances of pathways such as Peptidases, Energy metabolism and Lipopolysaccharide biosynthesis were increased in group NE, while that of the Glutathione metabolism pathway was decreased (all $P < 0.05$).
Conclusion: 1) Both groups had common kinds of bacterial taxonomic units, which indicates the shared pathogenesis of them. 2) EST may affect the composition of the biliary microbiota. 3) *Pyramidobacter*, *Akkermansia* and *Porphyromonas* may play key roles in the recurrence of choledocholithiasis. 4) The Peptidases, Energy metabolism and Lipopolysaccharide biosynthesis pathways might be involved in choledocholithiasis recurrence.
Disclosure: Nothing to disclose

P1329 FUNCTIONAL CHANGES OF PANETH CELL IN THE INTESTINAL EPITHELIUM OF MICE WITH OBSTRUCTIVE JAUNDICE AND AFTER INTERNAL AND EXTERNAL BILIARY DRAINAGE

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Introduction: Obstructive jaundice (OJ) is a condition that might lead to acute cholangitis and sepsis and multiorgan dysfunction, especially after surgical procedures. Intestinal mucosal barrier dysfunction and intestinal immune function decline might result in endotoxemia and intestinal bacterial translocation, which are important contributors to disease progression or death in patients. As one of the main effector cells of the intestinal mucosal barrier, paneth cell have several natural antibiotic peptides in their endocrine granules. Cell degranulation can be induced under certain conditions. The diversity of stimulants and cell endocrine particles suggests that paneth cell may play important roles in the construction of intestinal mucosal epithelial cells and the defense mechanism of host intestinal tract.
Aims and Methods: We aimed to investigate the functional changes of paneth cell in the intestinal epithelium of mice with OJ and after internal and external biliary drainage.
The experiment was divided into two stages. First stage: a total of 100 male C57BL/6J mice were randomly assigned to two groups: (I) sham operation (SH); (II) obstructive jaundice (OJ). The mice were respectively sacrificed before operation and on the 1st, 3rd, 5th and 7th days after operation to collect blood and terminal ileum specimens. Second stage: a total of 40 male C57BL/6J mice were randomly assigned to four groups: (I) SH; (II) OJ; (III) OJ and external biliary drainage (ED); and (IV) OJ and internal biliary drainage (ID). The animals underwent surgical ligation of the bile duct on day 0. They were reoperated on day 5 for biliary drainage procedure. Blood and terminal ileum specimens were collected on day 10. Various indicators were detected by Real-time PCR, immunohistochemistry, Western blot and other methods.
Results: The number of paneth cell and expression of lysozyme and cryptdin 4 were increased first and then decreased over time in OJ group, and the difference was statistically significant ($p < 0.05$). however, no obvious difference was found in different time points of the SH group ($P > 0.05$). The grade of mucosal injury, the level of plasma DAO and the rate of bacterial translocation increased gradually in the OJ group with the extension of time ($p < 0.05$). In addition, there were negative correlations between the level of plasma DAO and expression of lysozyme ($r = -0.729$, $p < 0.05$) and cryptdin-4 ($r = -0.718$, $p < 0.05$) in OJ group. After the secondary operation in mice to relieve OJ, the number of paneth cell and expression of lysozyme and cryptdin 4 were increased in ID group and ED group than that in OJ group, and more significant in ID group than that in ED group, with statistical differences ($p < 0.05$). In addition, the rate of bacterial translocation and plasma DAO were lower in ID group and ED group than those in OJ group, which were more obvious in ID group than that in ED group, and the differences were statistically significant ($p < 0.05$).
Conclusion: OJ could cause intestinal paneth cell dysfunction in mice, which was mainly manifested in the decrease of paneth cell number, as well as the decrease of cryptdin-4 and lysozyme expression levels. The change of paneth cell in OJ was strongly correlated with intestinal mucosal barrier dysfunction and bacterial translocation. ID was more significant than ED in restoring the function of paneth cell, thereby exerting a role in the functional recovery of the intestinal mucosal barrier. It might be one of the mechanisms that ID was superior to ED.
Disclosure: Nothing to disclose

P1330 EXPRESSION OF TLR4 IN DISTAL ILEUM OF MICE WITH OBSTRUCTIVE JAUNDICE AND ITS ROLE IN INTESTINAL MUCOSA BARRIER DAMAGE

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Introduction: OJ is a condition that might lead to acute cholangitis and sepsis and multiorgan dysfunction, especially after surgical procedures. Intestinal mucosal barrier dysfunction and intestinal immune function decline might result in endotoxemia and intestinal bacterial translocation, which are important contributors to disease progression or death in patients. Toll-like receptors (TLRs) is a class of transmembrane receptors widely existed in mammalian cells. TLRs can recognize a number of conservative pathogen associated molecular patterns of pathogenic microorganism, initiate signal transduction, eventually stimulate the activation of NF-κB and induce inflammatory mediators expression. TLRs may thus play a key role in innate immune system.
Aims and Methods: We aimed to investigate the role of TLR4 in intestinal mucosa barrier damage and bacterial translocation in mice with obstructive jaundice (OJ).
A total of 100 male C57BL/6J mice were randomly assigned to two groups: (I) sham operation (SH); (II) bile duct ligation (BDL). Mice were sacrificed at different time points (Before operation, as well as 1 d, 3 d, 5 d, and 7 d after operation). The blood, terminal ileum, liver, spleen and mesenteric lymph nodes ((MLNs) were collected under the aseptic condition simultaneously for further usage. The aminotransferase (ALT), total bilirubin (TB), alkaline phosphatase (ALP) and diamine oxidase (DAO) in blood were detected. The morphological changes of distal ileum tissue were observed using haematoxylin-eosin (HE) staining. The expression of Nuclear factor κB (NF-κB), TLR4 in different stage of OJ were observed by Western blot and Real-time PCR. The liver, spleen and MLNs were harvested for the detection of bacterial translocation.
Results: In the SH group, TLR4 protein and mRNA were rarely expressed in the intestinal mucosa of the mice and there were no significant differences at different time points ($p > 0.05$). By contrast, TLR4 protein (0.12 ± 0.06, 0.16 ± 0.08, 0.27 ± 0.10, 0.35 ± 0.12 and 0.41 ± 0.13 respectively) and mRNA (0.49 ± 0.19, 0.62 ± 0.23, 0.98 ± 0.32, 1.42 ± 0.41 and 1.72 ± 0.49 respectively) were increased gradually with the extension of OJ time in the BDL group ($p < 0.05$). The grade of mucosal injury, the level of plasma DAO and the expression of NF-κB increased gradually in the BDL group with the extension of OJ time ($p < 0.05$). In addition, the rate of bacterial translocation was also increasing in the liver, spleen and MLNs in the BDL group. There were positive correlations between the grade of mucosal injury and expression of TLR4 ($r = 0.781$, $p < 0.05$) and NF-κB ($r = 0.828$, $p < 0.05$) in BDL group. In addition, there were positive correlations between the level of plasma DAO and expression of TLR4 ($r = 0.775$, $p < 0.05$) and NF-κB ($r = 0.783$, $p < 0.05$) in BDL group. NF-κB expression was positively correlated with TLR4 expression ($r = 0.744$, $p < 0.05$).
Conclusion: The expression of TLR4 was significantly up-regulated in the distal ileum of mice with obstructive jaundice. Overexpression and activation of TLR4 were involved in the occurrence and development of intestinal mucosa barrier damage and bacterial translocation in mice with OJ.
Disclosure: Nothing to disclose

P1331 PREDICTING OUTCOMES OF PATIENTS WITH PRIMARY BILIARY CHOLANGITIS RECEIVING URSODESOXYCHOLIC ACID THERAPY USING THE GLOBE SCORE

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Introduction: Ursodeoxycholic acid (UDCA) is currently the only drug approved specifically for the treatment of primary biliary cholangitis (PBC), as it can delay histological progression and improve long-term outcome. Patients with inadequate response to UDCA are at increased risk of disease progression, need for liver transplantation, and death. Recently a risk score – the GLOBE score – have been proposed for prognosis of PBC. The aim of this study was to determinate the role of GLOBE score in predicting of response to UDCA in PBC.
Aims and Methods: We conducted a retrospective study of all patients with PBC who were treated with UDCA at the daily dose of 13 to 15 mg/kg between January 2008 and December 2017. The response to UDCA was defined according to Paris criteria after 1 year of therapy. The Globe score was calculated for all patients included in this study.
Results: A total of 71 patients with PBC were included. Sixty-six patients were females and only five were males. The average age was 55.23 years [23–81 years]. Accordingly to Scheur's classification, 28 patients with biopsy-proven were categorized as: stage 1, stage 2, stage3 and stage 4 respectively in 46.42%, 25%, 10.7% and 17.8% of cases. Of 71 patients, 34 were responded to UDCA (48%) and no-response to these therapy was observed in 37 cases (52%) after 1 year of UDCA therapy. The mean value of Globe score was 2.05 [-0.8; 4.68]. This value was found to be significantly elevated in PBC patients with poor response to UDCA comparatively with PBC patients responders to these therapy (2.27 vs 1.64; $p = 0.037$).
Conclusion: Our study showed that Globs score could be a new cheap and easily obtained marker in predicting of response to UDCA in PBC. Our findings need to be confirmed with larger scale prospective studies.
Disclosure: Nothing to disclose

P1332 EVALUATION OF THE POTENTIAL USE OF A SET OF MIRNAS IN INDETERMINATE BILIARY STRICTURES FOR EARLY DIAGNOSIS OF CHOLANGIOCARCINOMA

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Introduction: Early diagnosis of malignancy in biliary strictures can be challenging given the low rate of diagnostic accuracy of current modalities. Biliary strictures in Endoscopic Retrograde CholangioPancreatography (ERCP) with nondiagnostic brushings and/or biopsies, negative lab (CA19-9) and imaging tests are considered indeterminate. MicroRNAs (miRNA or miRs) are small non-coding RNA molecules that have been associated with pathophysiological processes in different organs and cell types, and are postulated as potential targets for diagnosis and therapy.
Aims and Methods: The aim of the study was to evaluate the potential diagnostic accuracy of a set of 3 miRNAs related to cholangiocarcinoma in indeterminate biliary strictures. We performed a prospective case-control observational study of 18 patients, diagnosed with cholangiocarcinoma, indeterminate stenosis or normal bile duct, who underwent ERCP and cholangioscopy. Biopsies under direct visualization and/or brush cytology were obtained. Specimens were evaluated histologically and miR-21, miR-483 and miR-675 expression was quantified using Reverse Transcription Polymerase Chain Reaction (RT-PCR, relative quantification).
Results: 18 patients underwent cholangioscopy (male 50%, mean age: 67.8). 8 patients had cholangiocarcinoma (mean age: 77.1), 6 had indeterminate biliary strictures (mean age: 63.3) and 4 had normal bile duct (mean age: 56). Normal bile duct cohort results were used as control. MiR-21 expression was upregulated in both cholangiocarcinoma [4.20 times ± 1.87, (1.43–7.06)] and indeterminate cohorts [1.45 times ± 0.28, (1.12–1.92)]. MiR-483 expression was upregulated in cholangiocarcinoma [5.59 times ± 2.09, (2.7–8.19)] and downregulated in indeterminate cohort [33.54 times ± 32.4, (2.32–90.9)]. Similarly, miR-675 expression was upregulated in cholangiocarcinoma [4.4 times ± 2.45, (2.19–9.21)] and downregulated in indeterminate cohort [3.16 times ± 0.99, (2.08–4.54)]. Surprisingly, all cases in cholangiocarcinoma and indeterminate cohorts upregulated or downregulated as above mentioned miR-483 and miR-675 expression, respectively.
Conclusion: Our limited data suggest that there may be a role for miRNAs in differential diagnosis for malignancy in indeterminate biliary strictures. MiRNAs represent a new research area. More trials are required for confirmation of the above results and establishment of cut-off values.
Disclosure: Nothing to disclose

P1333 A STUDY OF CORRELATION BETWEEN NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PROGNOSTIC FACTOR IN CHOLANGIOCARCINOMA

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Introduction: Neutrophil-to-lymphocyte ratio (NLR) is an indicator of the systemic inflammatory response, which has been proposed to be used as a prognostic marker in various types of cancers. Cholangiocarcinoma is a common cancer in Thailand. However, data regarding NLR in this cancer is still limited.
Aims and Methods: We would like to verify if NLR could be used as another prognostic factors in cholangiocarcinoma.
We conducted a retrospective study. Data were collected from eligible patients who were admitted to Siriraj Hospital, Mahidol University between January, 2006 and December, 2015. All patients with the diagnosis of cholangiocarcinoma were recruited. The diagnosis of cholangiocarcinoma was proven by pathological and/or imaging confirmation. The exclusion criteria were patients who received less than three cycles of chemotherapy, patients with other malignancy diagnosed within 5 years prior cholangiocarcinoma detected, patients who had active infection during the blood drawn of NLR was collected, and patients who were allocated into palliative care. Patients who received initial treatment at other hospital or unknown diagnosis date, who had been referred for adjuvant or systemic chemotherapy outside the study hospital, patients with missing data from medical record, who lost to follow-up and without definite diagnosis were also excluded. Baseline characteristics, laboratory data, modalities of treatment and therapeutic outcomes were collected. Associations between clinical characteristics, NLR, laboratory variables including tumor markers as well as survival were investigated by regression analysis. The proper cut off level of NLR also identified using sensitivity analysis. Comparison between patients with NLR < 2 and NLR ≥ 2 were performed using logistic regression analysis.
Results: 536 consecutive patients met the inclusion criteria, after considering the exclusion criteria, 171 patients were eligible for the final analysis. The mean age of patients was 59.26 ± 10.88 years. Eligible patients were categorized into 3 groups according to treatment modalities; palliative chemotherapy (N = 77, 45%), adjuvant therapy (N = 37, 21.6%) and surgery group (N = 57, 33%). The cut off NLR value of 2 was selected to predict prognosis with sensitivity of 74% and specificity of 53%. Patients who had NLR < 2 across the study timeline (before, during and after treatment) had the best survival (Median OS = 34.8 and 37.1 months). Patients with initial NLR < 2, had median overall survival (OS) and progression-free survival (PFS)/disease-free survival (DFS) of 34.8 and 50.6 months respectively compared to median OS of 21.6 months ($P = 0.001$) and median PFS/DFS of 16.6 months ($P = 0.004$) in patients with NLR ≥ 2. Multivariate analysis demonstrated that high level of CEA and CA19-9 were significant predictors of poor PFS/DFS with HR = 2.29 and 2.03, $P = 0.016$ and 0.04, respectively). Worse OS were predicted by NLR ≥ 2 (HR 1.76, $P = 0.021$), CA 19-1 > 300 (HR 1.79, $P = 0.009$), and ECOG ≥ 2 (HR 6.24, $P = 0.016$). Only patients in surgical group had significantly survival difference according to the change of NLR.
Conclusion: NLR can be considered as another independent prognostic factor to predict survival in patient with cholangiocarcinoma. As NLR is a cheap and simple, already available test, we proposed to use NLR as a useful biomarker to predict prognosis of cholangiocarcinoma.
Disclosure: Nothing to disclose

P1334 SURVIVAL OF PATIENTS WITH DISTAL CHOLANGIOCARCINOMA: A POPULATION-BASED DUTCH COHORT

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Introduction: Real-life treatment and outcomes of distal cholangiocarcinoma in the Western world are largely unknown. This study investigated treatment, outcomes, time trends and predictors for survival in a nationwide cohort of patients with distal cholangiocarcinoma.
Aims and Methods: A population-based cohort derived from the Netherlands Cancer Registry was studied. All patients (resected and unresected) registered to have distal cholangiocarcinoma between 2009–2015 were included. Missing data were handled using multiple imputation. Survival and predictors for survival were analyzed using Kaplan Meier and Cox regression analysis (backward selection).
Results: During the study period, 1152 patients were registered; 537 (46.6%) underwent resection, 376 (32.6%) had unresected non-metastasized disease (M0) and 239 (20.7%) had metastasized disease (M1). In the resected group, 30-day mortality was 5.4% (n = 29) and adjuvant chemotherapy was rarely used (8.4%, n = 45). Palliative chemotherapy was administered in 19 (5.1%) of the patients with non-resected M0 and in 74 (31.0%) of the M1 tumors. Median overall survival for patients with resected, unresected M0, and M1 tumors was 23 months (95% CI 20–25), 7 months (95% CI 6–8) and 4 months (95% CI 3–5) ($p < 0.001$), respectively. Over time, survival did not improve in any of the subgroups. Negative independent prognostic factors for survival in resected patients were increasing age ($p = 0.01$), T3/T4 stage ($p = 0.02$), higher lymph node ratio ($p < 0.001$), poor differentiation ($p < 0.001$), and microscopic ($p < 0.001$) or macroscopic ($p = 0.03$) residual disease.
Conclusion: This largest nationwide Western study on distal cholangiocarcinoma demonstrates a 47% resection rate with acceptable survival despite limited use of adjuvant chemotherapy, and poor survival and limited use of chemotherapy in unresected patients. The study identified predictors for survival which can be useful to stratify future clinical trials with (neo-) adjuvant or palliative treatment.
Disclosure: Nothing to disclose

P1335 ENDOSCOPIC SNARE PAPILLECTOMY (ESP) FOR AMPULLARY TUMOURS – SINGLE-CENTER EXPERIENCE

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Introduction: Ampullary tumors may be adenoma, adenocarcinoma or other rare lesions. Although it carries high morbidity, Whipple's pancreatico-duodenectomy is the recommended treatment modality in most. There is an increasing interest in endoscopic snare papillectomy (ESP) as an alternative minimally invasive treatment option. We report long-term results of ESP in a retrospective patient cohort from a single center.

Aims and Methods: Patients with localised ampullary tumors treated by ESP during 10-year period (2007–2017) were identified from a prospectively maintained ERCP database. All underwent pre-ESP endoscopic ultrasonography (EUS) to confirm localized disease and suitability for procedure. Exclusion criteria – tumor infiltration into pancreas, duodenal wall or distal bile duct on EUS. Endoscopic and EUS appearance was adequate to plan ESP and pre ESP histology was not considered mandatory. Enbloc ESP was performed using a diathermy snare followed by biliary and pancreatic stent placement; removed at 4–6 weeks with biopsies to look for residual tumor. Patients with final histology – adenocarcinoma were counselled for either close follow-up or surgical resection & those with benign histology were followed up. Follow up done at 3, 6, 12, 18, and 24 months, yearly thereafter. Duodenoscopy & appropriate imaging at every follow up.
Results: 63 patients underwent ESP. Mean age – 59.2 years (33–72) in adenoma group, 66.8 years (46–88) in adenocarcinoma group. Males – 36. Mean tumour size 20.3mm (5–52). Adverse events – 6 (9.5%) – post ESP bleed – 3 (2 – endotherapy, 1 – angio-embolization), delayed biliary stenosis – 2 (ERCP stenting), fatal pancreatitis after biopsy – 1. Final histology – adenocarcinoma (AC) – 29 (46%), adenoma (AA) – 27 (42.8%), neuroendocrine tumor (NET) – 3, chronic inflammation – 4. Base involved in 6 (9.5%) – underwent surgery. Follow up was as per final histology (Fig. 1). Follow up was available in 49 patients (78%), mean duration – 22.4 months (1–88). Recurrence was documented in 5 patients – 2/13 (15%) in AC (surgery – 1, palliative stenting – 1) & 3/25 (12%) in AA group. After correcting values for patients lost to follow up, 11/22 (50%) patients from AC group and 20/25 (80%) from AA group were disease free during follow up. All recurrences occurred around one-year (10.5 to 14). Therefore for the total cohort, 35/62 patients (56%) remained disease free during follow up.
Conclusion: Results of ESP in this single-center carefully selected patient cohort suggest that ESP may be curative for >50% patients with ampullary tumors. Curative resection may be achieved for 4/5 adenomas and every other localized adenocarcinoma. Given the fact that majority of these patients may be high-risk surgical candidates, these results are encouraging. Histologically confirmed clear resection margin is critical to minimize recurrence risk.
Disclosure: Nothing to disclose

P1336 THROMBOEMBOLISMS IN ADVANCED BILIARY TRACT CANCER: A RETROSPECTIVE ANALYSIS OF 174 CASES

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Introduction: A high incidence of thromboembolism (TE) has been reported in patients with malignancy, especially in pancreatic cancer patients. However, few data are available on patients with biliary tract cancer (BTC).
Aims and Methods: The aim of this analysis is to clarify the incidence of TE, risk factors for TE and its clinical impact in Japanese patients with BTC. Data on consecutive patients receiving systemic chemotherapy for advanced BTC between April 2008 and March 2017 were retrospectively studied. Both symptomatic and asymptomatic, arterial and venous TEs were included in the analysis. Risk factors for TE development were analyzed using a proportional hazards model with death without TE as a competing risk. The impact of TE on survival was also evaluated using a time-dependent covariate multiple Cox model.
Results: A total of 174 patients (105 male, a median age of 70 years) with advanced BTC were included in the analysis. Primary sites of cancer were intrahepatic in 66 (38%), gallbladder in 59 (34%), hilar bile duct in 27 (16%), distal bile duct in 17 (10%) and ampulla in 5 (3%). TE was identified in 21 cases (12%): 20 venous TEs and 1 arterial TE. The incidence of TE did not differ by the primary tumor site ($P = 0.66$). The median time to TE was 128 (95% CI; 66–230) days and the median survival from TE was 102 (95% CI; 29–171) days. In a multivariate analysis, female sex was the only significant risk factor for TE (subdistribution hazard ratio 4.10, 95% CI; 1.58–10.7, $P < 0.01$). In a multivariate analysis using a time-dependent covariate multiple Cox model, TE was significantly associated with poor prognosis (hazard ratio [HR] 1.98, 95% CI; 1.17–3.36 $P = 0.01$) as well as CA19-9≥300 (HR 1.55, 95% CI; 1.08–2.21, $P = 0.02$), gallbladder cancer (HR 1.51, 95% CI; 1.03–2.20, $P = 0.03$) and liver metastasis (HR 1.85, 95% CI; 1.27–2.70, $P < 0.01$).
Conclusion: TE was not uncommon in Japanese patients receiving chemotherapy for advanced BTC and was associated with poor prognosis. Female sex was the only risk factor for TE.
Disclosure: Nothing to disclose

P1337 PHOTODYNAMIC THERAPY OF PERIHILAR CHOLANGIOCARCINOMA – A RETROSPECTIVE COHORT ANALYSIS OVER A DECADE

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Introduction: Only a small proportion of patients with perihilar cholangiocarcinoma (hCCC) can be delivered to curative surgical resection. If surgery is impossible, the treatment consists of palliative chemotherapy and biliary drainage. In addition, local ablative therapy such as photodynamic therapy (PDT) can be offered. In previous studies, PDT showed ambiguous results regarding overall survival and clinical profit. Aim of this investigation is to analyse the therapeutic benefit of PDT in a clinical retrospective setting without restriction to combination of PDT with stent or concomitant chemotherapy.
Aims and Methods: We retrospectively analysed the data of 65 patients with histologically confirmed hCCC that were treated from 2003 until 2013. 30 patients received only stent therapy (group A), 35 patients received stent therapy with PDT (group B). PDT was performed with the photosensitzer porfimer sodium and an intraluminal photoactivation (wavelength: 630 nm, light dose: 180 J/cm^2). Survival time, numbers of needed ERCP and complication rate were statically evaluated. Subgroup analyses were done for patients with concomitant chemotherapy.
Results: PDT did slightly improve the survival time (A: 9.27 ± 6.27 months, B: 11.7 ± 8.8 months; $p = 0.348$) and reduced the numbers of needed ERCP within 3 months (A: 1.8 ± 1.2, B: 1.53 ± 0.49; $p = 0.115$). The complication rate per person was equal in both groups (A: $3.17 \pm 2.6\%$, B: $2.69 \pm 1.21\%$). Phototoxic skin reactions occurred in 17.4% of patients with PDT. 32.3% of the patients were able to receive additional chemotherapy which only minimally increased the survival time in both Groups (A: 10.7 ± 4.5 months, B: 16.1 ± 10.7 months; $p = 0.348$).
Conclusion: The impact of PDT on survival time in unselected patients with hCCC is low. The attributed advantages of PDT were not statistically significant and independent of additional chemotherapy.
Disclosure: Nothing to disclose

P1338 TRENDS IN INCIDENCE, TREATMENT AND SURVIVAL OF GALLBLADDER CANCER; A NATION-WIDE COHORT STUDY

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Introduction: Gallbladder cancer (GBC) is a rare but lethal malignancy, primarily diagnosed in an advanced stage unless detected incidentally after laparoscopic cholecystectomy for suspected benign gallbladder disease. Scarce data is available on GBC treatment and survival outcomes in Western populations. Consequently, controversy exists regarding surgical and systemic treatment. Aim of this study was to assess trends in incidence and evaluate treatment and survival of GBC patients.
Aims and Methods: Data on all patients with GBC diagnosed between 2000–2015 were retrieved from the nationwide population-based Netherlands cancer registry ($N = 2427$). Age-standardized incidence rates were calculated. Trends in incidence and demographics were assessed. Treatment strategies and associated survival were analysed using Kaplan-Meier methods and propensity score matching.
Results: Age-standardised incidence of GBC varied from 0.6 to 0.9 per 100.000 person years and did not change over time. Most patients were female (72%), over 75 years of age (44%), presented with stage IV (39.8%) disease and were diagnosed pre-operatively (67.2%). The overall median survival was 5.2 months and primarily determined by tumour stage, ranging from 36.2 months in stage I patients to 3.0 months in stage 4 patients. Between 2000 and 2015 overall median survival improved from 4.1 to 6.6 months ($p < 0.001$). After propensity score matching, median survival in surgically treated stage III + IV gallbladder cancer was 7.4 months, compared to 3.3 months for non-surgically treated patients ($p < 0.001$). Stage II GBC patients receiving additional liver bed resection showed superior median survival to those whom did not receive additional surgery (21.7 vs. 46.6 months, $p < 0.001$). Systemic therapy in advanced stage GBC improved median survival from 2.8 to 7.4 months ($p < 0.001$).
Conclusion: Incidence of GBC did not change significantly and overall survival increased slightly in this nation-wide cohort. Median survival was longer in patients with early GBC who underwent an additional resection and patients with advanced GBC who received systemic therapy compared to patients who did not receive these treatments. However, general outcome for GBC patients is still poor.
Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 09:00–14:00
Pancreas III – Hall X1

P1339 FEASIBILITY OF A THREE-DIMENSIONAL SPHEROID CULTURE USING ENDOSCOPIC ULTRASOUND-GUIDED TISSUE SAMPLING IN PANCREATIC CANCER

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Introduction: Pancreatic cancer is an extremely lethal malignancy, with a 5-year survival rate of less than 5%. Although chemotherapy is another option of therapy for advanced pancreatic cancer, the response was poor and unpredictable. Preclinical research is recently advanced for in vitro drug testing using cancer cell lines and organoids or xenograft tissue using human tumor tissues. However, obtaining tumor cells from patients with pancreatic cancer are limited because most patients were initially diagnosed as inoperable stage. Recently, methods to culture and/or propagate tumor tissue using specimens obtained from endoscopic ultrasound-guided tissue sampling (EUS-TS) were introduced.
Aims and Methods: The aim of our study was to evaluate the feasibility of a three-dimensional (3D) spheroid culture using EUS-TS in pancreatic cancer. Patients with suspected pancreatic cancer who were referred for EUS-TS were prospectively enrolled. Among them, patients with locally advanced or distant metastasis were included. After the acquisition of tissue specimen for pathologic diagnosis by EUS-guided fine needle aspiration using 20-gauge ProCore needle (Cook medical, Winston Salem, IN, USA), additional EUS-TS was performed for 3D spheroid culture. The acquired specimens were processed to cultivate in culture media and/or Matrigel and observed serially by phase contrast microscopy to evaluate the growth of tumor cells. After appropriate growth of tumor cells, the specimen was examined by Hematoxylin and Eosin staining to compare the similarity of histology between human cancer tissue and 3D spheroid tumor.
Results: Between June 2017 and November 2017, 12 patients were enrolled. Among them, two patients were excluded due to refusal of informed consent and nonpancreatic cancer. Finally, EUS-FNA specimen for 3D culture was obtained from 10 patients (male to female ratio, 2:3; median age of 67, range 54–78), who were diagnosed as ductal adenocarcinoma in EUS-TS. During mean observation period of 41.6 days, 3D spheroid culture was successfully constructed and observed tumor growth in 3 cases. The histology of 3D culture specimen was similar to that of human tumor tissue.
Conclusion: This model, which is successfully and rapidly created by means of EUS-guided core biopsy at the time of initial tumor diagnosis, can be a promising method for construction of in vitro models in the process of drug development and testing for pancreatic cancer.
Disclosure: Nothing to disclose

P1340 MAST CELL STABILIZERS AMELIORATE PAIN IN EXPERIMENTAL CHRONIC PANCREATITIS

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Introduction: In both chronic and acute pancreatitis (AP), pain is the cardinal symptom and notoriously difficult to managae. In recent studies, we detected a specific enrichment of mast cells around intrapancreatic nerves of patients with painful chronic pancreatitis (CP).
Aims and Methods: In the present study, we analyzed whether administration of mast cell stabilizers can improve the pain due to CP. For this purpose, AP and CP were induced in 8-week-old C57BL/6J mice via repeated i.p. injections of the cholecystokinin analogie cerulein. Mice were either prophylactically, i.e. beginning 2h (AP) or 1 week (CP) prior to disesase induction, or therapeutically, i.e. beginning in the third hour (AP) or at week 2 (CP) after disease induction, with one of the mast cell stabilizers ketotifen or cromoglycate. Metamizol was applied as the comparative agent, and solvent was applied as control. The mast cell stabilizers were applied i.p. during AP, and combined orally and s.c. during CP. The pain-associated behavior of mice was assessed via the von Frey mechanosensitivity test and via the open-field locomotion test.
Results: In dose-finding experiments, the effective analgesic doses for each drug were identified (metamizol: 500mg/kg BW, ketotifen: 10mg/kg BW, cromoglycate 500mg/kg BW). In the final therapy experiment, in AP, the mast cell stabilizers did not exert an anagelsic effect when administered as single therapeutics to the mice. However, in CP, we observed a prominent reduction in the von Frey pain scores and improvement in the locomotion scores of the mice treated with cromoglycate or ketotifen.
Conclusion: The present study showed for the first time a potential analgesic effect of mast cell stabilizers in pancreatic pain. Further preclinical studies analyzing mast cell stabilizers as adjunct analgesics are currently underway. This novel concept also needs testing in early phase clinical trials.
Disclosure: This abstract was also presented at the DGVS 2017 congress.

P1341 DOPAMINE D2 RECEPTOR SIGNALING CONTROLS INFLAMMATORY STATUS OF MACROPHAGES IN ACUTE PANCREATITIS THROUGH INHIBITION OF OXIDATIVE STRESS-INDUCED NF-κB AND INFLAMMASOME ACTIVATION

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Introduction: Acute pancreatitis (AP) is aninflammatory disease mediated by acinar cell injury andsubsequent inflammation with leukocyteinfiltration.[1,2] Innate immune cells are the first cells to arrive the injured pancreas in AP.[3] Macrophage activation is an important determinant of the severity of AP.[4] In response to different signals, macrophages may undergo two types of activation: M1 (classically activated macrophages) or M2 (alternatively activated macrophages). We have demonstrated the regulatory effects of dopamine and dopamine D2 receptor (DRD2) signaling pathway on AP in our previous studies.[5] Besides, cAMP – the second messenger of dopamine D1 receptor (DRD1) signaling,[6] can prevent macrophages to transform into M1 phenotype.[7] However, the relationship between DRD2 and macrophagepolarization in AP remains to be understood.
Aims and Methods: In the present study, we aimed to investigatethe changes of dopaminergic system in different macrophage phenotypes, the roleof DRD2 on macrophage polarization during AP. We analyzed changes of dopaminergic system both in M1 and M2 macophages, and the effects of DRD2 activation on macrophage polarization in bone marrow derived macrophages (BMDMs) *in vitro* or in caerulein and lipopolysaccharide (LPS) or L-arginine induced AP in wild-type and myoleid-specific $Drd2^{-/-}$mice *in vivo*. Intracelluar oxidative stress, NFκB and inflammasome activation were evaluated.
Results: Dopaminergic system was activated both in M1 and M2 macrophages, but DRD1 and DRD2 were decreased in M1 while increased in M2 macrophages. Compared to normal control, DRD1 and DRD2 were significantly reduced in macrophages from the pancreatic tissue of AP mice. DRD2 activation can significantly downregulate M1 markers (iNOS, TNFα, etc.) but upregulate M2 markers (CD206, etc.) both in LPS and IFNγ-induced BMDMs *in vitro* and in the pancreas of caerulein and LPS-induced or L-arginine-induced AP model *in vivo*. Myeloid-specific Drd2 deficiency aggravated pancreas injury of AP, elevated serum amylase and lipase levels and more M1 macrophages were obsevered in the pancreas. Furthermore, we revealed that DRD2 activation can inhibit the membrane translocation of $p47^{phox}$- one cytoplasmic subunit of NADPH oxidase, and reduce ROS generation, which influence the NFκB and inflammasome activation in the downstream in LPS and IFN-γ-induced BMDMs. And we confirmed these phenomena in the BMDMs isolated from myeloid-specific $Drd2^{-/-}$mice. Our datas showed that DRD2 activation can inhibit NADPH oxidase-mediated ROS generation, NFκB and inflammasome activation in $Drd2^{-/-}$BMDMs.
Conclusion: Our data showed that in the progress of AP, DRD2 can inhibit M1 macrophages, and pherhaps promote them to M2 profile by inhibiting NADPH oxidase-mediated ROS generation and its downregulating NFκB and inflammasome activation. Therefore, therapeutic approaches that activate DRD2 receptor signaling may represent a novel strategy for attenuating inflammation in AP clinically.
Disclosure: Nothing to disclose

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P1342 FUNCTIONAL GENOMIC SCREENING DURING SOMATIC CELL REPROGRAMMING IDENTIFIES DKK3 AS A ROADBLOCK OF PANCREATIC REGENERATION

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Introduction: The reprogramming process partly eliminates disease- and aging-associated phenotypes, inducing a ''partial cure'' or ''rejuvenation'' in pluripotent stem cells as shown in studies using somatic cells from centenarians or chronically sick patients as templates. Interestingly, adult stem cells share common features with their pluripotent counterparts, such as differentiation potential and self-renewal, and at least partially share certain molecular programs.
Aims and Methods: We propose that studying somatic cell reprogramming could serve as a tool to gain valuable insights into adult stem cell fitness and organ regeneration. As logical consequence we have successfully applied a straightforward functional genomics approach using RNA-interference techniques during iPS formation.
Results: We identified a set of factors limiting both cellular reprogramming and stem cell fitness in the hematopoietic system. Dkk3 (Dickkopf 3) was found to be a factor limiting these two features. Consequently we aimed to investigate the role of Dkk3 during liver and pancreas regeneration upon injury. To do so, we used Dkk3 null mice to examine its role in a cerulein-induced acute pancreatitis context. First, there was no effect on the acute injury but Dkk3 loss appeared relevant in the regeneration phase of the pancreas. Specifically, we demonstrated that DKK3 inactivation triggers a better pancreatic acinar regeneration four days after pancreatitis induction. Furthermore, DKK3 knockout mice display a significant decrease of acinar-to-ductal metaplasia lesions, correlated with lower

edema and inflammation scores, and a diminished fibrotic content. Additional mechanistical insights are given by organoid cultures derived from wild type and Dkk3 null pancreata. In contrast, partial hepatectomy in Dkk3 null mice revealed just a trend toward better regeneration.
Conclusion: DKK3 appears to act as a brake of acinar regeneration after pancreatic insult in a tissue-specific manner.
Disclosure: Nothing to disclose

P1343 SMALLER PORTAL SYSTEM VEIN DIAMETERS PREDICT COMPLICATIONS AND OUTCOME IN ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) progresses to necrotizing pancreatitis in 15% of cases [1]. An important pathophysiological mechanism in AP is third spacing of fluids, which leads to intravascular volume depletion that may progress to hypovolemic shock [2, 3]. This compromises the splanchnic circulation and reduces venous return [4–6]. Smaller diameters of portal system veins (portal, splenic and superior mesenteric) as a result of decreased venous return might contribute to increased morbidity and mortality in acute pancreatitis. Computed tomography (CT) scan enables identification of the diameter of these veins in early acute pancreatitis.
Aims and Methods: We conducted a post-hoc analysis of data from two randomized controlled trials that included patients with predicted severe and mild AP. One trial included patients with a predicted severe disease course at admission [7]. All patients had a CT scan 7–10 days after admission. The other trial included patients with mild biliary pancreatitis [8]. From this trial we included patients who underwent a CT scan within 7 days of admission. We performed additional CT measurements of portal system vein diameters and calculated their prognostic value through univariate and multivariate Poisson regression. In the multivariate regression we corrected for possible confounders. Additionally, we performed an analysis in which we compared the mean vein diameters in patients with predicted mild and severe AP by Student's t-test. The primary endpoint was AP-related mortality. The secondary endpoints were (infected) necrotizing pancreatitis and (persistent) organ failure.
Results: The total sample consisted of 177 patients. Multivariate regression analysis showed a significant inverse association between splenic vein diameter and mortality (RR 0.75 (0.59–0.97)), a smaller diameter was a risk factor for mortality. Furthermore, there was a significant inverse association between splenic and superior mesenteric vein (SMV) diameter and (infected) necrosis. The diameters of all veins were inversely associated with organ failure and persistent organ failure. The results of the univariate and multivariate analysis are displayed in the table. Patients with predicted mild AP had significantly larger diameters of the portal, splenic and SMV compared to those with predicted severe AP.
Conclusion: We observed that a smaller diameter of the splenic vein is a risk factor for mortality and a smaller diameter of all portal system veins is a risk factor for morbidity in AP. These findings could be used in the optimization of radiological scoring systems to predict the severity of pancreatitis.

Mortality	Univariate analysis	Multivariate analysis
Portal vein	0.87 (0.70–1.08)	
Splenic vein	0.78 (0.62–0.98)	0.75 (0.59–0.97)
SMV	0.88 (0.71–1.09)	
Necrosis		
Portal vein	0.90 (0.80–1.01)	
Splenic vein	0.80 (0.71–0.91)	0.78 (0.68–0.89)
SMV	0.84 (0.75–0.94)	0.83 (0.74–0.93)
Infected necrosis		
Portal vein	0.85 (0.72–1.01)	
Splenic vein	0.76 (0.64–0.92)	0.72 (0.59–0.88)
SMV	0.78 (0.66–0.93)	0.76 (0.64–0.91)
Organ failure		
Portal vein	0.83 (0.72–0.95)	0.79 (0.67–0.94)
Splenic vein	0.80 (0.68–0.94)	0.76 (0.64–0.90)
SMV	0.84 (0.73–0.97)	0.81 (0.70–0.94)
Persistent organ failure		
Portal vein	0.81 (0.70–0.94)	0.77 (0.65–0.92)
Splenic vein	0.78 (0.66–0.93)	0.73 (0.61–0.88)
SMV	0.78 (0.67–0.91)	0.75 (0.64–0.87)

Values depict relative risk (95% confidence interval).
SMV: superior mesenteric vein.

[Univariate and multivariate analyses of association between vein diameter and mortality and AP-related morbidity]
Disclosure: Nothing to disclose

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P1344 DIAGNOSTIC WORK-UP IN IDIOPATHIC ACUTE PANCREATITIS, A POST-HOC ANALYSIS OF A PROSPECTIVE MULTICENTER OBSERVATIONAL COHORT

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Introduction: After standard diagnostic work-up, the etiology of acute pancreatitis remains unknown in up to 25% of cases, a condition referred to as idiopathic acute pancreatitis (IAP). Determining the etiology of pancreatitis is essential, as it may direct treatment in the acute phase of the disease and guide interventions to prevent recurrent pancreatitis.
Aims and Methods: We explored the use and yield of additional diagnostic tests (i.e. endosonography, MRI/MRCP, CT, diagnostic ERCP and IgG4). Furthermore, we analyzed the recurrence rate of acute pancreatitis after a first episode of IAP and assessed what the impact was of establishing an etiological diagnosis treatment on recurrence rates.
Between 2008 and 2015, patients presenting with acute pancreatitis were registered prospectively in fifteen Dutch hospitals. Patients who initially had a negative diagnostic work-up with regard to the etiology of their pancreatitis were labelled IAP. This initial work-up included: personal history (signs of a biliary cause, alcohol use, medication use, metabolic disorders, prior abdominal trauma, surgery, or ERCP); family history (chronic or hereditary pancreatitis); transabdominal ultrasound; and laboratory tests (i.e. liver enzymes, calcium, triglycerides) We performed a post-hoc analysis including the type and number of all diagnostic tests performed, the yield of these test to establish an etiological diagnosis, and recurrence rates after treatment.
Results: Out of the 1632 patients that were registered, 191 patients were diagnosed with a first episode of IAP. Out of these 191 patients, 176 (92%) underwent one or more additional diagnostic test: CT (n = 124, yield 8%), EUS (n = 62 patients, yield 35%), MRI/MRCP (n = 56, yield 33%), repeat ultrasound

(n = 97, yield 21%), IgG4 (n = 54, yield 9%), and ERCP (n = 15, yield 47%). In 64 patients (36%) these test revealed an etiologic diagnosis. During a median follow-up of 4 years (IQR 3–6), 50 out of 191 patients (26%) had at least one recurrence, 26 of whom had more than one recurrent episode. There were 101 recurrences in total with a median of 2 per patient (IQR 1–2). Out of 141 patients with only one single episode of idiopathic pancreatitis, 128 patients underwent additional diagnostic testing. In 35 cases (27%) an etiology was found: biliary (n = 22; 1 combined with pancreas divisum), autoimmune (n = 3), pancreatic carcinoma (n = 3), chronic pancreatitis (n = 3), ampullary carcinoma (n = 2), pancreas divisum (n = 1), and a neuroendocrine tumor (n = 1). Of the 50 patients with recurrent episodes of acute pancreatitis, an etiologic cause was identified after additional testing in 29 patients (58%): biliary etiology (n = 17; 1 combined with pancreas divisum), pancreatic carcinoma (n = 6; 1 combined with biliary stones and chronic pancreatitis), autoimmune pancreatitis (n = 3), chronic pancreatitis (n = 2) and an IPMN (n = 1). In 13 out of 176 of patients (7%) additional testing showed an ampullary or pancreatic neoplasm. EUS and MRI/MRCP had a high diagnostic etiological yield, both in the single episode patients (EUS 35%; MRI/MRCP 30%) and the ones with recurrent episodes (EUS 35%; MRI/MRCP 35%).

Conclusion: In over one-third of patients initially labelled as idiopathic pancreatitis an etiological diagnosis is established after additional diagnostic testing. The rate of etiologies detected was twice as high in patients with recurrent IAP (58%) than in patients with only one pancreatitis attack (27%). The etiology found was mostly biliary, but neoplasms were not a rarity which prompts for extra vigilance not to lose an opportunity for timely resection.

Disclosure: Nothing to disclose

P1345 DIFFERENCES BETWEEN THE OUTCOME OF RECURRENT ACUTE PANCREATITIS AND ACUTE PANCREATITIS

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Introduction: Recurrent acute pancreatitis (RAP) can occur in 10–30% of patients who recover from first episode, with patients having milder disease and lower mortality. Overall, a handful of studies are available on outcome of RAP, in comparison to first episode of acute pancreatitis (AP).

Aims and Methods: We aimed to provide more complete and updated picture of RAP and how it is different from initial episode of AP.

Consecutive patients admitted with an episode of acute pancreatitis over 8 years were included in study. Patients with prior episodes (≥1) of acute pancreatitis, with atleast a 2-month gap between each episode were labelled as RAP. Patients with underlying chronic pancreatitis were excluded. Blood investigations including fasting triglyceride levels, calcium, parathormone, MRCP and EUS were used to find an etiology. Severity assessment was done using BISAP, APACHE II and revised Atlanta scoring. All patients were managed as per standard guidelines for fluid resuscitation, antibiotics for infection and drainage of infected necrosis using PCD when indicated. Primary outcome measures were need for surgical necrosectomy and mortality.

Results: Of the 724 patients (age 39.22 ± 13.25 years, 68% male) with an episode of pancreatitis, 632 (87.3%) had presented with first episode (AP) and 92 (12.7%) with at least one prior episode (RAP). Regarding the etiology of RAP patients, biliary etiology (32.6%) and alcohol (30.4%) were the two most frequent factors, and no etiology could be identified in 19.6%. SIRS, BISAP and APACHE II scores were less in RAP group. The incidence of severe pancreatitis was significantly less in RAP patients (10.9%) in comparison to AP patients (48.6%). The mean duration of hospitalization (10.5 + 9.5 versus 21.6 + 16.4 days), ICU admission (10.9% versus 43.7%) and need of PCD (38.6% versus 55.1%) were significantly lower in RAP group. Fluid collections were present in 57 (62%) RAP patients and in 573 (90%) patients with AP. The requirement of surgical intervention and mortality were less in patients with RAP (1.1% and 2.2%) in compared to patients with AP (9.3% and 18%, respectively). The mean number of episodes per RAP patients was 2.97 ± 1.66 (range 2–10) and 64.1% had only 2 episodes.

Conclusion: Patients with RAP had milder disease course and lesser mortality when compared to the initial episode of AP. Appropriate evaluation and dealing with etiological factors at the initial episode of AP can prevent a majority of RAP.

Disclosure: Nothing to disclose

P1346 DOES THE TIMING OF PERCUTANEOUS CATHETER DRAINAGE IMPACT OUTCOME IN PATIENTS WITH ACUTE FLUID COLLECTION IN PATIENTS WITH ACUTE PANCREATITIS

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Introduction: Percutaneous catheter drainage (PCD) is used as a first step in the management of symptomatic fluid collections in acute pancreatitis (AP). Data is lacking for the ideal time of PCD for fluid collections in AP. We aimed to compare the indication and outcome of PCD in patients with acute necrotic collection (ANC) and walled-off necrosis (WON).

Aims and Methods: Consecutive patients of AP with symptomatic ANC or WON undergoing PCD were evaluated in a tertiary care centre in North India between January 2011 and December 2017. The two were compared for indications and outcome measures (need for additional surgical necrosectomy, mortality, need for up-gradation of first PCD, need for additional drain, total duration of PCD and length of hospital stay). Complications related to PCD were also compared.

Results: Of the 650 patients [mean age was 38.58 ± 12.28 years; 71.5%males; etiology: alcohol (51.5%), gall stone disease (35.5%) with AP, 375(57.6%) underwent PCD as a part of their management. 258 (68.8%) patients underwent PCD for ANC and 117 (31.2%) for WON. The mean time to admission to our hospital was 10.47 ± 9.82 days and 36.79 ± 30.69 days in patients who underwent PCD for ANC and WON respectively (p = 0.001). The commonest indication for PCD in both ANC (n = 135, 52.3%) and WON (n = 79, 67.5%) was suspected infection of pancreatic necrosis. Persistent organ failure as an indication for PCD was significantly more common in patients with ANC than WON (38% vs 16.2%, p = 0.001). Pressure symptoms formed the indication for PCD in 9.7% patients with ANC and 16.2% with WON (p > 0.05). Infection of pancreatic necrosis was proven with culture of drain fluid in 146 (56.6%) patients with ANC and 75 (64.1%) patients with WON (p = 0.104). One PCD was placed in 152 (58.9%) patients with ANC and 72 (61.5%) patients with WON with a mean of 1.50 ± 0.66 and 1.50 ± 0.72 PCDs per patient respectively (p = 0.915). The total duration of PCD in ANC was 28.38 ± 20.72 days versus 30.16 ± 26.20 days in WON (p = 0.479). Surgical necrosectomy was needed in 14% patients with ANC versus 12% patients with WON (p = 0.364). Mortality was 19% in patients with ANC as compared to 13.7% in those with WON (p = 0.132). Complications of PCD included external pancreatic fistula (27.5%), blockade of PCD catheter (12.3%), slippage of PCD catheter (10.9%), and bleed through PCD catheter. External pancreatic fistula which occurred more often in WON than in ANC (24.4% versus 34.2%, p = 0.034).

Conclusion: Outcome of PCD is similar in patients with ANC and WON. However, persistent organ failure formed an indication for PCD in greater number of patients with ANC than WON. External pancreatic fistula occurred more often in WON than ANC.

Disclosure: Nothing to disclose

P1347 FACTORS AFFECTING OUTCOME AFTER PERCUTANEOUS CATHETER DRAINAGE OF FLUID COLLECTION IN PATIENTS WITH ACUTE PANCREATITIS

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Introduction: Percutaneous catheter drainage (PCD) is the initial step of step-up approach for management of acute pancreatitis (AP). Currently no reliable criteria are available to predict which patients may benefit from PCD.

Aims and Methods: The aim of this study was to identify factors that lead to surgical intervention or mortality after initial management with PCD. In a prospective observational study, 101 consecutive AP were managed by step up approach. Patients who had worsening after conservative management were subjected to PCD under image (USG/CT) guidance. Patients who did not improve at 72 hours were considered for up gradation of the PCD. Patients who did not improve were considered for surgical necrosectomy. Various factors evaluated were, demographic parameters (age, sex, aetiology, comorbidities), severity parameters (CTSI, APACHE II, CRP and IAP), full morphologic characteristics on USG/MRI/EUS (solid component), characters collection before PCD (infected or sterile, volume, site & number), PCD parameters (indication, initial size, maximum size, number and duration of drainage) and factors after PCD insertion (fall in CRP, fall in IAP, reduction in volume of collection. PCD success (survival without necrosectomy) was correlated with baseline and outcome measures.

Results: Out of 101 patients of AP, 50 patients were treated conservatively and 51 required PCD. A total 87 PCD catheters were placed. The success rate of PCD in our study was 66.66% (34/51) and 4 patients required additional surgical necrosectomy after PCD. Overall mortality rate in our study was 29.4% (15/51, including 2 after surgery). PCD alone improved organ failure in 72.54% patients. Patients were divided into two groups, PCD success group (i.e. survival without necrosectomy) and failure group. Size of first PCD was significantly larger in PCD success group (13.94 ± 2.48 vs 12.58 ± 1.17 Fr, **p = 0.011**). There was a

significant percent volume reduction in PCD success group than in failure group **(74.35±21.35% and 44.49± 31.02% respectively, p = 0.000).** More than 50% reduction in fluid collection after PCD (**p = 0.005**) correlated with the PCD success. Amount of collection (114.21 ± 125.47 vs 388.99 ± 341.03 CC, **p = 0.005**) and percentage of volume reduction after PCD insertion (74.35 ± 21.35% and 44.49 ± 31.02% respectively, **p = 0.000**) were significant between groups. ICU stay was significantly longer in PCD failure group (6.35 ± 7.96 vs 13.23 ± 12.21, **p-0.046**). Higher number of patients had volume of collection more 750 CC before PCD **(p = 0.05)** in PCD failure group

Conclusion: Larger size of the first PCD and more than 50% reduction of collection after PCD were positive predictors of PCD success. Total volume of collection more than 750 CC before PCD was a negative predictor of PCD outcome.

Disclosure: Nothing to disclose

P1348 COMPARISON OF PROGNOSTIC SCORES IN THE CRITICALLY ILL PATIENT WITH SEVERE ACUTE PANCREATITIS

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Introduction: A large number of studies have focused on identifying severe forms of acute pancreatitis (SAP) within heterogeneous groups of patients most of whom exhibit non-severe forms. However, the value of such predictors in the identification of patients with the worst prognosis in pre-selected groups, such as the critically ill patient with SAP, has been less studied.

Aims and Methods: We aimed to compare the accuracy of non-specific and specific scores on predicting intra-hospital mortality, need for surgery and complications in SAP. We have also evaluated the accuracy of individual clinical and laboratory parameters.

Single-center retrospective cohort including all adult patients with severe acute pancreatitis admitted between January 2007 and February 2017 at a general intensive care unit (ICU). Severity and local complications were defined according to the 2012 Atlanta classification. Clinical (age, sex, body mass index, vasopressor use, mechanical ventilation, hemodialysis and blood transfusions), laboratory (c-reactive protein (CRP), hematocrit, blood urea nitrogen, serum creatinine, albumin levels) data and Acute Physiologic and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment (SOFA) Simplified Acute Physiology Score (SAPS), Systemic Inflammatory Response Syndrome (SIRS), Ranson's criteria, Bedside Index for Severity in Acute Pancreatitis (BISAP), Pancreatitis Outcome Prediction (POP) were collected on admission. Laboratory parameters were also recorded at 48 hours from admission. Statistical analysis was performed with SPSS v.24 and STATA v.14

Results: 57 consecutive patients were included in the study (59.6% male, median age 71 ± 13 years). 49.1% had cardiovascular comorbidity. 42.1% of the SAP cases were biliary and 43.9% had necrotizing pancreatitis. 49.1% had SAP complications mostly intra-abdominal ischemia. 19 patients required surgery after admission to the ICU. The ICU mortality was 42.1%.

APACHE II, SAPS, POP and SOFA scores were significantly higher in the non-survivor group when compared to the survivor group ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p = 0.004$, respectively). Significantly higher serum levels of creatinine (Cr0) and blood urea nitrogen (BUN0) were also observed in the non-survivor group ($p = 0.048$ and $p = 0.001$ respectively). Other scoring systems and laboratory parameters did not differ significantly. ICU related variables associated with increased mortality included need of hemodialysis ($p = 0.001$), and vasopressor requirement ($p = 0.002$).

POP (AUC: 0.79 [0.68–0.91]), APACHE II (AUC: 0.78 [0.67–0.9]), SAPS (AUC: 0.77 [0.65–0.89]) and Cr0 (AUC: 0.74 [0.61–0.87]), outperformed all other evaluators in predicting ICU mortality

POP score had the highest prediction accuracy for mortality without statistical significance ($p > 0.5$). None of the scoring systems were able to predict with high accuracy the need for surgery or SAP complications. Necrotic pancreatitis correlated significantly with need for surgery during ICU stay and complications as expected ($p < 0.0001$ and $p = 0.047$ respectively) but not with mortality ($p = 0.057$). Age, Body Mass Index, and comorbidities had no statistical correlation with any of the outcomes.

Conclusion: Severe acute pancreatitis is associated with high intensive care unit mortality rates. POP, APACHE II, SAPS and Cr0, were able, in this group of patients, to predict mortality with high accuracy. We believe that an early risk stratification of the critical patient influences subsequent management and outcomes positively and should be used in everyday clinical practice.

Disclosure: Nothing to disclose

P1349 ACUTE PANCREATITIS AS A RARE COMPLICATION OF HYDATID LIVER DISEASE. REPORT OF 16 CASES

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Introduction: Acute pancreatitis (AP) due to hydatid cyst is an exceptional complication of hydatid liver cyst (HLC). Its pathogenesis is probably due to pancreatic duct obstruction secondary to fistulization of the HLC in the biliary duct. Its treatment combines the general measures of AP and endoscopic retrograde cholangiopancreatography (ERCP) to unclog the biliary duct andthe cure of the HLC and bili cystic fistula in order topreventrecurrence. We report a first case serie of 16 patients diagnosed and treated at the University Hospital Hassan II to analyze the clinicopathological and evolutionary features.

Aims and Methods: This retrospective study was conducted between January 2013 and April 2018. Sixteen patients were hospitalized in our center for acute pancreatitis associated with biliary fistulating HLC assessed by ultrasound and computed tomography (CT) and ERCP. The data collected were: age, sex, severity of pancreatitis, imaging data, modalities and outcomes of endoscopic and surgical treatment

Results: The average age of our patients was 44.33 years (20–66). We observed a female predominance with a sex ratio F/H of 1.3. All patients had acute pancreatitis associated with angiocholitis. Only 12.5% (n = 2) of the patients had past history of surgical cure of HLC. Nine patients (56.25%) had systemic inflammatory response syndrome (SIRS) at admission. In CT, Balthazar's pancreatitis stages A, B, and C accounted for 87.5% (n = 14) and the E stage for 12.5% (n = 2). The hyatid liver cyst was classified stageIII according to GHARBI classification in 62.5% of patients (n = 10). The size of the cyst varied between 4 and 9cm. The common bile duct (CBD) was dilated in all patients and the cystobiliary fistula was identified in 68.75% patients (n = 11). ERCP showed cystic fistula and lacunar images at the level of VBP followed by evacuation of membranes after sphincterotomy in 87.5% of patients (n = 14) and two of our patients had free CBD with visualization of cystic fistula. All patients had surgical cure of their HLCby the technique of resection of the salient dome and closure of the cystobiliary fistula. After treatment, one patient had anaphylactic shock following intraoperative rupture of the cyst, and another patient had infection of the residual cavity, he benefited from percutaneous drainage afterwards.

Conclusion: Acute pancreatitis is an exceptional complication of hydatic liver cyst. It is often associated with angiocholitis. Imaging allows diagnosis and visualization of cystic fistula in 2/3 of cases. The ERCP combined to surgery of HLC remain the key treatment.

Disclosure: nothing to disclose

P1350 WHOLE-EXOME SEQUENCING TO IDENTIFY GENETIC RISK FACTORS FOR MULTIPLE-ORGAN FAILURE IN SEVERE ACUTE PANCREATITIS

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Introduction: Acute pancreatitis has a severe disease course in 20% of the patients, often characterized by persistent (multiple-) organ failure. It is largely unknown what factors contribute to this severe complication. Genetic risk factors are thought to enhance severity in complex traits like acute pancreatitis, and this could be an explanation for observed difference in phenotype. However, discovery and validation of novel genetic associations often requires large sample sizes. One strategy to maximize power is to select and compare patients with extreme phenotypes.[1]

Aims and Methods: A case-control study with an extreme phenotype approach was performed to identify genetic risk factors for multiple organ failure in patients with acute pancreatitis. The study population was a Dutch cohort of 387 patients that were potentially eligible for inclusion in a randomized clinical trial that investigated the efficacy of prophylactic probiotics in patients with predicted severe acute pancreatitis (PROPATRIA).[2] Consent was given for the use of stored blood for genetic studies in acute pancreatitis. Nine patients with early multiple-organ failure were case-matched with mild patients in a 1:1 ratio. After DNA isolation and exome capture, the samples were sequenced on an Ion-Proton platform. Candidate variants that are associated with multiple-organ failure were identified using bio-informatics approaches.

Results: Exome sequencing resulted in 161.696 variants that passed quality control, of which 38.333 were synonymous and subsequently selected for downstream analyses. Of these, 153 variants were overrepresented in patients with multiple-organ failure. Gene-set enrichment analyses showed that one gene-set, *KEGG antigen presentation and processing*, harbors more variants than can be expected by chance. Among the highest ranking candidate variants were in the caspase gene family, *CASP8* and *CASP10*, which are key regulators of apoptosis. Other promising variants are in genes involved in the innate immunity, such as *HLA-DQB1*, *KIR2DS4* and *FCGR3A*. Finally, a candidate list of 52 variants was constructed for the validation process.

Conclusion: This is the first study that identifies genetic risk factors of multiple-organ failure in acute pancreatitis using Next-Gen sequencing. Whole-exome

sequencing discovered novel candidate variants that are related to multi-organ failure during acute pancreatitis. These results are currently being validated in a larger international cohort. Discovery of causal genetic risk factors could potentially give insight in the mechanisms that lead to multiple-organ failure and even provide for highly needed, novel targets for drug development.
Disclosure: Nothing to disclose

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P1351 PULMONARY FUNCTION IN THE EARLY PHASE OF ACUTE PANCREATITIS: A PROSPECTIVE COHORT STUDY

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Introduction: During the early phase of acute pancreatitis (AP), which lasts about one to two weeks, about two-thirds of the patients develop respiratory complications [1]. The pathophysiological mechanisms are complex. Activated pancreatic enzymes are important mediators of severe pancreatic inflammation and systemic toxicity including activation of the complement system, over activation of the leucocyte system, and the involvement of the inflammatory mediators, which in turn lead to pulmonary endothelial and epithelial barrier dysfunction [2]. Pulmonary complications based on gas exchange, chest x-rays and computerized tomography scans have been evaluated [3,4]. Only few studies have attempted to evaluate the pulmonary function in the early phase of AP and with conflicting results [5,6].
Aims and Methods: To evaluate the changes in pulmonary function tests during the early phase of acute pancreatitis (AP). We included patients with their first attack of AP regardless of aetiology or disease severity admitted to our department in the period February 2016 to June 2017. The diagnosis of AP was based on revised Atlanta criteria [7].
Severe AP was defined as C-reactive protein (CRP) >150 mg/l. Patients were evaluated on day 1, 2, 3, 6, and 10, and one month after hospital discharge in our outpatient clinic. We measured plasma values of CRP, white blood count (WBC), amylase and albumin, and performed chest x-rays. Pulmonary function tests included the % predicted: forced expiratory volume during the first second (FEV1), forced vital capacity (FVC), total lung capacity (TLC), diffusion lung capacity (DLCO) and the ratio between DLCO and alveolar volume (DLCO/VA). Patient characteristics were summarized using means with standard errors (SD) or proportions. Groups were compared using t-test or one-way analysis of variance (ANOVA) with Bonferroni's correction for multiple comparisons.
Results: A total of 44 patients (52% men; mean age 52 years; gallstone pancreatitis 66% and alcohol related pancreatitis 20%) admitted with their first attack of AP and 22 healthy controls were included. Eighteen patients (41%) developed severe AP. Six patients (14%) required treatment at the intensive or semi-intensive care unit. Three patients died (7%) during admission. Twenty-eight percent developed pulmonary complications with pneumonia, atelectasis and/or pleural effusion. Thirty-four percent required oxygen therapy, and 34% required continuous airway pressure. None required mechanical ventilation or pleural drainage.
From day one, patients had impaired FEV1, FVC, DLCO, and TLC compared with controls ($p < 0.0001$ in all analyses). The pulmonary dysfunction was greater for patients with lung complications compared with controls ($p < 0.001$) and patients without lung complications ($p < 0.001$). Evidence of pulmonary dysfunction, especially DLCO, was also seen after discharge.
Conclusion: This study suggests that patients with AP develop pulmonary dysfunction, probably due to combination of extra-pulmonary causes and alveolar damage, from the first day after hospital admission and that the dysfunction may last for several weeks after hospital discharge.
Disclosure: L.L.G. acted as investigator in clinical trials funded by Merck, Abbvie, Intercept, and Norgine, got travel expenses covered by Novo Nordisk, and gave lectures funded by Eli Lily and Norgine. The remaining authors declare no conflicts of interest.

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P1352 DEVELOPMENT OF A SCORE TO DETERMINE THE RISK OF ACUTE BILIARY PANCREATITIS RELAPSE BEFORE CHOLECYSTECTOMY

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Introduction: International guidelines for Acute Pancreatitis (AP) recommend that patients with Acute Biliary Pancreatitis (ABP) should undergo cholecystectomy during index admission or in 4 weeks' time after discharge. However, this recommendation is not consistently followed and the disease recurs in a proportion of patients. A system is needed to determine the risk of recurrence after ABP to prioritize patients for cholecystectomy in the surgical waiting list.
Aims and Methods: We developed a model to determine the recurrence of ABP, based on demographic data, endoscopic procedures and laboratory tests at admission for a first episode of ABP.
A retrospective cohort study of patients admitted at our Department from 2010 to 2015 with a first episode ABP was carried out. All patients were prospectively enrolled in a central electronic medical record (EMR), which is shared by all the hospitals and health centres around the north-west of Spain. Biliary aetiology was defined by the presence of stones, or sludge/microlithiasis in the CBD or gallbladder at abdominal ultrasound, EUS or MRCP, together with the absence of AP relapse over at least 2-year follow-up after cholecystectomy. Liver laboratory tests at admission were recorded. Primary outcome was ABP recurrence during the six-month period after first admission for ABP. Survival analysis was performed using the Kaplan-Meier method. Factors associated with ABP recurrence were scored and patients were classified as low, intermediate and high risk of relapse according to the total score. A Cox regression to compute hazard ratios (HR) and 95% CIs to determine associations between risk of progression and scores were used.
Results: 353 patients with a first episode of ABP were included. The median time for cholecystectomy was 135 days (range 72–199). After exclusion of patients who waited longer than 6 months for cholecystectomy, 221 patients were finally included; 135 (60.5%) were female, mean age 67.6 years (range 51.2 to 77.7). ABP relapsed in 56 patients (25.1%). Serum levels of alkaline phosphatase, endoscopic sphincterotomy (EE) and severity of AP were significantly associated with the risk of ABP relapse. Scores assigned (Table) identified patients at risk of ABP relapse with a c-statistic of 0.63 (95% CI 0.57–0.68), ($p < 0.001$), HR 3.33 (95% CI 1.73–6.40). Patients in the high, intermediate and low-risk group had a rate of ABP relapse of 21.5%, 3.6 and 0%, respectively.
Conclusion: A score system (named Recurrence Acute Biliary Pancreatitis (RABP) score) was developed based on admission serum levels of alkaline phosphatase, EE and severity of AP. The RABP score identified patients with ABP at low, intermediate and high risk of recurrence, allowing patients in the cholecystectomy waiting list to be prioritized.

Serum alkaline phosphatase	Score
0 to 263 (Normal limit)	5
264 to 526 (1–2 ULN)	4
527 to 789 (2–3 ULN)	3
790 to 1052 (3–4 ULN)	2
>1052 (>4 ULN)	0
Severity of AP	
Mild AP	4
Moderate AP	2
Severe AP	0
ERCP + EE	
No	4
Yes	0

ULN, upper limit of normal.
Low risk: 4 to 8 points; intermediate risk: 9 to 11 points; high risk: 12 to 13 points

[Relapsing Acute Biliary Pancreatitis Score.]
Disclosure: Nothing to disclose

P1354 UTILITY OF ERCP IN ACUTE BILIARY PANCREATITIS

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Introduction: The timing of, and indication for ERCP in acute biliary pancreatitis (ABP) is an unresolved issue. Whilst expert opinion suggests early ERCP (<72 hours) should be performed in the setting of cholangitis and ongoing obstruction, lack of consensus guidelines means that practise is variable. Data suggests that often ERCP is not necessary as most ductal gallstones pass spontaneously.

Aims and Methods: The purpose of this study was to assess the use of ERCP in the setting of ABP, specifically evaluating timing and findings at ERCP. We retrospectively reviewed the case notes of all patients admitted to Brighton and Sussex University Hospitals NHS Trust with a diagnosis of ABP between 1st January 2015 and 31st December 2017. Data recorded included age, sex, LFTs on admission, length of stay, and imaging findings. If ERCP was performed, the timing and ERCP findings were analysed, and details of any subsequent cholecystectomy were recorded.

Results: One hundred and fifty seven patients (64 male, 93 female) were admitted with acute biliary pancreatitis during the three-year period with a median age of 63 (Range 14–101). 69 patients (44%) underwent ERCP. 16 patients (23%) had ERCP within 72 hours. The median time to ERCP from admission was 10 days (range 1- 48 days). ERCP was unsuccessful in 4 cases (5.7%). Stones were found in less than half the cases (32/65, 49%). Compared with definite imaging findings, equivocal imaging findings (eg possible stone and biliary dilatation only) was associated with no stone being found at ERCP (66% in equivocal, vs 42% in definite, $p = 0.05$). There was a trend towards lower chance of finding stones at ERCP in those who had the procedure 3–14 days from admission compared with those ERCP'd within 72 hours (46% vs 75%, $p = 0.09$). 26 patients proceeded to cholecystectomy and median number of days before cholecystectomy is 33.5 days (range 4–663 days)

Conclusion: In ABP, ERCP is not always indicated even when stones are seen in the CBD on imaging. Our data suggests that stones often pass spontaneously after the imaging and that unnecessary ERCPs are performed. We suggest that in selected cases (eg those with equivocal imaging), repeat imaging/clinical evaluation is performed at 10–14 days to reassess the need/indication for ERCP.

Disclosure: Nothing to disclose

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P1355 CLINICAL AND NUTRITIONAL FEATURES ARE PREDICTABLE FOR HOSPITALIZATION IN PATIENTS WITH CHRONIC PANCREATITIS: A COHORT STUDY

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Introduction: The majority of deaths (60–75%) in patients with chronic pancreatitis (CP) are due to extra-pancreatic consequences of the disease like cardiovascular events, osteoporosis, and infections. Data are lacking regarding the risk of such events and their relation with exocrine (EPI) or endocrine pancreatic insufficiency and the nutritional status during the FU. Recent guidelines recommend the use of the MUST score to assess the nutritional status of CP patients.

Aims and Methods: To evaluate the incidence of extra-pancreatic events in patients with CP during the follow-up and their association with CP features, pancreatic function and nutritional status.

Retrospective analysis of a single-centre cohort of CP patients prospectively enrolled and followed-up. Epidemiological data, risk factors, new hospitalizations were recorded at the diagnosis and at FU visit. EPI assessed by fecal elastase, MUST score evaluated as a nutritional tool. The occurrence of death and of extra-pancreatic events was recorded. Differences in terms of clinical features, risk factors and nutritional factors analysed by fisher and t-test. Hospitalization -free survival was evaluated with Kaplan-Meier and Cox regression analysis.

Results: 110 patients (64% male; mean age 57) enrolled with a median FU of 36 months. 52% had a toxic aetiology and 53% had EPI. 10% of patients had severe CP and 29% had a MUST score ≥2 at diagnosis. During the FU, 2% of patients died, 2% had cardiovascular events, 8% had infections and 16.4% needed endoscopic/surgery treatment. 34% needed hospitalization, in 49% for extra-pancreatic events. There was no association between EPI and extra pancreatic events. A BMI <20 and a MUST score≥2 were borderline significant for being associated with an increased risk of hospitalization (HR 2.1 95% CI 0.7–6 p 0.07; HR 1.8 95% CI 0.8–3.9 p 0.09). Toxic aetiology had a two-fold risk of new hospitalization (HR 2.9 95% CI 0.9–5.7 p 0.001). Patients with severe disease had a higher risk of hospitalization (HR 4.5 95% CI 0.9–22 p 0.0002) and more often needed endoscopic/surgery treatment (55% vs 13% p 0.006).

Conclusion: About 30% of patients were at high risk of malnutrition at diagnosis, and 34% of them were hospitalized during the FU, often for extra-pancreatic events that caused death in 2%. Toxic aetiology and severe disease are associated with hospitalization and MUST score seems to be less useful in predicting these events.

Disclosure: Nothing to disclose

P1356 OCTREOTIDE AMELIORATES PANCREATIC FATTY ACID SYNTHESIS AND β-OXIDATION IN HIGH FAT DIET-INDUCED PANCREATIC STEATOSIS

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Introduction: Pancreatic steatosis is an uncommon pathological condition caused by adipose ectopic deposition and metabolic disorder. Somatostain, a neuroendocrine hormone, can suppress the release of gastrointestinal peptides, including suppression of pancreatic secretion. Octreotide, a synthetic analogue of Somatostain with a longer half-life, is used as a replacement of somatostain due to the similar effects.

Aims and Methods: This study aims to investigate the underlying mechanisms of pancreatic steatosis and octreotide effects. A total of 60 C57BL/6J mice were randomly allocated to normal chow (NC), high-fat diet (HFD), and HFD + Octreotide groups. Body weight, food intake, pancreatic weight, serum and pancreatic lipid levels, level of serum insulin, glucose tolerance test and pancreatic tissue alteration at histology were investigated. Expression of fatty acid synthesis pathway genes and proteins—adenosine monophosphate-activated protein kinase (AMPK), sterol regulatory element binding protein-1c (SREBP-1c), fatty acid synthetase (FASN), acetyl-CoA carboxylase (ACC), and fatty acid β-oxidation pathway—peroxisome Proliferator activated receptor α (PPAR α), acyl-CoA oxidase-1 (ACOX-1) and carnitine palmitoyltransferase-1 (CPT-1) were measured with RT-PCR and western blot.

Results: Mice with HFD showed increased body and pancreatic weight, serum and pancreatic lipid levels, accompanied by aggregated lipid droplets in pancreatic acinar cells, which were declined with octreotide treatment. In HFD group the mRNA and protein levels of SREBP-1c and its target genes were significantly elevated, while the expression of β-oxidation related genes were decreased compared to NC group. Octreotide reduced fatty acid synthesis pathway, at the same time increased β-oxidation pathway.

Conclusion: Octreotide can improve pancreatic steatosis in high-fat diet mice, probably by inhibiting pancreatic fatty acid synthesis and β-oxidation pathways.

Disclosure: Nothing to disclose

P1357 PROSPECTIVE STUDY EVALUATING THE ENDOCRINE AND EXOCRINE PANCREATIC FUNCTIONS AFTER ENDOSCOPIC TREATMENT OF CHRONIC PANCREATITIS

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Introduction: Studies reporting on function after endoscopic treatment of chronic pancreatitis are scarce.

Aims and Methods: The aim of the study was to investigate prospectively the evolution of pancreatic endocrine and exocrine function in patients undergoing endoscopic treatment based on endocrine function parameters and fecal tests for exocrine function. Between November 2013 and December 2016, patients

requiring endoscopic drainage for chronic pancreatitis with symptomatic ductal obstruction were enrolled in the study. Endocrine function was evaluated by HbA1c, fasting blood insulin level, C-peptide level and HOMA test before endotherapy and at 1, 3, 6 and 9 months following endotherapy. Exocrine function was evaluated by 72h fecal fat test, fecal acid steatocrit and elastase level. A comparative analysis between follow-up points (1,3,6 and 9 months) and baseline values of variables was performed.
Results: Thirty-four patients (age: 54+12 yr, 67.6% male) were included. Statistically significant improvement in HbA1c was attained at 1 (6.6 vs. 6.2, *p=0.001*), 3 (6.6 vs. 6.1, *p=0.005*) months and at maximum follow-up (6.6 vs. 6.0, *p=0.006*) compared to before drainage. HOMA-B values were statistically higher at 1 (53.0 vs. 67.2, *p=0.002*), 3 (53.0 vs. 68.6, *p=0.001*), 6 (53.0 vs. 75.4, $p < 0.001$) months and at maximum follow-up (53.0 vs. 75.0, $p < 0.001$). Clinical success of endoscopic drainage defined as 50% reduction in VAS score as compared to before drainage was recorded in sixty-eight, seventy-nine, seventy-five and seventy-two percent of patients at 1, 3, 6 and 9 months respectively. Exocrine function was not assessable due to patients' poor compliance to stool sampling.
Conclusion: To our knowledge, our study is the first to evaluate prospectively the effect of endoscopic treatment on the endocrine function of the pancreas as the principal aim. Our study has shown significant improvement in endocrine function at 1, 3, 6 and 9 months following endoscopic drainage. All endocrine function variables (HbA1C, FPG, FBIL, C-peptide, HOMA-B) improved their values at each follow-up point. Similar results were obtained in diabetic patients under insulin therapy or oral antidiabetic medications as well as in non-diabetic patients. In conclusion, endoscopic therapy in chronic pancreatitis improves glycaemic control and pancreatic endocrine function in the short-and mid-term follow-up. We therefore suggest that it might become a new indication for treatment even in non-diabetic patients.
Disclosure: Nothing to disclose

P1358 THERAPEUTIC EFFICACY OF PANCREATIC ENZYME SUPPLEMENT AND CLINICAL CHARACTERISTICS IN EARLY CHRONIC PANCREATITIS

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Introduction: Chronic pancreatitis (CP) is a progressive and permanent destruction of the pancreas resulting in exocrine and endocrine insufficiency and often causing chronic disabling pain. Recently, early CP has been recognized by typical pancreatic-type pain, normal conventional imaging examinations, and subtle findings of CP using endoscopic ultrasound (EUS). However, it remains unclear whether the clinical characteristics including EUS findings and symptoms of early CP are reversible. In this study, we retrospectively evaluated the efficacy of treatment for early CP during long-term follow up.
Aims and Methods: Thirty-four patients with early CP were treated with protease inhibitors and pancreatic enzymes for at least two years. They showed typical EUS findings for early CP, presented with repetitive abdominal pain and elevated serum pancreatic enzyme levels. The outcomes measured were changes in abdominal symptoms, serum pancreatic enzyme levels, pancreatic exocrine functions, and EUS findings.
Results: The median treatment duration was 66.5 months, during which 80% of the patients showed decreased pain intensity. The face rating scale significantly improved compared to before treatment (1.1 vs. 2.4 points, $p < 0.01$). Serum pancreatic enzyme levels (amylase, lipase, and elastase-1) significantly decreased compared to before treatment ($p < 0.05$). Although EUS findings revealed some differences compared to before treatment in 4 of the 24 patients, the changed EUS findings were not related to the presence or absence of improvement in abdominal symptoms and serum pancreatic enzyme levels.
Conclusion: Our results indicate that therapeutic intervention for early CP should have clinical significance. However, the changes of early CP may be irreversible because there was no correlation between time-dependent changes in EUS findings and the improvement of clinical parameters.
Disclosure: Nothing to disclose

P1359 CLINICAL OUTCOME OF EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY COMBINED WITH ENDOSCOPIC TREATMENT FOR CHRONIC PANCREATITIS WITH PANCREATIC STONE

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Introduction: In ESGE guidelines, also in Japanese guidelines, endoscopic treatment and extracorporeal shock wave lithotripsy (ESWL) for symptomatic chronic pancreatitis with/without pancreatic stone is recommended, however, the selection of treatment methods and procedures are not established yet.
Aims and Methods: Evaluating the clinical outcome of the chronic pancreatitis with pancreatic stone patients underwent ESWL in our center.
59 consecutive patients underwent ESWL for pancreatic stone with chronic pancreatitis between January 2010 and December 2014 at our tertiary referral center in Japan.
ESWL was performed under X-ray fluoroscopy using a device of MODULITH SLX (Storz Medical, Switzerland). If it was difficult to recognize stone by X – ray, ENPD tube was indwelled and it was performed under the contrast.
In patients with pancreatic duct stricture, pancreatic stent insertion for 2 to 3 months was applied in addition to ESWL. After the initial treatment, we deployed ENPD tube and clinical success was evaluated by pancreatography via ENPD tube. If the outflow was well confirmed, the patients were observed without additional procedure. If clinical success was not obtained, the patients underwent additional ESWL and/or upgraded the size of the stent or placing of multiple stents.
Primary endpoints were the results of the treatment and the asymptomatic period, and secondary endpoints were the complications of the procedures, and the risk factors for the recurrence.
Results: Of the 59 patients, the median age was 60 years old, 44 males and 15 females. The etiologies of pancreatitis were alcohol (n = 40), idiopathic (n = 12), autoimmune pancreatitis (n = 5) and pancreas divisum (n = 2). The region of the stones were pancreas head (n = 41), body (n = 9), tail (n = 3) and multiple regions (n = 6). 31 patients (52.9%) needed pancreatic stenting for the main pancreatic duct strictures.
In all patients the treatments were successful. The median period of the treatment were 62 days (2–637). The median number of all procedures were four (1–10), ESWL were two (1–6). During the median observation period of 412 days (4–2794), one year asymptomatic duration rate was 76.7%, and three years rate was 55.9% using Kaplan-Meier method.
The risk of recurrence was high in the patients with non-alcoholic pancreatitis and the obstruction/stricture of body-tail. Seven patients (12%) had the complications after ERCP: pancreatitis (n = 3), incompetence of basket catheter (n = 2), guidewire penetration (n = 1), cholangitis (n = 1). They had improvement with conservative or endoscopic therapy.
In order to detect the risk factors for the recurrence of the symptoms we performed univariate analyses, non-alcoholic patients (p = 0.02) and the obstruction/stricture of body-tail (p = 0.009) resulted as significantly correlated with the recurrence.
We also performed a multivariate logistic regression analysis, non-alcoholic patients (OR = 3.71, 95% C.I.: 1.09–12.6, p = 0.036) and the obstruction/stricture of body-tail (OR = 4.42, 95% C.I.: 1.28–15.3, p = 0.019) also resulted as significantly correlated with the recurrence.
Conclusion: ESWL combined with endoscopic treatment for chronic pancreatitis with pancreatic stone is the safe and effective treatment.
The risk of recurrence was high in the patients with non-alcoholic pancreatitis and the obstruction/stricture of body-tail.
Disclosure: Nothing to disclose

P1360 PANCREATIC EXOCRINE AND ENDOCRINE INSUFFICIENCY AND CARDIOVASCULAR RISK IN PATIENTS WITH CHRONIC PANCREATITIS (CP). A PROSPECTIVE, LONGITUDINAL COHORT STUDY

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Introduction: Previous studies have suggested that chronic pancreatitis (CP) is associated with increased risk of cardiovascular (CV) disease independently of other major risk factors.
Aims and Methods: We evaluated the risk of CV events in a well-phenotyped cohort of patients with CP and its association with pancreatic exocrine insufficiency (PEI) and pancreatic endocrine insufficiency (pancreatogenic diabetes) among other CV risk factors.
Prospective, longitudinal cohort study of patients with CP, followed-up at the Pancreas Unit of the University Hospital of Santiago de Compostela, Spain.
Results: 430 patients were included (mean 47.8 ± 14.4 years of age, 79.1% male). Mean follow-up was 8.6 ± 4.6 years. CP etiology was toxic (alcohol and/or smoking) in 290 patients (67.4%). PEI and pancreatogenic diabetes mellitus (DM) were present in 29.3% and 29.5% of the patients, respectively. A total of 45 cardiovascular events was prospectively recorded (10.5%); 21 patients had a major cardiovascular event (stroke or myocardial infarction) and 27 developed clinically relevant peripheral arterial disease. A higher incidence of cardiovascular events was recorded in patients with PEI than in those without (incidence rate ratio 3.67, 95% confidence interval (CI) 1.92–7.24; p < 0.001). In the multivariate analysis, PEI without DM (OR 4.96; IC95%: 1.68 to 14.65), coexistence of PEI and DM (OR 6.54; IC95%: 2.71 to 15.77), arterial hypertension (OR 3.40; IC95%: 1.50 to 7.72) and smoking (OR 2.91, IC95%: 1.07 to 7.97) were independently associated with increased CV risk.
Conclusion: Together with known major cardiovascular risk factors like smoking and hypertension, PEI is significantly associated with the risk of cardiovascular

events in patients with CP. Coexistence of pancreatogenic diabetes increases the CV risk associated with PEI in CP.

	Univariate		Multivariate	
Variable	OR (95% CI)	P value	OR (95% CI)	P value
Age at CP diagnosis, years (categorized)				
≤38	1.00			
39–48	3.27 (1.02–10.47)	0.046		
49–57	4.49 (1.43–14.13)	0.01		
≥58	4.49 (1.44–14.01)	0.007		
Male Gender	13.23 (1.8–97.39)	0.011	7.16 (0.92–55.99)	0.061
Pancreas (categorized)				
No DM/No PEI	1.00			
DM (No PEI)	2.27 (0.76–6.84)	0.144	1.05 (0.28–3.95)	0.947
PEI (No DM)	3.97 (1.51–10.42)	0.005	4.96 (1.68–14.65)	0.004
PEI and DM	8.64 (3.93–19.01)	0.000	6.54 (2.71–15.77)	0.000
Tobacco consumption	4.38 (1.81–10.60)	0.001	2.91 (1.1–7.97)	0.037
Alcohol consumption	2.26 (1.09–4.70)	0.029		
Hypercholesterolemia	0.9 (0.47–1.7)	0.734		
Hypertension	3.25 (1.63–6.47)	<0.001	3.40 (1.50–7.21)	0.003

CI, confidence interval; CP, chronic pancreatitis; CV, cardiovascular; EUS, endoscopic ultrasound; OR, odds ratio PEI, pancreatic exocrine insufficiency; SD, standard deviation

[Analysis of variables associated with CV events (logistic regression model)]

Disclosure: Nothing to disclose

P1361 OVERALL CARDIOVASCULAR RISK ASSESSMENT IN PATIENTS WITH CHRONIC PANCREATITIS AND EXOCRINE INSUFFICIENCY RECEIVING ENZYME REPLACEMENT THERAPY

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Introduction: Patients with chronic pancreatitis (CP) and pancreatic exocrine insufficiency (PEI) are at increased risk of cardiovascular events. Cardiovascular risk (CVR) assessment leads to proper primary and secondary prevention and may improve the quality of life.

Aims and Methods: To investigate CVR in patients with CP and PEI. Study enrolled 82 patients (48 males, mean age 49.46 years), receiving pancreatic enzyme replacement therapy due to PEI. CVR was assessed by Framingham risk score (FRS) used to predict an individual chance of developing cardiovascular disease in the next 10 years; by routine lipid profile and apolipoproteins (apo): apo A-I (protective against CV events, HDL-associated), apo B and C-III (proatherogenic), Apo B/Apo A-I ratio (associated with myocardial infarction prediction) and by vitamin D levels (using a validated, DEQAS certified ID-LC-MS/MS method with accuracy and precision within 7.5% and linearity range 3.0–300.0nmol/L). Malnutrition risk was evaluated by MUST (Malnutrition Universal Screening Tool). Severity of CP and pancreatic structural changes were assessed by M-ANNHEIM and Cambridge classifications, respectively. Statistics was performed via SPSSv22.

Results: According to FRS 25.61% of the patients were with high CVR, 20.73% – with moderate and 53.66% – with low. We observed a tendency to increase CVR (FRS) as the severity of both morphological changes and CP by M-ANNHEIM worsened. Vitamin D levels were significantly lower in patients with moderate CVR by FRS versus those at low risk, $p = 0.05$. Statistically significant correlations occur between CVR by FRS and HDL ($p = 0.0002$), total cholesterol ($p = 0.02$), LDL ($p = 0.02$), non-HDL ($p = 0.003$), VLDL ($p = 0.0002$), total cholesterol/HDL ratio ($p = 0.0001$). In patients with high CVR by FRS we found significantly higher apo B ($p = 0.02$) and lower apo A-I ($p = 0.007$) levels, as well as an increased risk of myocardial infarction using Apo B/Apo A-I ratio ($p = 0.04$). Dyslipidemia with borderline high and high levels of the atherogenic total cholesterol, triglycerides and/or LDL was evaluated in 50.68% of patients with CP. There was no significant difference in the incidence of dyslipidemia compared to both CP severity and structural changes. Low HDL levels were found in 35 of the studied patients (21 men) and high non-HDL levels – in 71.23%. There was a statistically significant difference in HDL levels between mild and moderate CP, $p = 0.04$. High total cholesterol/HDL ratio (above 5), which is associated with higher CVR, was observed in 41.1% of the patients. A progressive increase in the total cholesterol/HDL ratio was observed as the CP severity increased. Significant lower apo A-I and vitamin D levels were found with malnutrition risk and lipid malabsorption worsening ($p = 0.047$, $p = 0.032$). A significant difference was found in apo A-I levels between mild and moderate CP ($p = 0.007$) and between mild and advanced CP ($p = 0.04$) and in Apo C-III between mild and advanced CP ($p = 0.047$). With morphological changes worsening significantly lower apo A-I levels were found between Cambridge grade I and Cambridge grade III ($p = 0.03$) and between Cambridge grade I and Cambridge grade IV ($p = 0.005$). Similar observation was made for apo C-III between Cambridge grade I, II and Cambridge III, IV ($p = 0.000$).

Conclusion: Overall CVR assessment using FRS, lipid profile and apolipoproteins could identify patients at high risk of cardiovascular events and allows the proper control of the risk factors.

Disclosure: Nothing to disclose

P1363 THE COMMON TRUNCATION VARIANT P.W358X OF THE PNLIPRP2 LIPASE IS NOT ASSOCIATED WITH CHRONIC PANCREATITIS

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Introduction: Pancreatic Lipase-Related Protein 2 (PNLIPRP2) is a lesser lipase isoform which can digest long chain triglycerides, diglycerides and monoglycerides. In vitro experiments showed that thecommon nonsense variant c.1074G>A (p.W358X) causes the formation of a shorter misfolded protein that is not secreted well but induces endoplasmic reticulum (ER) stress. ER stress is a known susceptibility factor for chronic pancreatitis, suggesting that the p.W358X mutation of the PNLIPRP2 gene might contribute the development of pancreatitis.

Aims and Methods: Our aim was to investigate whether the p.W358X mutation of the PNLIPRP2 gene is associated with idiopathic and alcoholic chronic pancreatitis. In our study we enrolled 115 patients with idiopathic and 142 patients with alcoholic chronic pancreatitis and 200 controls recruited by the Hungarian Pancreatic Study Group (HPSG – www.pancreas.hu). Exon 11 and its flanking intronic regions were analyzed by Sangersequencing. Expression of the PNLIPRP2 gene was studied by RT PCR using human donor pancreas cDNA samples.

Results: When allele frequencies were considered, the p.W358X mutation was not overrepresented either in the idiopathic or the alcoholic chronic pancreatitis groups compared to the controls (54.8% and 50% vs. 52%, respectively). RT-PCR on a homozygous cDNA sample indicated drastically reduced PNLIPRP2 expression at the mRNA level. Additionally, we identified 5 more PNLIPRP2 variants (c.1071–379delG, c.1071–321C>T, c.1084A<G p.I362V, c.1161A>Gp.S387=and c.1181+55C>A) but none were associated with chronic pancreatitis.

Conclusion: The p.W358X mutation of the PNLIPRP2 gene is not associated with chronic pancreatitis. Expression of the truncated protein is inhibited at mRNA level likely by "nonsense-mediated mRNA decay", therefore, this variant does not cause ER stress in the human pancreas.

Disclosure: Nothing to disclose

P1364 SERUM ALBUMIN LEVEL, PROGNOSTIC NUTRITIONAL INDEX, AND CA19–9 ARE TREATMENT-PREDICTIVE MARKERS FOR DISEASE CONTROL RATE IN PATIENTS WITH UNRESECTABLE PANCREATIC CANCER

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Introduction: Pancreatic cancer (PC) is one of the most difficult human malignancies to treat with poor outcome. A combination of gemcitabine plus *nab*-paclitaxel (GN) as well as FOLFIRINOX (FFX) is preferentially used for unresectable PC. However, it is not clear which regimen is appropriate for unresectable PC. For practicing evidence-based chemotherapy, we tried to find treatment-predictive markers in PC patients treated with GN and/or FFX.

Aims and Methods: We retrospectively investigated 68 advanced-stage (III and IV) of PC patients treated with GN. Patients backgrounds, hematological and chemical laboratory tests just before the chemotherapies were evaluated to detect the predictive factors for survivals and therapeutic effects with logistic regression analyses.

Results: Statistical differences ($p < 0.15$) were observed in neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), neutrophil count, prognostic nutritional index (PNI), platelet count, CA19-9 level, white blood cell count, and serum albumin level between longer OS group (OS ≥1 year) and shorter OS group (OS <1 year) by univariate analyses. Kaplan-Meier analysis revealed that no statistical difference ($p = 0.3144$) on median OS between GN (375 days) and FFX (393 days) treatments. The ratio of PR/SD (disease control rate) was shown to be statistically higher than PD ratio in higher PNI ($p = 0.03$) or higher albumin ($p = 0.05$) group treated with GN, and also in lower CA19-9 group ($p = 0.08$) treated with FFX.

Conclusion: PNI, serum albumin level, and CA19-9 are treatment-predictive markers for disease control rate in patients with unresectable PC treated with GN, GN, and FFX, respectively. Statistical difference in median OS was not determined between GN therapy and FFX therapy.
Disclosure: Nothing to disclose

P1365 DIAGNOSTIC ACCURACY OF CARCINOEMBRYONIC ANTIGEN IN DIFFERENTIATING MUCINOUS AND NON-MUCINOUS PANCREATIC CYSTIC NEOPLASMS: SYSTEMATIC REVIEW AND INDIVIDUAL PATIENT DATA META-ANALYSIS

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Introduction: Distinction between the different types of pancreatic cystic neoplasms (PCNs) is essential, since non-mucinous PCNs are mostly benign without need for surveillance, whereas mucinous PCNs are considered premalignant and require either surveillance or surgical resection. We aimed to systematically review the diagnostic accuracy of CEA in differentiating mucinous and non-mucinous PCNs and to determine the optimal cut-off value of CEA using individual patient data meta-analysis.
Aims and Methods: A systematic literature search was performed in PubMed, EMBASE and the Cochrane Library for studies investigating the accuracy of CEA in differentiating mucinous and non-mucinous PCNs. Individual data of patients with histopathological confirmation of the type of PCN were extracted if available from the included studies to determine the optimal cut-off value of CEA.
Results: Nineteen studies were included, with a total of 1477 patients. Meta-analysis of 16 studies with 1298 patients showed that the pooled sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of the most commonly used cut-off CEA >192ng/ml for the differentiation between mucinous and non-mucinous PCNs were: 63.8% (95% CI 60.6%-67.0%); 85.2% (95% CI 81.3%-88.5%); 90.5% (95% CI 88.2%–92.3%) and 51.7% (95% CI 49.2%–54.0%).
Individual data of 408 patients from seven studies were available and could be extracted to determine the optimal cut-off value of CEA. A cut-off CEA≥20ng/ml achieved the highest accuracy for differentiating between mucinous and non-mucinous PCNs with pooled sensitivity of 91.1% (95%CI 87.5%-93.9%) and 93% specificity (95% CI 84.3%-97.7%). The positive predictive value and negative predictive value were 98.4% (95% CI 96.3%–99.3%) and 68.8% (95% CI 60.9%–75.7%), respectively. With CEA ≥20ng/ml, 5 (1.2%) patients would have been over diagnosed, whilst 30 (7.4%) mucinous cysts (15 IPMNs, 9 MCNs and 6 mucinous ductal adenocarcinoma) would have been missed. Whereas with a CEA >192ng/ml, 0 (0%) patients would have been over diagnosed, but 116 (28.4%) mucinous cyst (69 IPMNs, 35 MCNs and 12 mucinous ductal adenocarcinoma) would have been missed.
Conclusion: In conclusion, pancreatic cyst fluid CEA can accurately differentiate histologically verified mucinous cysts from non-mucinous cysts with an optimal cut-off value ≥20ng/ml,which is much lower than previously reported values. For further validation large prospective studies are encouraged.
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P1366 SCREENING TO DETECT PRECURSOR LESIONS OF PANCREATIC ADENOCARCINOMA IN HIGH-RISK INDIVIDUALS EXPERIENCED FROM RAMBAM HEALTH CARE CAMPUS

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Introduction: Pancreatic cancer is a deadly disease that is often detected in late stages due to the unobtrusive nature of its evolution. Various centers around the world are currently investigating the feasibility and yield of surveillance for pancreatic cancer in high-risk individuals. Evidence is beginning to accumulate that surveillance may lead to the early detection of precursor lesions and asymptomatic pancreatic cancer. Proper screening methods and identification of such precursor lesions can allow prophylactic measures and interventions to be administered in order to prevent further fatalities. The primary objective of this project was to check feasibility of identifying precursor lesions in high-risk individuals by endoscopic ultrasound surveillance in attempt to prevent the development of pancreatic cancer or at least detect early cancer.
Aims and Methods: Between 2008 and 2018, a cohort of 123 high-risk individuals came for annual/biannual endoscopic ultrasound screening for pancreatic cancer. Referrals were from both physicians and self-referrals. Inclusion criteria included at least one first-degree relative with pancreatic cancer within 10 years of the age of that first-degree relative, or otherwise within the consensus guidelines recommended criteria. Retrospective and prospectively collected data was obtained, analyzed and compared on the basis of several variables. These variables include age at beginning of screening, gender, smoking, obesity, diabetes and presence of tumor markers. Genetic mutations were taken into account as well as the patients personal and family history of cancer. Each screen date and their respective results and plan were recorded. Pancreatic cancer screening guidelines, based on consensus opinions, have been applied in various centers around the world; however, evidence for effectiveness is lacking. At Rambam Health Care Campus, we have established a cohort of high-risk individuals and herein report our results of screening for pancreatic cancer.
Results: Detection of precursor pancreatic lesions is feasible with endoscopic ultrasound screenings, however adherence remains an important challenge to surveillance of findings. Patients may best be categorized based on specific risk factors, including genetics and family history, as an indication of when to initiate screening.
Average age at first screening was 57. 210 EUS exams have been performed. 22% also submitted to genetic consultations. Overall two patients underwent pancreatic surgery and both have survived long-term. 40% of patients showed any EUS abnormalities.
Conclusion: International Collaborations, such as the International Cancer of Pancreas Screening (CAPS) consorstium, are needed to collate evidence for screening to prevent pancreatic cancer morbidity and mortality, and are essential to achieve proof of concept. Pancreatic cancer is a challenging field and endoscopic ultrasounds alone cannot prevent all cases of pancreatic adenocarcinoma. Screening programs, however, within research protocols may yield actionable results to prevent or at least detect some pancreatic cancers at an early stage. Different countries with varying healthcare systems and budgets may find that variance of screening procedures may be appropriate.
Disclosure: Nothing to disclose

P1367 ASSOCIATION BETWEEN PROGRESSION OF LOW-RISK IPMNS AND DIABETES MELLITUS

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Introduction: Although the incidence of pancreatic cystic lesions has increased, the majority do not progress to pancreatic cancer and the burden of surveillance is significant. In previous studies we and others have identified metabolic parameters, in particular diabetes and obesity, to be associated with pancreatic malignancy. In our cohort of low-risk intraductal papillary mucinous neoplasms (IPMN) surveyed at our institution we sought to evaluate the relationship between progression and the diagnosis of baseline diabetes and new onset diabetes in the presence and absence of obesity.
Aims and Methods: We conducted a retrospective review of prospectively collected data of patients evaluated for a pancreatic cyst between 2003 and 2016. Patients who met clinical criteria for presumed IPMN with no worrisome features or high-risk stigmata at baseline imaging, as defined by the 2012 international Fukuoka guidelines, and ≥12 months of follow-up were included. We collected data on random and fasting glucose values, known clinical diagnosis of diabetes and HbA1C as well as BMI data throughout surveillance. New onset diabetes was defined as a random plasma glucose concentration of ≥200 mg/dl or an HbA1c ≥6.5% at least 3 months after initial diagnosis. Obesity was defined as having a BMI≥30. Statistical analysis was performed with the chi square test and relative risk analysis.

Results: Of 2562 patients who underwent evaluation of a pancreatic cystic lesion, 468 met inclusion criteria. 132 patients (28.2%) had diabetes at index imaging. 32 patients (6.8%) developed diabetes during the period of IPMN surveillance. BMI data was available for 364/468 patients (77.8%). 90/ 364 patients (24.7%) were obese at baseline. 58/468 patients (12.4%) progressed to have IPMNs with worrisome features and 21/468 patients (4.5%) progressed to have IPMNs with high risk stigmata or cancer. Baseline diabetes, with or without obesity, was not associated with a significantly increased risk of progression. New onset diabetes was not associated with a significantly increased risk of developing worrisome features. However, we found new onset diabetes was associated with a significantly increased risk of developing high-risk stigmata or cancer in both the entire cohort (RR 1.14–7.74; p = 0.028) and in non-obese patients (RR 2.16–16.02; p < 0.001).
Conclusion: In this cohort of low-risk clinically suspected IPMNs we found new onset diabetes to be associated with development of high-risk stigmata or cancer. This data further supports the inclusion of new onset diabetes mellitus as a risk factor for IPMN progression.

	Yes	*No*	*p-value*	*Relative Risk (95% CI)*
Diabetes Mellitus at Baseline				
Non-Progressor (n = 389)	28.5%	71.5%	—	—
Progressed to WF (n = 58)	25.9%	74.1%	0.673	0.91(0.57–1.44)
Progressed to HR/ Cancer (n = 21)	28.6%	71.4%	0.997	1.00(0.50–2.00)
Diabetes Mellitus Baseline and Non-Obese (BMI < 30)				
Non-Progressor* (n = 306)	19.0%	81.0%	—	—
Progressed to WF* (n = 42)	11.6%	88.4%	0.266	0.63(0.27–1.48)
Progressed to HR/ Cancer* (n = 16)	18.8%	81.2%	0.984	0.99(0.35–2.82)
New Onset Diabetes Mellitus				
Non-Progressor (n = 389)	6.4%	93.6%	—	—
Progressed to WF (n = 58)	5.2%	94.8%	0.713	0.80(0.25–2.58)
Progressed to HR/ Cancer (n = 21)	19.0%	81.0%	0.028	2.96(1.14–7.74)
New Onset Diabetes Mellitus and Non-Obese (BMI < 30)				
Non-Progressor* (n = 306)	4.2%	95.8%	—	—
Progressed to WF* (n = 42)	2.4%	97.6%	0.564	0.57(0.08–4.18)
Progressed to HR/ Cancer* (n = 16)	25.0%	75.0%	<0.001	5.88(2.16–16.02)

BMI, body mass index; WF, worrisome features; HR, high-risk stigmata; CI, confidence interval * only patients with available BMI data were included in this analysis
[Table 1. Metabolic Parameters and Cyst Progression]
Disclosure: Nothing to disclose

P1368 PREDICTION OF LOCAL RESECTABILITY OF PANCREATIC DUCTAL ADENOCARCINOMA: ARTIFICIAL INTELLIGENCE BEATS HUMAN INTELLIGENCE?

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Introduction: Pancreatic ductal adenocarcinoma (PDA) is the fourth leading cause of cancer-related death with a 5-year survival rate of approximately 7%. While surgery is currently the only potentially curative therapy, only 15–20% of the patients are considered for resection. However, in some 25% of patients the tumor cannot be resected due to unexpected liver or peritoneal metastases. As of now, it is not possible to accurately determine whether PDA patients are suitable for resection and they have to undergo invasive surgery in order to determine the resectability status. Therefore, applying image analysis techniques to routine abdominal CT scans, i.e. quantitative radiomics, could be helpful to predict local resectability of PDA and aid in treatment planning.
Aims and Methods: The aim of our study was to compare the performance of an expert radiologist to that of quantitative radiomics for prediction of local resectability of pancreatic ductal adenocarcinoma on routine abdominal contrast-enhanced CT. We included 50 patients (m:f = 28:22; range 48–79 yrs) with histologically proven pancreatic ductal adenocarcinoma who were operated within 4 weeks of an initial routine portal-venous phase multidetector-row CT examination. An expert abdominal radiologists scored CT data for tumor resectability. Another expert abdominal radiologist drew tumor contours to obtain a volume of interest, from which we computed 90 intensity, shape and texture features. During training the number of features was reduced with a feature selection algorithm and combined with several classifiers to predict local resectability using radiomics.
Results: There were 33 hypo- and 17 iso-attenuating tumors, of which 29 were resectable and 21 non-resectable. The best classification result was obtained with a support vector machine classifier with the feature vector reduced by regularized discriminative feature selection. Accuracy for predicting resectability was 68% for the radiologist, and 74% for radiomics. Sensitivity, specificity, positive and negative predictive value for resectability were 90%, 38%, 67% and 73%, respectively, for the radiologist and 97%, 42%, 70%, and 90%, respectively, for radiomics.
Conclusion: Quantitative CT-based radiomics for prediction of local resectability of pancreatic ductal adenocarcinoma on routine CT, may outperform expert radiologists.
Disclosure: Nothing to disclose

P1369 DOES ABO BLOOD TYPE INFLUENCE LONG-TERM OUTCOMES OF PANCREATIC CANCER IN JAPANESE?

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Introduction: An association between ABO blood type and risk of developing cancer is recognized in some cancers such as pancreatic cancer (PC) and gastric cancer. Additionally, long-term effect of ABO blood type on the clinical course of various cancers are reported i.e. PC, renal cell carcinoma, non-small cell lung cancer. Studies with regards to PC from the western countries investigated the effect of ABO blood type on the survival mostly in resected patients. Within Asia, to date, there is a study from China. However, the results are inconclusive and its impact on the Japanese patients with PC, long term outcomes in particular, is poorly understood.
Aims and Methods: The Ehime Pancreato-Cholangiology (EPOCH) Study Group aimed to determine whether ABO blood type influence long-term outcomes of the Japanese patients with PC. Chart review for patients with PC diagnosed between 2011 and 2013 was conducted within the EPOCH Study Group. Data collection includes age, sex, ABO blood type, Union for International Cancer Control (UICC) stage at diagnosis of PC and outcomes. The chi-square test and Student's t-test were used for statistical analysis, where appropriate. Outcomes were analyzed using the Kaplan-Meier method and Cox proportional hazards regression. Differences in survival analyses were determined using the log-rank test. Local ethic boards approved the study but written consent form was waived due to the retrospective manner.
Results: Distribution of UICC stage of the entire cohort (N = 409, mean age 72.9 ± 9.5, male 52.3%) was as follows: stage 0 (N = 7, 1.7%), stage IA (N = 20, 4.9%), stage IB (N = 22, 5.4%), stage IIA (N = 104, 25.4%), stage IIB (N = 50, 12.2%), stage III (N = 63, 15.4%) and stage IV (N = 144, 35.2%). Distribution of ABO blood type were as follows: type A (N = 192, 47.0%), type B (N = 86, 21.0%), type O (N = 91, 22.2%) and type AB (N = 12.2, 12.2%). Mean age did not differ among ABO blood type (71.0 ± 10.6, 72.9 ± 9.5, 72.9 ± 9.2 and 70.5 ± 10.1, respectively). Sex (male rate) did not differ among ABO blood type (53.2%, 52.3%, 60.4%, and 50%, respectively). However, type O was diagnosed at earlier stage than type non-O when UICC stages 0-IIA was considered as earlier stage (47.3% vs. 34.6%, P = 0.027) and the difference was much more significant between type O and type AB (47.3% vs. 26.0%, P = 0.019). Furthermore, median survival time (MST) of type O was longer than that of type non-O (P = 0.058) and statistically significant when compared with type AB (P = 0.045): type A 370 days, type B 408 days, type O 521 days, type AB 301 days.
Conclusion: ABO blood type, type O and type AB in particular, influenced long term outcomes of Japanese patients with PC presumably due to the difference in disease onset.
Disclosure: Nothing to disclose

P1370 INFLAMMATION AND PROFILE OF IL-6,10 AND 17 INTELEUKINS IN PATIENTS WITH CHRONIC PANCREATITIS AND PANCREATIC CANCER

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Introduction: Inflammation plays an important role in pancreatic carcinogenesis. Interleukin-6 promote cell proliferation, migration, invasion and angiogenesis. IL -10 inhibits pro-inflammatory cytokine release from lymphocites via STAT3, downregulates MHCII co-stimulatory molecules CD80/CD60, reducing clonal expansion of T-lymphocytes. Recently several report showed that IL-17 have an important role in initiation and progression of pancreatic intraepithelial neoplasia PanIN and early pancreatic cancer. Family history of pancreatic cancer and several genetic syndromes must be taken into account for early detection of pancreatic cancer.

Aims and Methods: To evaluate IL-6, 10 and 17 profiles in patients with: pancreatic adenocarcinoma (PAC), chronic pancreatitis (CP), risk conditions for PAC (e.g Familial pancreatic cancer, hereditary pancreatitis, Brest ovarian cancer syndrome, HNPCC, FAMMM, PJS, juvenile polyposis, FAP) comparative with a group of controls.

A total of 138 patients (mached by sex and median age), were enrolled in the study. These were grouped in the pancreatic cancer group (n = 77), chronic pancreatitis group (n = 34), risk conditions groups (n = 8) and the control group (n = 19).

The diagnosis of PAC was made histopathologically by biopsy specimen analysis (fine needle aspiration guided by echoendoscopy or surgery resection). The diagnosis of CP was based by medical history, imaging methods and echoendoscopy data according to Rosmond criteria. The control group consisted of healthy volunteers who were matched by gender and age. It was collected 10 mL of peripheral blood from all individuals. Plasma was separated, frozen and stored at −80°C. Systemic concentrations of IL-6, 10 and 17 were measured using ELISA kits.

Results: The seric levels of IL-6 were significant statistically higher in patients with PAC and CP vs. control groups ($P < 0.0001$). There was no statistical significance between IL-10 levels in PAC and risk conditions groups ($P = 0.1777$) and between CP and control groups ($P = 0.1775$). We found statistically significant difference between IL-10 level in PAC group vs CP group ($P = 0.0023$) but no significant statistical between risk conditions group and control group. IL-17 levels were significant higher in PAC patients and in CP vs risk conditions group ($P < 0.0001$) and in PAC group vs CP group also ($P < 0.0001$).

Conclusion: We detected higher serum levels of IL-6, 10 and 17 in patients with CP and PAC suggesting their role in initiation and progression of early pancreatic cancer with implications in diagnostic and therapeutic management. These cytokines can be non-invasive biochemical markers for the screening of PAC in high risk or moderate risk population. Prognostic roles need to be established.

Disclosure: Nothing to disclose

P1372 HETES IN PATIENTS WITH PANCREATIC CANCER: A PRELIMINARY REPORT

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Introduction: Lipoxygenase (LOX)-derived bioactive lipids represent a family of important biological molecules that can be of great importance in the pathogenesis of pancreatic neoplasms. We hypothesized that systemic levels of LOX-derived Hydroxyeicosatetraenoic acids (HETEs) may be associated with clinical presentation of pancreatic neoplasms in humans, as well as with previously reported phenomenon of intensified circulation of various populations of bone marrow-derived stem cells in these patients.

Aims and Methods: In the current study, we comprehensively evaluated the systemic levels of selected HETEs such as 5-, 12-, and 15-HETE in patients with pancreatic adenocarcinoma (n = 36), chronic pancreatitis (n = 39), and in healthy individuals (n = 35).

Results: Compared to healthy individuals, patients with pancreatic adenocarcinoma showed 3–8-fold higher levels of 5-, 12-, and 15-HETE (at least $p < 0.003$). Similar results were observed in patients with chronic pancreatitis, who had elevated concentrations of all examined HETE acids compared to healthy volunteers (in all cases at least $p < 0.03$). Interestingly, the levels of the examined HETEs were not significantly associated with the TNM stage of pancreatic cancer in our patients. However, 12-HETE and 15-HETE concentrations were correlated with peripheral circulation of selected populations of bone marrow-derived stem cells, such as very small embryonic/epiblast-like stem cells and mesenchymal stem cells. Finally, analyses of receiver operating characteristic curves demonstrated that all HETEs examined had relatively low area under the curve values for discriminating pancreatic adenocarcinoma from non-cancerous conditions ($p > 0.05$ in each case).

Conclusion: Our study provides first clinical evidence for the significance of the examined HETEs in the clinical pathogenesis of pancreatic cancer and other pancreatic diseases in humans. Moreover, our study identifies significance of HETEs in the phenomenon of intensified peripheral circulation of selected populations of bone marrow-derived stem cells in patients with pancreatic cancer. Finally, our data demonstrate that the HETEs examined here do not show sufficient clinical potential to be used as independent biomarkers for differentiating pancreatic adenocarcinoma from other non-cancerous conditions in humans.

Disclosure: Nothing to disclose

P1373 SARCOPENIA AS A PREDICTOR OF COMPLICATIONS AFTER PANCREATIC RESECTIONS IN PATIENTS WITH PANCREATIC ADENOCARCINOMA

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Introduction: Sarcopenia can be a predictor of complications after pancreatic resections.

Aims and Methods: We performed a retrospective analysis of treatment of 104 patients with pancreatic adenocarcinoma, who underwent pancreaticoduodenectomy in our institution in the period 2012–2017. Preoperative computed tomography (CT) was performed for all patients. Sarcopenia was quantified using Hounsfield Unit Average Calculation (HUAC). They were measured at the level of the third lumbar vertebral body (L3).

Results: Sarcopenia was diagnosed in 44 (42.3%) patients *vs* 60 (57.7%) patients without this diagnosis. Postoperetive complications occurred in 26 (59.0%) patients in the group with sarcopenia and in 17 (28.3%) patients in the group without sarcopenia ($c^2 = 9.9$, $p = 0.0017$). Mortality was 2 (4.5%) and 1 (1.6%) respectively ($c^2 = 0.75$, $p = 0.38$).

In patients with sarcopenia infectious complications occurred in 5 patients, pancreatic fistula Grade B or C in – 14 patients, delayed gastric empting – in 2, haemorrhage- in 5.

In patients without sarcopenia infectious complications occurred in 5 patients, pancreatic fistula Grade B or C in – 4 patients, delayed gastric empting – in 4, haemorrhage- in 4. We did not find any significant difference in the increase in the number of infectious complications ($c^2 = 2.1$, $p = 0.14$), delayed gastric empting ($c^2 = 2.1$, $p = 0.14$) and haemorrhage ($c^2 = 0.11$, $p = 0.7$), but sarcopenia was revealed as an independent, significant risk factor for incidents of postoperative pancreatic fistula Grade B or C ($c^2 = 3.8$, $p = 0.04$).

Conclusion: HUAC could be easily calculated preoperatively in patients with pancreatic cancer. Present results suggest that sarcopenia, determined by HUAC, is a reliable indicator of the surgical outcome and significantly influences on total level of postoperative complications. It is also a strong predictor of clinically relevant postoperative pancreatic fistula occurrence. The assessment of sarcopenia can be used to improve the selection of patients with pancreatic cancer prior resection.

Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 09:00–14:00

Endoscopy and Imaging III – Hall X1

P1374 ANALYSIS OF VOLUME ADJUSTMENT IMPACT, RESULTS AND COMPLICATIONS USING THE SPATZ BALLOON FOR EXCESS WEIGHT TREATMENT: A LARGE BRAZILIAN EXPERIENCE IN FOUR HUGE CENTERS

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Introduction: Intragastric Balloons (IGB) are used for decades worldwide in excess weight treatment with well-established success. SPATZ adjustable IGB approved for 12-month may provide greater weight loss due to a longer period of treatment and reduce early removals in intolerant patients.

Aims and Methods: We aimed to evaluate weight loss and complications in 04 private Brazilian clinics with a high volume of patients; To report whereas download and upward balloon adjustments and longer period of therapy have impact in treatment results regarding weight loss and early removal rates. We included patients that underwent Spatz3 IGB implantation and concluded at least the 1 year treatment. Minimum initial body mass index (BMI) was 27 kg/m2. We analyzed the complications and BMI reduction, percent total body weight loss (%TBWL) and percent excess weight loss (%EWL), weight loss in kilograms, early removal rates between patients submitted to adjustments or not. Data were analyzed using descriptive statistic and the Student t test. The level of significance was set at $p < 0.05$.

Results: 487 patients were analyzed (339 females). Mean age 40.1 years. Mean BMI 36.4 kg/m2; mean weight 101.3 kg, and mean initial balloon volume 620.34 ml (360 -700 ml). Balloon volume adjustments offered for intolerance and weight loss plateau. There were 34(6.98%) early removals (all refused adjustment), 15(3.08%) deflations, 19(3.90%) gastric ulcers (1 requiring balloon removal), 2(0.41%) gastric perforations, 1(0.22%) Mallory-Weiss Syndrome and 2(0.41%) Bezoars, 11(2.25%) gas production inside the balloon. 437 patients completed treatment. Mean weight loss was 18.3 kg; mean EWL 64.33% and mean TBWL 19.1%. The final BMI (29.80 Kg/m2) was significant lower than the initial (36.40 Kg/m2) (mean BMI reduction 6.6 Kg/m2). Success rate (>25%EWL) occurred in 392 (89.7%). Downward adjustments performed in 57(11.7%) cases (mean reduction 280.87 ml ± 64.58) and all continued treatment. Upward adjustment was performed in 232 patients (47.6%) (mean 5.7 ± 1.52 months; mean 230 ± 70.4 ml) and did not show statistically improvement in weight loss (Kg) in comparison to the group that did not adjust (mean weight loss 17.80 Kg vs 18.10 Kg, $p = 0.063$). 71%(mean 12.54 Kg) of the excess weight loss happened in the first 6 months and the other 29% (mean 5.48 Kg) in the subsequent period of treatment.

Conclusion: Spatz3 IGB is a very effective device to induce weight reduction, safe (no mortality), even though with a little higher morbidity when compared to traditional IGBs. The downward adjustment certainly reduces the incidence of early balloon removals in intolerant patients. On the other hand, the upward adjustment seems to be ineffective in providing a greater weight loss, but a longer treatment period probably brings better results when compared to shorter treatments.
Disclosure: Nothing to disclose

P1375 A NOVEL TECHNIQUE FOR ENDOSCOPIC ENBLOC RESECTION FOR LESIONS UP TO 30 MM (EMR+)

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Introduction: Endoscopic mucosal resection (EMR) is the most common technique for endoscopic resection (ER) of intestinal mucosal neoplasia. However, successful enbloc resection depends on tumor size and decreases under 40% for lesions >20 mm. In consequence, piecemeal EMR is usually performed for lesions >20 mm. This technique is associated with a higher rate of recurrency and R0 resection is difficult or impossible to determine after piecemeal resection. Endoscopic submucosal dissection (ESD) allows enbloc resection for lesions >20 mm but the technique is difficult, time-consuming and associated with a higher risk for complications. Submucosal injection is well investigated and essential for both resection techniques. The standard solution used for injection is saline solution, but the created submucosal cushion disappears quickly as saline is absorbed by the adjacent mucosa. Frequent re-injections and prolonged procedure times are the consequences.
Aims and Methods: Development of a technique (EMR+) which allows endoscopic enbloc resection of lesions up to 30 mm.
The technique was developed and evaluated in an explanted pig stomach. The stomach was adjusted in a special simulation model to be accessible to endoscopy. An additional working channel was mounted on a standard gastroscope and used for a resection snare. The conventional working channel of the scope was used for an anchor device. For submucosal injection a new developed agent with a temperature-dependent viscosity was used. The agent has liquid consistency at room temperature which allows submucosal injection. At body temperature the agent gels and forms a stable cushion within seconds which allows stable resection (no absorption, re-injections are not necessary). The safety of this agent has already been shown in vivo in domestic pigs. Imaginary lesions of 30 mm were marked by coagulation. After injection the anchor device was used simultaneously with the snare to facilitate resection. After the resection technique was established 22 resections (11 with a frontal and 11 with a tangential approach) were performed and evaluated.
Results: The median size of the enbloc resection specimens was 30 × 26 × 11 mm (maximum 40 × 33 × 14). The procedure times were between 6–7 minutes (Table 1). No perforations occurred.
Conclusion: The technique (EMR+) allows fast enbloc resection and obtains resection specimens of 30 mm. The technique needs to be evaluated in vivo.
Disclosure: Nothing to disclose

P1376 FEASIBILITY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL NEOPLASMS IN ELDERLY PATIENTS: A SINGLE-CENTER, LARGE-SCALE, RETROSPECTIVE STUDY

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Introduction: Although the number of elderly patients with superficial esophageal neoplasms (SENs) has been steadily increasing, there is still an evident lack of studies focused on the clinical outcome of esophageal endoscopic submucosal dissection (ESD) in the elderly. We investigated the feasibility and safety of ESD for SENs in elderly patients.
Aims and Methods: Patients who underwent ESD for SENs between December 2005 to December 2017 were eligible. Clinical features and treatment outcomes according to the three age groups (not-old, <65 years; young-old, 65–74 years; middle and oldest-old, >74 years) were retrospectively reviewed using medical records.
Results: ESD was performed in 426 patients with 475 lesions, including 97 cases (20.4%) of dysplasia, 364 cases (76.6%) of squamous cell carcinoma and 14 cases (3%) of adenocarcinoma. The age was divided into three groups, the not-old (n = 200), young-old (n = 179) and middle & oldest-old (n = 47). Gender, Smoking and characteristics of tumor (circumference, location, lesion size, resected specimen size, histology and depth of invasion) did not differ. Underlying disease such as hypertension (not-old vs. young-old vs. middle & oldest-old; 30.0% vs. 41.9% vs. 40.4%, p = 0.045), chronic kidney disease (0.5% vs. 0.0% vs. 4.3%, p = 0.033) and cardiovascular disease (2.0% vs. 7.8% vs. 4.3%, p = 0.028) significantly differed between the three groups. En bloc resection (96.8% vs. 95.5% vs. 100.0%, p = 0.260), complete resection (88.2% vs. 87.5% vs. 83.3%, p = 0.622) and curative resection rates (77.2% vs. 77.0% vs. 81.5%, p = 0.768) were no significant differences between the three groups. Complications of procedure such as bleeding (2.3% vs. 0.0% vs. 1.9%, p = 0.075), perforation (4.5% vs. 3.0% vs. 5.6%, p = 0.601) and stricture (5.4% vs. 6.0% vs. 11.1%, p = 0.297) also occurred similar in the three groups. During the follow-up period (median, 27.4 months; interquartile range, 7 to 40), among the patients with curative resection, cumulative recurrence rate did not differ significantly between the three groups (local recurrence, 0.7% vs. 0.0% vs. 0.0%; synchronous recurrence, 4.0% vs. 3.7% vs. 2.6%; metachronous recurrence, 5.4% vs. 6.0% vs. 10.3%).
Conclusion: ESD is a feasible and effective procedure for the treatment of SENs in elderly patients as in non-elderly patients which showed favorable outcomes.
Disclosure: Nothing to disclose

P1377 ENDOSCOPIC HAND-SUTURING FOR MUCOSAL DEFECTS AFTER GASTRIC ESD IN CASES WITH ANTITHROMBOTIC AGENTS: A CASE SERIES STUDY IN 8 PATIENTS

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Introduction: Endoscopic submucosal dissection (ESD) for gastric neoplasms is gaining an acceptance as one of curative treatment options. The major post-operative adverse event of gastric ESD is delayed bleeding. Although effective countermeasures for post-ESD bleeding are proton pump inhibitors and

Abstract No: P1375
Table 1: EMR+

Number	L × W × H (mm)	Time Injection*	Time Procedure**	Number	L × W × H (mm)	Time Injection*	Time Procedure**
F#1	30 × 27 × 10	3 min 55s	6 min 44s	T#1	30 × 26 × 9.6	1 min 41s	9 min 31s
F#2	25 × 24 × 10.4	3 min 13s	3 min 16s	T#2	30 × 28 × 12,4	2 min 31s	4 min 4s
F#3	30 × 24 × 9.2	3 min 1s	3 min 10s	T#3	25 × 22 × 8.5	3 min	3 min 45s
F#4	22 × 20 × 7	4 min 2s	3 min 3s	T#4	30 × 29 × 10.5	4 min 48s	3 min 20s
F#5	31 × 25 × 13.3	2 min 56s	3 min	T#5	36 × 30 × 13.5	3 min 13s	3 min 59s
F#6	35 × 25 × 11.6	2 min 22s	3 min 44s	T#6	33 × 30 × 16.6	3 min 59s	4 min 40s
F#7	34 × 29 × 12.7	2 min 25s	3 min	T#7	32 × 28 × 14.4	2 min 34s	5 min 12s
F#8	40 × 33 × 14.4	3 min 3s	2 min 23s	T#8	25 × 25 × 12.7	3 min 12s	3 min 49s
F#9	29 × 25 × 8.8	3 min 20s	3 min 59s	T#9	26 × 22 × 6.5	3 min 44s	4 min 49s
F#10	32 × 26 × 10.3	3 min 40s	2 min 50s	T#10	29 × 29 × 11.5	4 min 2s	3 min 39s
F#11	30 × 25 × 11.4	2 min 58s	2 min 21s	T#11	37 × 30 × 10.1	2 min 30s	4 min 12s
Median	30.7 × 25.7 × 10.8	3 min 10s	3 min 25s		30.3 × 27.2 × 11.5	3 min 12s	4 min 38s
F = frontal approach	* from begin injection to end of flushing lesion with warm water						
T = tangential approach	** from begin positioning snare to extracting resection specimen						

prophylactic coagulation of visible vessels on mucosal defect after ESD, the incidence of post-ESD bleeding is not negligible. Furthermore, patients receiving antithrombotic agents are increasing because of population ageing and progress of treatment for cardio-cerebrovascular disease, which may increase the risk of post-ESD bleeding.
Aims and Methods: To prevent postoperative bleeding after gastric ESD of the patients receiving antithrombotic agents, we conducted endoscopic hand suturing (EHS), which was a suturing technique using a through-the-scope needle holder and an absorbable barbed suture attached to a curved needle, for mucosal defects after ESD (Goto O, et al. *Endoscopy* 2017). Eight patients who were receiving antithrombotic agents and underwent ESD for gastric neoplasm (less than 3 cm in size) were recruited. The details of antithrombotic agents were as follows: aspirin in 2 patients, aspirin and clopidogrel in 2 patients, triple antiplatelet agents in 1 patient, warfarin in 1 patient, apixaban in 1 patient, and aspirin and warfarin in 1 patient. In all cases, aspirin were continued and warfarin were replaced to heparin during perioperative period. Other antithrombotic agents were interrupted before ESD and resumed immediately after ESD. We performed EHS for the mucosal defects after successful lesion resection by ESD. Success rate, adverse events, and suture maintenance of EHS and the incidence of delayed bleeding were subsequently investigated.
Results: EHS was successfully completed in 9 lesions in 8 patients without severe adverse events. The tumor locations, the mean size of mucosal defects and the mean procedure time of EHS were U/M/L: 1/4/4, 26.0 ± 9.5 mm and 40.6 ± 12.6 min, respectively. The mean number of stitches for a lesion and the mean time per one stitch were 6.3 ± 1.4 stitches and 6.9 ± 3.0 min, respectively. The sutures of 8 lesions in 7 patients were completely maintained in second endoscopy on third day after ESD. In one patient who had acute myocardial infarction on 2 days after ESD under taking aspirin underwent second endoscopy on 7th day after ESD, which showed that the defect remained closed. In all cases, there was no post-ESD bleeding.
Conclusion: This small-numbered case series showed that the mucosal defects after ESD were successfully closed and no post-ESD bleeding occurred. EHS appears to be feasible and useful for prevention for gastric post-ESD bleeding.
Disclosure: Research funds and supply of devices: Olympus Co. Ltd., Tokyo, Japan

Reference

1. Goto O, Sasaki M, Akimoto T, et al. Endoscopic hand-suturing for defect closure after gastric endoscopic submucosal dissection: a pilot study in animals and in humans. *Endoscopy* 2017; 49: 792–7.

P1378 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC INDEFINITE FOR NEOPLASIA: WHICH SHOULD BE RESECTED?

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Introduction: The management plan for gastric indefinite for neoplasia is yet to be determined and endoscopic forceps biopsy might be inconclusive to decide to resect or not. The aim of this study was to evaluate the clinical outcomes of endoscopic submucosal dissection (ESD) for gastric indefinite for neoplasia and to know the highly suspicious factors associated with true neoplasia.
Aims and Methods: Between November 2008 and December 2015, a retrospective study was conducted in a single, tertiary, referral hospital. A total of 109 gastric indefinite for neoplasia from endoscopic forceps biopsy which resected by ESD were enrolled. The clinical outcomes and endoscopic factors for prediction of true neoplasia were analyzed.
Results: A total of 99 patients (90.8%) were diagnosed as definite neoplasia after ESD; category 3 ($n = 42$), category 4 ($n = 50$) and category 5 ($n = 7$) according to the revised Vienna classification. The patients' mean age was 65.8 ± 9.8 years. The mean lesion size was 10.7 ± 6.1 mm. The patient population was male predominant (70.6%). The en-bloc and complete endoscopic resection rate were 98.2% and 94.5%, respectively. Associated factors with true neoplastic lesions were male sex (OR 8.596, $p = 0.008$) and lesion size $\geq$ 5 mm (OR 11.355, $p = 0.003$). Associated factors with category 4–5 were male sex (OR 3.165, $p = 0.021$) and erosive change (OR 2.841, $p = 0.031$).
Conclusion: Endoscopic resection for indefinite for neoplasia with larger lesions size with erosive changes especially in male sex should be considered when possible.
Disclosure: Nothing to disclose

P1379 SAFETY AND EFFICACY OF SUBMUCOSAL TUNNELING ENDOSCOPIC SEPTUM DIVISION FOR EPIPHRENIC DIVERTICULUM

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Introduction: Symptomatic epiphrenic diverticula are mostly treated with laparoscopic diverticulectomy. Recently, submucosal tunneling endoscopic septum division (STESD) has been used for the treatment of esophageal diverticulum. Our study aimed to demonstrate the safety and efficacy of STESD for treatment of symptomatic epiphrenic diverticula and elucidate the possible of STESD combined with POEM for treating patients with epiphrenic diverticula and achalasia.
Aims and Methods: Data of patients with symptomatic epiphrenic diverticula who underwent STESD between October 2016 and January 2018 at Jiangsu Province Hospital (Jiangsu, China) were retrospectively reviewed. The parameters analyzed were the modified Eckardt score, total procedure time, hospital stay, the number of clips used, the incidence of complications and patient satisfaction.
Results: A total of 7 patients were enrolled in our study. There were 4 men and 3 women with the mean age of 66.42 ± 6.68 years. The most common symptoms were dysphagia, heartburn and regurgitation. The mean size of epiphrenic diverticula was 3.70 ± 1.95cm. One patient had Zenker's diverticula while the others had supradiaphragmatic diverticula. One patient had multiple diverticula. In four patients with co-existent achalasia, peroral endoscopic myotomy (POEM) was simultaneously performed by the same tunnel. The mean procedure time was 56.42 ± 24.10 minutes. The median number of clips applied was 6 (range: 3–16). The modified Eckardt score significantly decreased after STESD ($P = 0.002$). The mean hospital stay was 5.57 ± 0.79 days. No complications were observed during the median follow-up of 7.83 months.
Conclusion: STESD is an effective and safe procedure for the treatment of epiphrenic diverticula. STESD can be combined with POEM for treating patients with epiphrenic diverticula and achalasia.
Disclosure: Nothing to disclose

P1380 THE YIELD OF BIDIRECTIONAL ENDOSCOPY IN YOUNG MALES WITH IRON DEFICIENCY ANAEMIA

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Introduction: Current British Society of Gastroenterology (BSG) guidelines advise bidirectional endoscopy in all males and postmenopausal women with iron deficiency anaemia (IDA). Endoscopy findings are reported to be significant in anywhere between 42 and 85% of patients in this group. The aim of this study was to investigate the yield of bidirectional endoscopy specifically in males 18–55 with iron deficiency anaemia (IDA).
Aims and Methods: The endoscopy database was searched for all synchronous bidirectional endoscopies undertaken at Queen Elizabeth Hospital in males aged 18–55 in 2017 with the indication of IDA. Endoscopic findings were retrieved for each procedure and the hospital results system provided levels of haemoglobin (Hb), mean corpuscular volume (MCV), ferritin, iron and haemoglobin electrophoresis, if performed, at the time of referral. Histology samples from endoscopy were also assessed. Significant findings were defined as malignancy, grade C/D oesophagitis (Los Angeles scoring system), coeliac disease, colitis, polyps >1cm, oesophageal stricture, Barrett's oesophagus, ulcers, arteriovenous malformation and Giardia infection.
Results: Forty six patients fit the inclusion criteria, with an average Hb of 109 g/L and average MCV of 77 fL. Fourteen patients (30%) were found to have significant findings. These included 3 diagnoses of malignancy (7%) and 2 diagnoses of IBD (4%). Eight of the significant findings (57%) were on oesophagogastroduodenoscopy, with the remaining 6 findings (43%) being on colonoscopy.
Conclusion: These results indicate that bidirectional endoscopy has a high yield in young men with IDA. While the yield is lower than that reported in all males and post menopausal women, significant findings, including malignancy, indicate that bidirectional endoscopy should continue to be recommended in this population.
Disclosure: Nothing to disclose

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P1381 NEOANGIOGENESIS IN LOCALLY ADVANCED GASTRIC CANCER TREATED BY NEOADIUVANT CHEMOTHERAPY EVALUATED BY PROBE CONFOCAL LASER ENDOMICROSCOPY (PCLE)

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Introduction: Angiogenesis is a hallmark of cancer development inducing the formation of new vasculature to support its growth. Probe based confocal laser endomicroscopy (pCLE) is an advanced technique which provides imaging of gastrointestinal mucosa at subcellular resolution and of microvasculature during endoscopic examination. The evaluation of the tumoral vascular pattern could predict response to chemo-antiangiogenetic-radiotherapy.
The aim of our study was to evaluate tumor neoangiogenesis through pCLE imaging in locally advanced gastric patients, before and after neoadjuvant radio-chemotherapy (RT/CT).
Aims and Methods: 50 consecutive patients with Gastric Cancer (GC, 24F, 26 M mean age: 65 years) underwent endoscopy with pCLE-GastroFlex UHD probe (Mauna Kea Technologies) and i.v. fluorescein infusion in order to evaluate intratumoral vascularization and to evaluate the efficiency of blood flow. After RT/CT treatment, 12 GC (5F, 7M) patients were revaluated using pCLE. Vascular assessment was based on vessel shape and size, vessel permeability and blood flow, and allowed the creation of an angiogenic score ranging from 0, for normal vasculature, to 4: Cannizzaro-Spessotto (CS) scale. A first evaluation of angiogenic status was given in real time by the endoscopist during the pCLE analysis. Images were stored digitally and then reviewed with a dedicated software package.
Results: 5 out of 12 (41.6%) GC patients showed an improvement of angiogenesis index, while in the remaining 7 GC (59.4%) no substantial changes were documented. The unchanged vascular alterations in gastric cancer patients correlated positively with stable or progressive disease. Since a small remission was detected in only 25% of gastric cancer patients it was possible that the unaltered angiogenic score could be ascribed to the lack of treatment efficacy.
Conclusion: In GC patients median angiogenesis index remained unmodified, without positive changes in vascular morphology, probably due to the presence of fibrosis.
The evaluation of tumor vasculature may provide vital information for predicting the efficacy of treatments and for achieving tailored interventions for individual patients. The analyses performed on gastric cancer patients suggest that these patients could especially benefit from neoadjuvant angiogenetic tailored therapy, thereby improving also the efficacy of the standard therapy. The results of our work demonstrate that pCLE is a valid method for real-time analysis of the vascular density and efficacy in gastric cancers.
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to R.C.
Disclosure: Nothing to disclose

P1382 FLUORESCENT ENDOSCOPY DURING ESOPHAGEAL CARCINOGENESIS IN A MOUSE MODEL

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Introduction: Barrett's Esophagus (BE) represents an early stage in carcinogenesis leading to esophageal adenocarcinoma (EAC), but current screening and surveillance strategies are limited by the absence of specific molecular markers highly predictive of increased risk for EAC. In our previous translational study, we provided new insights into the kinetics and pathogenesis of esophageal cancer, and introduce CXCR4-based imaging of the tumor microenvironment as a potential approach for diagnosis and surveillance of EAC[1]. In the present study, we investigate the attractive molecular targets such as fluorescent labelled neutrophils, CXCR4 expressing cells and HSP70 expressing cells for endoscopy imaging.
Aims and Methods: We utilized a IL-1b transgenic mouse model of BE and EAC[2] for fluorescent endoscopy imaging to analyse the importance of immune cells, CXCR4 expressing cells and Hsp70 expressing cells during esophageal carcinogenesis. The dual channel murine upper endoscopy is performed with a highly sensitive fluorescence/color endoscope imaging system[3] with a design to offer video-rate simultaneous color and near-infrared (NIR) fluorescence endoscopy.
Results: Our Immunohistochemistry (IHC) and flow cytometry (FACS) data show that specific recruitment of neutrophils and CXCR4-positive (CXCR4+) immune cells correlated with dysplasia progression, suggesting that the immune population may be a key contributor to esophageal carcinogenesis. Furthermore, stronger CXCR4 signal intensity was accumulated in ex vivo fluorescence imaging in advanced dysplasia mice. Moreover, fluorescent endoscopy studies showed that fluorescently labelled CD45 immune cells and fluorescently labelled CXCR4 cells could be detected in low grade and high grade dysplasia in L2-IL-1b mice. Most importantly, elevated CXCR4-fluorescence signal intensity was observed in high grade dysplasia in L2-IL-1b mice. In addition, IHC data showed that HSP70 was expressed in BE regions of dysplasia in L2-IL-1b mice. These findings support that immune cells, CXCR4 and HSP70 are suitable molecular markers for endoscopy imaging of the tumor microenvironment during esophageal carcinogenesis.
Conclusion: The recruitment of neutrophils, CXCR4+ immune cells in esophageal dysplasia highlight the potential of immune cells and CXCR4 as molecular targets for diagnostic imaging of the tumor microenvironment in BE and EAC. We hypothesize that the early detection of a tumorigenic niche by fluorescence endoscopy based imaging could define a novel modality that allows to define a population at risk to develop EAC. Therefore, we are currently developing a dual channel murine upper endoscopy that can detect and overlap 2 molecular markers for parallel evaluation of early dysplasia surveillance. A series of case studies are under investigation to confirm the ability to detect early dysplastic lesions.
Disclosure: Nothing to disclose

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P1383 ENDOSCOPIC VACUUM THERAPY FOR POSTOPERATIVE ESOPHAGEAL LEAK

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Introduction: Anastomotic leak is one of the most common complications of esophagectomy. The endoscopic vacuum-assisted closure (EVAC), which is based on continuous negative pressure applied to the wound with a sponge, has advantages of effective drain of infected fluid and accelerating would healing by inducing formation of granulation tissue over fully covered self-expanding metal stent (SEMS) treatment.
Aims and Methods: We aimed to evaluate the efficacy and to identify factors associated with longer ($\geq$ 21 days) treatment duration of EVAC for esophageal anastomotic leak following esophagectomy for cancer. We retrospectively analyzed 20 esophageal cancer patients who had undergone EVAC for esophageal leak after esophagectomy between October 2016 and December 2017 at the Samsung Medical Center.
Results: All 20 patients were male. Of these, 10 (50.0%) received neoadjuvant treatment and 6 (30.0%) had one or more comorbidities. The median size of fistula opening was 1.75 cm. During a median of 14.5 days of EVAC treatment, a median of 5 interventions were performed. Treatment success was achieved in 19 patients (95.0%). Neoadjuvant treatment was significantly associated with longer EVAC treatment. There was a non-significant trend toward the need for longer treatment duration for a larger fistula opening size.
Conclusion: EVAC treatment is a good non-surgical option for anastomotic leak following esophagectomy. Long duration of treatment is associated with neoadjuvant treatment and a large leakage opening.
Disclosure: Nothing to disclose

P1384 PER ORAL ENDOSCOPIC MYOTOMY USING TRIANGLE TIP KNIFE WITH OR WITHOUT WATER JET FUNCTION

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Introduction: The procedure of Per Oral Endoscopic Myotomy (POEM) is becoming standardized for treatment of Achalasia. Recently, the new Triangle tip (TT) knife is equipped with water-jet function which could hasten the operative time. We retrospectively compared the use of TT knife with and without waterjet function on the clinical outcomes of POEM for treatment of Achalasia
Aims and Methods: This is a retrospective cohort study comparing use of TT knife against TT knife with water jet function (TTJ) for performance of POEM. All patients who received POEM using TT knife for treatment of Achalasia at our institution were recruited. The POEM procedures were all performed under general anesthesia by single endoscopist. The outcomes including baseline demographics, operative time, hospital stay and efficacy were compared.

Results: From 2010 to 2017, 91 patients received POEM performed by using TT knife (81 patients with conventional TT and 10 patients with TTJ). There was no difference between two groups in the age, gender and baseline demographics. The preoperative Eckhardt score was 5 (1–11) for TTJ group and 6 (1–12) for TT group ($p = 0.875$). The mean myotomy length was 9.8 ± 0.9cm for TTJ group and 10.8 ± 2.4cm for TT group ($p = 0.223$). The operative time was significant shorter for the TTJ group as compared to the conventional TT group (79.3 ± 21.6 vs 101.6 ± 34.3 mins; $p = 0.05$). There was no difference in the hospital stay between the two groups (2.7 ± 0.5 (TTJ) vs 3.1 ± 1.1 (TT); $p = 0.409$). There was no perioperative mortality, and no difference in the morbidities between two groups (1 (TTJ) vs 6 (TT); $p = 1.0$). The postoperative Eckhardt score was 0 (0–1) for TTJ group and 0 (0–6) for TT group (n.s).
Conclusion: In this retrospective cohort study, we showed that the use of TT knife with waterjet function significantly reduced operative time of POEM while achieving similar length of myotomy, clinical efficacy as well as safety for treatment of Achalasia.

Parameters	TT Jet (10)	TT (81)	p value
Gender: M (%)	5 (50)	29 (35.8)	0.492
Age	47.3 ± 18.6	49.3 ± 17.2	0.735
Duration of symptoms (months)	42.8 ± 35.3	61.0 ± 83.9	0.548
Comorbidities	1 (0–1)	0 (0–5)	0.839
Previous therapy (%)	2 (33.3)	14 (17.7)	0.315
Baseline Eckhardt score (Median)	5 (1–11)	6 (1–12)	0.875
Mean OT time	79.3 ± 21.6	101.6 ± 34.3	0.05
Mean total Myotomy length (cm)	9.8 ± 0.9	10.8 ± 2.4	0.223
Mean Hospital stay (days)	2.7 ± 0.5	3.1 ± 1.1	0.409
Complications (%)	1 (10)	6 (7.4)	1.0
Postop Eckhardt score	0 (0–1)	0 (0–6)	n.s.
FU (months)	13.7 ± 15.4	37.8 ± 21.4	0.002

[Table 1 – TT Jet compare to non-jet for POEM]
Disclosure: I am serving as chairman of ANBIG, which received sponsorship from Olympus Co Ltd

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P1385 UPPER GASTROINTESTINAL CAPSULE ENDOSCOPY AS AN ALTERNATIVE TO OESOPHAGOGASTRODUODENOSCOPY

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Introduction: Conventional oesophagogastroduodenoscopy (OGD) is uncomfortable, unpopular with patients and may result in non-attendance. When mean examination time using this invasive modality exceeds 7 mins, the chance of detecting neoplasia increases by 3-fold compared to mean examination times of less than 7 minutes (1). Capsule endoscopy (CE) is better tolerated than OGD (2) and upper gastrointestinal capsule (UGIC) endoscopy has been evaluated in the screening and surveillance of varices in liver disease (3) and screening for Barrett's oesophagus (4).
Aims and Methods: We aim to examine patient's tolerability of UGIC and outcomes following UGIC in those who refused or did not tolerate OGD.
Consecutive patients undergoing UGIC were prospectively recruited between December 2016 and 2017. UGIC was performed by two specialist nurses using a novel simple positional interchange technique as previously described (5). The UGIC (Medtronic Ltd., Dublin, Ireland) is a novel device with cameras at both ends taking up to 35 frames per second (FPS) for 10 minutes and up to 18 FPS for the remaining 80 mins. Clinical records and endoscopy findings were reviewed and data on patients expected and actual discomfort and pain scores were collected before and after UGIC respectively.
Results: Thirty-four patients who refused (88.2%) or did not tolerate OGD (11.8%) had UGIC with a median follow up period of 119 days (19–670 days). Indications for UGIC were variceal screening ($n = 20$), dyspepsia ($n = 6$), reflux ($n = 3$), iron deficiency ($n = 3$), Barrett's screening and gastric ulcer healing ($n = 1$ each). Half the patients had previous OGDs. In patients for variceal screening, 45% were index examinations and the remainder surveillance procedures, of which 10% have had variceal haemorrhage.
UGIC was successful in 91% with 3 patients being unable to swallow the capsule. The capsule spent a mean time of 26 (±9.7) secs in the oesophagus, 1 hour 25 mins (±16.6 min) in the stomach, entered the duodenum in 87% in whom it spent 12 (±2.2) mins. Normal exams were found in 35.4% ($n = 11$). Pathologies detected on UGIC include oesophageal (OV; $n = 6$) and gastric ($n = 1$) varices, portal hypertensive gastropathy ($n = 4$), gastric erosions ($n = 7$), oesophageal erosions or ulcers ($n = 1$ each), hiatus hernia ($n = 2$) and benign fundic cystic gland polyps ($n = 4$).
Only 6.5% ($n = 2$) had a further gastroscopy during their follow up period. They were performed to confirm OV in one and in another to rule out malignancy in a patient with a suspicious lymph node found on imaging, who had earlier UGIC for variceal surveillance. No additional findings were seen on OGD.
Mean procedural distress, discomfort and pain were excellent (scores from best to worse = 0–10; 0.3, 0.1, 0.1) despite patients expecting more discomfort and pain prior to investigation (2.9 and 2.3 respectively). Overall, 96.6% of patients with successful UGIC would have a repeat examination.
UGIC changed patient management in 25.8% ($n = 8$). In patients with liver disease, 2 were placed on variceal surveillance (with UGIC), 2 patients had beta blockers started or increased and in one omeprazole initiated for incidental erosive gastritis. In 9 patients with dyspepsia and/or reflux, a third had their PPIs changed or doses altered.
Conclusion: UGIC is extremely well tolerated and highly acceptable to patients, almost all of whom would agree to having repeat procedures. A range of oesophageal and diffuse gastric pathologies were identified. No focal gastric lesions were identified in this small study, but the longer examination duration suggest that a blinded comparison with OGD is warranted.
Disclosure: Nothing to disclose

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P1386 CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR NON-AMPULLARY DUODENAL LESIONS

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Introduction: Because of thin anatomical structure and high risk of complication including perforation, endoscopic resection (ER) for non-ampullary duodenal lesions (NADLs) is technically more difficult than lesions of stomach. However, with development of therapeutic endoscopy, endoscopic treatment of duodenal lesions has been performed recently.
Aims and Methods: The aim of this study was to evaluate the efficacy and safety of endoscopic resection for NADLs. Retrospectively, patients who underwent ER for NADLs between December 2004 and June 2017 were included. We analyzed clinical and pathologic features of the lesions including the clinical outcomes and adverse events.
Results: The study included fifty-two patients (57.7% male) with NADLs. The median age of patients was 55.5 years (range 22 to 80 years). The mean NADL size was 10.19 ± 7.72 mm and the mean procedure time was 14.55 ± 12.08 min. After resection, final histological data showed 39 adenomas (61.5%), 10 Brunner's gland tumors (19.2%) and 3 pyloric gland tumors (5.8%). The en-bloc resection rate was 92.3% (48/52), and the complete resection rate with clear margins was 86.5% (45/52). According to the location of NADLs, half (26/52) of the lesions were located in duodenal bulb including superior duodenal angle. Even though micro-perforation occurred from 2 out of 52 patients, it was treated only with conservative treatment.
Conclusion: ER for NADLs might be an effective treatment method with favorable long-term outcomes. However, it should always be performed with the possibility of perforation complication in mind.
Disclosure: Nothing to disclose

P1387 OVER-THE-SCOPE CLIPS (OTSC) FOR THE TREATMENT OF STOMACH AND DUODENAL ULCERS WITH HIGH-RISK STIGMATA OF BLEEDING – ONE AND DONE?

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Introduction: The risk of treatment failure as well as short-term recurrence of bleeding after standard endoscopic therapy of high-risk peptic ulcer bleeding (HRUB) is high even after successful primary control of bleeding. We evaluated the use of OTSC in patients with HRUB.
Aims and Methods: Between 04/2014 and 03/2018, N = 100 patients (pts) with peptic ulcer bleeding and HRUB (Forrest Ia – IIb), who received primary treatment with OTSC or secondary treatment after unsuccessful standard endoscopic therapy, were recorded in a database.
The primary endpoint of the study was either uncontrolled bleeding or recurrence after primary control (within 30 days). Furthermore, we examined factors that influenced the clinical success of OTSC treatment.
Results: OTSC as a single procedure for bleeding control was possible in N = 76 (76%) of all cases. OTSC as the primary and only treatment was performed in 64 pts, with clinical success in 50 pts (78.1%). Another 36 pts received the OTSC as a rescue treatment after failed initial standard endoscopic treatment. In 26 pts (72.2%) the treatment by OTSC alone was successful.
In 8 pts the bleeding could not be controlled by OTSC. 5 pts received a successful angiographic treatment, one pt underwent surgery and two pts died during active bleeding.
In 16 pts the bleeding was initially controlled by OTSC but recurrent bleeding occurred after 1–12 days. 11 pts received subsequent endoscopic retreatment, 5 pts angiography, one pt underwent surgery and one pt died.
OTSC failure occurred more often in large ulcers (> 3 cm $p = 0.03$), in the duodenal bulb ($p = 0.03$) and in ulcers with negative helicobacter test ($p = 0.045$). The patients with OTSC failure received more blood transfusions ($p = 0.002$). We found no statistically significant difference for the Rockall Score (median 7.5), the Glasgow Blatchford score (median 15.5), NSAID use or anticoagulation.
Conclusion: OTSC has a good clinical success rate in primary and secondary bleeding control in peptic ulcers with high-risk stigmata of bleeding. Potential risk factors for treatment failure are large ulcer size, location in the duodenal bulb and a negative helicobacter status.
Disclosure: Nothing to disclose

P1388 SPORADIC NON-AMPULLARY DUODENAL LESIONS: TWO TERTIARY-CENTERS STUDY ON ENDOSCOPIC RESECTION EFFICACY AND RECURRENCE

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Introduction: Sporadic duodenal adenomas (SDA) are rare lesions, accidentally diagnosed during endoscopy. Larger lesions (≥15mm) are usually referred to tertiary centers because of the challenging endoscopic resection and the reported high complication.
Aims and Methods: The aim of our study was to evaluate efficacy and safety of endoscopic mucosal resection for the treatment of SDA in two tertiary centers. This is a retrospective analysis of a cohort of patients with SDA referred to 2 tertiary centers (Humanitas Research Hospital, Milan; Queen Alexandra Hospital, Portsmouth), for resections of SDA between 2013 and 2017. Patients with familial adenomatous polyposis or ampullary lesions were excluded. All patients were included in a prospectively maintained database. Data regarding size of the lesion, site, morphology (Paris classification), type of endoscopic resection (en-bloc endoscopic mucosal resection (EMR), piece meal (PEMR), endoscopic submucosal dissection (ESD), histological findings, intra and post-procedural adverse events were recorded and analyzed. Lesions were divided into: small (<15 mm), large (≥15–30mm) and giant (≥30mm). Outcomes considered for this study were technical success, adverse events, and recurrence. Statistical analysis included descriptive statistics, Chi square tests (p. values of <0.001 was considered statistically significant) and Kaplan-Meier with survival estimation.
Results: A total of 120 patients (mean age 66 ± 11.9 years, 53 male) were enrolled in the study. Mean size of the lesions was 23.3 mm (range 5–80). Most common morphology (54.7%) was flat elevated (type IIa) with almost 1/3 of the lesions located in the second part of the duodenum (68.3%). En-bloc EMR was performed in 56 (46.6%) cases, PEMR in 41 (34.1%), 23 patients (19.1%) underwent ESD. LGD was the most common histology type (65.8%). HGD was found in 23 cases (19.1%). Five lesions were neuroendocrine tumors. We found 10 hyperplastic lesions and 3 amartoma. No cancer was detected. Ninety-eight (81.6%) lesions were resected uneventfully with no intra or post-operative complications. Intraprocedural perforation was observed in 4 patients (3.3%) all successfully treated by clips. Fourteen post-procedural (11.6%) complications were recorded: 11 bleedings (78.5%) (4 self-limited not requiring treatment, 3 endoscopically treated, 1 requiring transfusion). Four delayed perforations (3.3%) needed surgery. One patient who underwent surgery for perforation died. Considering the size of the lesions, 3/4 of intraprocedural perforations and all post-procedural perforations occurred in giant lesions. We found a significant correlation between giant lesions and development of complications ($p < 0.001$). 119 patients were still alive at last follow-up. Recurrence was observed in 11 patients (9.5%) during a median follow-up of 29 months: HGD was found in 6 patients. All recurrences but one were successfully managed endoscopically. Only one patient required surgically.
Conclusion:
1. Histological analysis found no cancer in any of the resected specimen demonstrating that the optical diagnosis alone can help exclude polyps with cancers from endoscopic resection.
2. Endoscopic resection can be successfully carried out in majority of patients
3. Adverse event rate of duodenal resection is high at just below 20%.
4. Size >3 cm seems to be the predictor of high risk polyps as most complications happened in this group.
5. Most of the complications can be managed endoscopically in expert hands. We recommend that such polyps should only be resected at expert centres.
Disclosure: Nothing to disclose

P1389 SAFETY OF ENDOSCOPIC FULL-THICKNESS RESECTION OF SUPEPITHELIAL TUMORS IN THE STOMACH AFTER PRIOR FULL-THICKNESS SUTURING

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Introduction: Endoscopic resection of gastric supepithelial tumours after application of full-thickness sutures with a device originally designed for endoscopic anti-reflux therapy was proven to be feasible and efficient in a recent study on 31 patients (Schmidt A, et al. *Endoscopy*. 2015)
Aims and Methods: The aim of this study was to extend the above-mentioned study and further analyse safety of endoscopy full-thickness resection of gastric supepithelial tumours in a larger cohort. The above-mentioned study was extended until January 2018 and patients were identified retrospectively. The tumour was resected as following: after prior full-thickness suturing underneath the tumour with either the Plicator device or the GERDX device, the tumour was then resected with a snare. Besides basic demographic and health characteristics we as well included information on peri- and post-interventional complications.
Results: 50 patients were finally included in the study. The tumour was located in the gastric antrum in 12, the corpus in 26, the fundus in 7 and the cardia in 5 patients. Median tumour size as measured by endoscopic ultrasound prior to resection was 20 mm (range: 7–60). In 27 patients the resection was done with the Plicator and in 22 with the GERDX device. A median of 3 (range: 1–12) sutures was applied in total, of which a median of 2 were applied before resection; in 23 patients at least one further suture was applied after snare resection. Endoscopic resection was feasible in all patients. Bleeding during resection occurred in 29 patients and could be managed endoscopically in all patients; peri-interventional transfusion of red blood cells was necessary in only 1 patient. A perforation or dehiscence of the gastric wall after resection occurred in 14 patients and could be closed by application of furthers sutures or clips in all cases. A control endoscopy the following day was routinely performed. Treatment of bleeding was necessary in 7 patients during control endoscopy and in 3 patients treatment of perforation was performed. An episode of further bleeding after control endoscopy occurred in 7 patients and could again be managed endoscopically. During follow-up the most severe complication was noted in one patient who died 8 days after resection due to delayed perforation and peritonitis. One patient experienced oesophageal perforation and pleural empyema, who finally could be discharged 36 days after resection. Median hospital stay in all patients was 4 days (range: 2–36).
Conclusion: The endoscopic resection of subepithelial tumours in the stomach after prior full-thickness suturing is safe. Bleeding or perforations commonly occur during resection, but can be managed sucessfully endoscopically in all cases. The most important postinterventional complication is bleeding, which again can be treated endoscopically. Severe complications are rare.
Disclosure: Nothing to disclose

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P1390 DELAYED REMOVAL INCREASED THE COMPLICATION OF SHARP FOREIGN BODY IN THE UPPER GASTROINTESTINAL TRACT: AN EXPERIENCE FROM MULTIPLE CENTERS IN CHINA

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Introduction: Foreign bodies (FBs) ingestion is a common medical emergency accounting for 4% of all emergency endoscopies, secondary only to the GI bleeding.[1] 70∼75% of FBs are located in the esophagus[2]. The need of endoscopic management reached up to 63∼76%[3–5] with 3%∼20% of incidence of complications[6]. According to the latest guidelines from ESGE, emergent endoscopy is recommended for the impaction of sharp-pointed objects within 24 hours[5]. However, there were still different opinions on the endoscopic methods with different FBs.
Aims and Methods: The study was performed from October 2015 to August 2016 among 595 patients with clinical suspicion of foreign body ingestion from 18 general hospitals in China. The patient data including age, gender, clinical features, and data about endoscopic management including types and locations of

foreign bodies, retrieval devices, outcomes and complications were collected and analyzed.
Results: 1) The most common types of foreign bodies were sharp ones (75.9%), including fish bones (34.0%), chicken bones (22.1%), and fruit nucleus (17.1%). A few were non-sharp ones (24.1%), such as food bolus (14.6%). The majority of them were short objects (<2.5cm, 74.0%), subsequently followed by middle objects (2.5~6.0cm, 24.5%) and long objects (>6cm, 1.5%). Most objects were lodged in the proximal esophagus (75.9%), followed by the middle segment (15.2%) and the distal segment (8.9%) of esophagus. 2) Complication rate was as high as 34.0%, which was increased with long retention time and sharp objects ($P < 0.001$). The rate was increased by 2.2- and 6.1- folds after impacted for over 24 hours or 48 hours as compared to in 12 hours. Logistic regression analysis indicated that sharp objects had obviously more complications than non-sharp ones (OR 3.36, 95% CI: 1.97–5.74). In particular, the incidence of perforation was 5.6%, which was strongly related with long retention time and sharp objects ($P < 0.01$), but not with locations or lengths of the objects ($P > 0.05$). For sharp objects (75.9%), complication rate was increased by increased retention time ($P < 0.001$).
Conclusion: Foreign bodies, especially sharp ones, should be removed as soon as possible within 24 hours, to further decrease severe complications.
Disclosure: Nothing to disclose

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P1391 ENDOSCOPIC MUCOSAL AUTOGRAFT FOR REVERSING THE REFRACTORY ESOPHAGEAL CAUSTIC STRICTURE: THE PRELIMINARY HUMAN EXPERIENCE

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Introduction: Esophageal caustic stricture is the stubborn disease and postoperative restenosis limits clinical efficacy for endoscopic dilation. Some refractory cases with frequent recurrence or anatomic abnormality may require surgical intervention. Autologous mucosa graft has been successfully applied for treating urethral stricture and preventing stricture after extensive mucosal resection. We aimed to use mucosal autograft endoscopically to treat the refractory esophageal stricture.
Aims and Methods: Three patients with intractable corrosive esophageal stricture were treated endoscopically via combining dilation with autologous mucosal transplantation. For donor graft, the autologous normal esophageal mucosa was firstly chosen considering with tissue homology. The standard ESD was successfully performed as described. The isolate normal mucosal patch was spread in 37°C 0.9% saline, then rapidly delivered to the defect region endoscopically following gastric intubation. The basolateral side of mucosal patch should orient towards the defect surface. The graft was fixed by clips (Olympus, Japan). All patients received postoperative anti-acid and anti-infection intervention, and were fasted for 5–7 days.
Results: All procedures were successful without severe complications. Mucosa regeneration were shown at the transplanted segments. One patient maintained normal diet with complete remission after one-year follow-up. Intraluminal stenosis and dysphagia were significantly improved in another two cases.
Conclusion: Our preliminary human experience achieved the amazing success for refractory caustic stricture. The findings need to be verified in more controlled trials. The standard modality of operation and post-operational care are urgently required for clinical practice. If effective and reproducible, this strategy might substantially benefit patients suffering from corrosive esophageal stricture.
Disclosure: Nothing to disclose

P1392 ENDOSCOPIC SCREENING FOR BIERMER'S DISEASE: EXPERIENCE OF A MOROCCAN ENDOSCOPY UNIT

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Introduction: Biermer's Disease is an auto immune affection that is a preneoplasic situation and can lead to carcinoid tumors and gastric adenocarcinoma. Thus, the endoscopic screening of patients with Biermer's disease is necessary should be evenly performed. The aim of our work is to relate the experience of our gastroenterology and endoscopy unit concerning the endoscopic screening of Biermer's disease.
Aims and Methods: This study was run from January 2006 to January 2018 and reported all the cases of Biermer's disease admitted to the unit. All patients underwent an upper gastrointestinal endoscopy with antral and fundic biopsies and biopsies of the lesions if any. We reported the clinical, endoscopic and histological and therapeutic aspects.
Results: Within 18165 upper gastrointestinal endoscopies run during this period, 251 Biermer's disease were reported, with a frequency of 1.38%. The age of patients was from 21 to 80 with an average of 40 years. There was a slight male predominance of 56.5%. The upper gastrointestinal endoscopy found a fundus congestion in 67% of the cases, polypoid lesions in 25% of the cases, they were located in the fundus in 21% of the cases and the antrum in 4% of the cases. The endoscopy was normal for 6% of the patients.
Histological analysis revealed a chronic atrophic fundal gastritis in 32% of the cases, an intestinal and pyloric metaplasia with ECL cells hyperplasia was associated to the gastritis in 40% of the cases, a neuroendocrine tumor with ECL cells hyperplasia was described in 15% of the cases, hyperplasic polyps were present in 9% of the cases, and polyadenoma in low grade dysplasia were found in 3% of the cases. Hp infection was found in 75% of the hyperplasic polyps, and in 50% of the gastric adenomas, and in 50% of neuroendocrine tumors.
Conclusion: Biermer's disease is a preneoplasic state that can degenerate into neuroendoscrine tumors and gastric adenocarcinoma. In our series, 18% of the patients had a tumoral evolution, and none presented a gastric adenocarcinoma. The gastric screening through upper gastrointestinal endoscopy and histology for pernicious anaemia is necessary.
Disclosure: Nothing to disclose

P1393 PER-ORAL ENDOSCOPIC MYOTOMY FOR ESOPHAGEAL DIVERTICULA WITH OR WITHOUT ESOPHAGEAL MOTILITY DISORDERS

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Introduction: Mid-esophageal and epiphrenic diverticula are frequently associated with esophageal motility disorders [1, 2]. Optimal treatment of mid-esophageal and epiphrenic diverticula is still debated. Of note, in case of esophageal motility disorder, several authors suggest to perform a surgical myotomy of the lower esophageal sphincter associated to diverticulectomy [2, 3]. In the absence of esophageal motility disorder, instead, diverticulectomy alone may be considered [3].
Per-oral endoscopic myotomy (POEM) has become an accepted treatment for major esophageal motility disorders and has been recently used to perform a diverticulotomy [4], a technique similar to the one used for the treatment of Zenker's diverticulum [5].
Aims and Methods: The aim of this study is to report our experience with POEM for the treatment of patients with mid-esophageal or epiphrenic diverticula with or without underlying esophageal motility disorder.
Data were prospectively collected from a cohort of patients with mid-esophageal or epiphrenic esophageal diverticula treated with POEM between April 2017 and March 2018. Preoperative evaluation included in all patients barium contrast radiographic study, high-resolution manometry (HRM) and esophagogastroduodenoscopy. Eckardt score was used to report the severity of patient symptoms before POEM and at each postoperative evaluation [6]. POEM was performed under general anesthesia by two expert endoscopists following the procedural steps described by Inoue et al [7]. In case of esophageal motility disorder, myotomy of the circular muscle bundle was performed on the opposite side of the diverticulum using a triangular tip knife. When no motility disorder was observed, myotomy was then performed homolateral to the diverticulum to achieve diverticulotomy, as previously described by Mou et al [4]. Barium contrast radiographic study was performed on postoperative day 1. Postoperative HRM was performed 3 months after endoscopic treatment. Follow-up visits were scheduled every 3 months.
Results: Four patients were treated with POEM for mid-esophageal or epiphrenic diverticula with or without underlying esophageal motility disorder. One patient suffered from distal esophageal spasm, one from jackhammer esophagus, one from esophago-gastric junction outflow obstruction. In one case no esophageal motility disorder was detected. Patients' age ranged from 65 to 77 years. Diverticulum size was 3 cm in one case and 6 cm in the others three cases. Pre operative Eckard score ranged from 6 to 8. No procedural related adverse events were reported. Patients with esophageal motility disorders were asymptomatic at 6–8 months follow-up except from one case of pathological reflux that was

treated with proton pump inhibitor. The patient without motility disorder had an Eckard score of 2 at 1 month follow up.
Conclusion: Mid-esophageal and epiphrenic diverticula may be associated with esophageal motility disorders. In this case, POEM performed contralateral to the diverticulum allows to treat the cause underlying the diverticulum and seems to achieve good early clinical outcomes. In the absence of a motility disorder, endoscopic diverticulotomy appears feasible in experienced hands with promising early clinical outcomes, and might be offered as an alternative to surgical diverticulectomy in selected patients.
Disclosure: Nothing to disclose

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P1394 PERORAL ENDOSCOPIC MYOTOMY (POEM) IS EFFECTIVE IN TREATMENT OF NON CARDIAC CHEST PAIN CAUSED BY HYPERCONTRACTILE ESOPHAGEAL MOTILITY DISORDERS

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Introduction: Non cardiac chest pain (NCCP) is recurrent angina pectoris like pain without evidence of coronary heart disease in conventional diagnostic evaluation. The treatment options and therapeutical results for patients with hypercontractile esophageal motility disorders are disappointing so far. Recently, peroral endoscopic myotomy (POEM) was established as treatment option in achalasia. However, limited data exist on the effectivity of POEM in NCCP with hypercontractile esophageal motility disorders.
Aims and Methods: In this prospective study 18 patients (female = 8, mean age 63.2 ± 13.2 years) with NCCP and hypercontractile esophageal motility disorders (type III achalasia n = 8, Jackhammer esophagus n = 9, distal esophageal spasm n = 1) were included. All patients underwent standardized diagnostic work-up including esophagogastroduodenoscopy with esophageal biopsies, high-resolution esophageal manometry and combined intraluminal impedance and pH testing before and 3 weeks after procedure. The POEM procedure was executed standardized (Hybridknife®, t-type, electric generator VIO 300D®, Erbe, Tuebingen, Germany) with myotomy of the lower esophageal sphincter and the manometrically identified hypercontractile segments in the esopahgeal body. A standardized symptom questionnaire was disposed before POEM, 3 weeks after and every 6 months after the intervention.
Results: 15 patients (clinical success rate 83.3%) showed significant symptom relief after POEM (pre-Eckardt-score: 7.9 ± 1.4, 3 weeks post: 1.8 ± 1.8, 6 months post: 2.3 ± 2.9 and 1.9 ± 2 after a mean follow-up of 10.5 ± 10.0 months). High-resolution-manometry showed significant reduction in IRP (pre-POEM: 22.8 ± 17.8 mm Hg, post-POEM: 12.9 ± 14.7 mm Hg) and DCI (pre-POEM: 4208 ± 3334 mmHg*s*cm, post-POEM: 1133 ± 1017 mmHg*s*cm). Two moderate adverse events classified with ASGE lexicon severity grading system were handled endoscopically. One case of gastroesophageal reflux disease (Type B, LA-Classification) occurred after intervention and was handled successfully with PPI. Two patients required secondary intervention because of persisting hypercontractile segments in HR-manometry.
Conclusion: The results suggest that POEM is an effective and safe therapeutic option for patients with NCCP and hypercontractile esophageal motility disorders.
Disclosure: Nothing to disclose

P1395 NATIONAL TRENDS IN HEALTHCARE OUTCOMES AND UTILIZATION OF ENDOSCOPIC AND SURGICAL INTERVENTIONS IN PATIENTS HOSPITALIZED WITH OESOPHAGEAL FOREIGN BODY

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Introduction: The incidence and prevalence of oesophageal foreign body (OFB) is on the rise. However, its impact on the rate of inpatient admissions, utilization of endoscopic and surgical interventions and healthcare outcomes is poorly understood. We conducted a study to analyze these outcomes using the national inpatient sample (NIS) database.
Aims and Methods: Data on all adult (≥18) patient admitted with OFB was extracted from the NIS database from 1998 to 2013. ICD-9-CM code, 935.1 was used to identify patients with a primary discharge diagnosis of OFB. The temporal trends in discharge rates as well as in length of stay (LOS), hospital charges and in-hospital mortality rates were assessed by linear and polynomial regression. A p value of <0.05 was considered as statistically significant.
Results: Average age, gender and race of inpatients with OFB were not significantly different between 1998 and 2013. Patients were more likely to be smokers, alcoholics with higher Charlson comorbidity index in 2013 as compared to 1998. The rate of OFB admissions increased significantly from 1998 to 2005 followed by a decline thereafter ($p = 0.01$). LOS and hospital charges increased by 0.02 days/year ($p = 0.015$) and \$1547/year ($p < 0.001$) respectively. Patients undergoing oesophago-gastro-duodenoscopy (OGD) within 24 hours of admission were higher in 1998 as compared to 2013 ($p = 0.026$). The rates of surgical intervention and inpatient mortality did not change significantly over the study period.
Conclusion: The rate of inpatient admissions for OFB is on the decline in recent years, suggesting the modern-day practice of cost-effective medicine. LOS and hospitalization cost have increased, whereas rates of surgical intervention and inpatient mortality have not changed significantly over the study period.
Disclosure: This abstract has been accepted for a poster presentation in Digestive Disease Week (DDW) meeting at Washington DC, June/2018

Abstract No: P1395
Table 1: Patient, Procedural characteristics and Outcomes in 1998 and 2013. [OGD=Oesophago-gastro-duodenoscopy, CCI=Charlson comorbidity index

Factor	Oesophageal foreign body in 1998	Oesophageal foreign body per 10,000 Admissions in 1998	Oesophageal foreign body in 2013	Oesophageal foreign body per 10,000 Admissions in 2013	p-value
Age (years), mean ± se	65.5 ± .0.76		64.6 ± 0.65		0.39
Smoking	151 (3.6%)	0.74	1150 (27%)	1.5	<0.001
Alcohol abuse	70 (1.7%)	0.65	185 (4.3%)	1.3	0.037
Congestive heart failure	254 (6.1%)	1.05	410 (9.6)	1.6	0.019
Renal failure	15 (0.37%)	0.2	410 (9.6)	1.1	0.001
Fluid and electrolyte disorders	629 (15%)	1.7	860 (20.2%)	1.2	0.005
CCI, mean ± se	0.67 ± 0.05		1.1 ± 0.06		<0.001
OGD performed	3694 (88%)	30.5	3505 (82.4%)	30.2	0.86
OGD within 24 hours of admission	2008 (56.9%)	118.5	2225 (53.8%)	97.6	0.026
Surgical procedure to remove Oesophageal foreign body	58 (1.4%)	62	65 (1.5%)	82.4	0.49
Length of stay (days), mean ± se	2.5 ± 0.12		2.7 ± 0.13		0.39
Inflation-adjusted costs (2013 \$), mean ± se	5261.2 ± 243.5		28739.5 ± 1177.1		<0.001

P1397 EFFECT OF VONOPRAZAN ON THE TREATMENT OF POST-ENDOSCOPIC SUBMUCOSAL DISSECTION ARTIFICIAL GASTRIC ULCER

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Introduction: Proton pump inhibitors (PPI) are effective for the treatment of gastric ulcers (GU) after endoscopic submucosal dissection (ESD). Vonoprazan, a potassium-competitive acid blocker, has a strong inhibitory effect for gastric acid secretion. However, the efficacy of Vonoprazan is unclear in this field.

Aims and Methods: The aim of this study is to clarify which factors are more important for healing of GU after ESD procedure. We compare the healing status of ESD-induced GU and incidence of post-ESD bleeding between subjects treated with Vonoprazan and Rabeprazole.

Two hundred twenty-two patients who were performed ESD for the treatment of gastric neoplasms between April 2014 and April 2017 at our hospital were enrolled in this study. Twenty mg per day Vonoprazan (V group) or 10mg per day Rabeprazole (R group) for 4 weeks after ESD. Endoscopic images on 30th day after ESD were used for the evaluation of the shrinking rate of ESD ulcers. For the assessment of healing effect, age, sex, past history, smoking, drinking, drugs, the status of *Helicobacter pylori* (HP) infection, tumor location (Upper/Middle/Lower), tumor size, tumor depth, and tumor histopathology were analyzed by multivariate analysis.

Results: The ulcer healing was only related to the tumor size ($P < 0.01$) and drugs. The ratio of treated lesions with scar-stage was significantly higher in the V group than in R group (30.1% < 40 of 133 > vs 16.9% < 15 of 89 >, $P = 0.027$). In the V group, patients got good healing regardless of HP infection although patients with HP infection had the low rate of ulcer scar-stage as compared with patients without HP infection in the R group ($P = 0.021$). The factors affecting post-ESD bleeding incidence were the patients who has a diabetes and renal failure past history ($P < 0.05$). There were no statistically significant differences between the two group with regard to use of anticoagulants, antiplatelet agents, steroid, and non-steroidal anti-inflammatory drugs (NSAIDs).

Conclusion: Vonoprazan was significantly superior to Rabeprazole for the healing of post-ESD artificial ulcer. Post-ESD bleeding did not have the significant difference between drugs, but the contraction rate is significantly faster in Vonoprazan and may be a medical care drug to contribute to economically at the point. Therefore Vonoprazan may supersede PPI in treating post-ESD artificial ulcers.

Disclosure: Nothing to disclose

P1398 FLEXIBLE ENDOSCOPIC MYOTOMY IN ZENKER'S DIVERTICULUM: NO CORRELATION BETWEEN OUTCOME AND DIVERTICULUM SIZE OR PRETREATMENT AFTER COMPLETE SEPTOTOMY

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Introduction: Flexible endoscopic myotomy offers several advantages over competing techniques like surgery or rigid endoscopic myotomy because of less invasiveness. Nevertheless different studies displayed a declining success rate with rising diverticulum size or in pretreated patients.

Aims and Methods: This is a single-center retrospective study including 42 patients with symptomatic Zenker's diverticulum between 4/2014 and 12/2016. Patient characteristics showed a male-female ratio of 3:2, mean age was 73 years (range 43–94). 26% of patients were pretreated (flexible endoscopic myotomy (5), open surgery (2), rigid endoscopic diverticulotomy (4). Mean size of diverticulum was 3.3 cm (range 1.5–6.5 cm). The intervention was performed following a standardized protocoll. On first day routine endoscopy and barium esophagogram was performed.

On day 2 mucomyotomy under conscious sedation took place using a needleknife (Zimmon knife, Cook medical, Winston-Salem, NC) with a diverticuloscope (Cook medical, Winston-Salem, NC) or a standard transparent cap. The complete incision of the septum was intended in one session. On first postinterventional day water-soluble contrast-esophagogram excluded perforation and oral intake was started. Clinical success was defined as complete resolution of clinical symptoms and disappearance of diverticulum in esophagogram.

Clinical success rate was interpreted in relation to the variables diverticulum size and pretreatment. Level of significance was evaluated with fisher's exact test.

Results: Overall clinical success rate was 88%. Adverse events occurred in 3 patients: bleeding (2), microperforation (1), all treated conservatively (complication rate 7.1%).

Mean follow-up was 19 ± 10 months, 6 patients developed recurrance of disease (14%), 4 of them were treated successfully with second endoscopic intervention. Mean time until recurrance was 8 ± 5 months. There were no significant changes in outcome in relation to the variables diverticulum size or pretreatment.

Conclusion: Flexible endoscopic myotomy is a safe and effective treatment in Zenker's diverticulum.

Our retrospective data suggest that clinical success rate is indepent of diverticulum size or state of pretreatment when complete septotomy is performed.

Disclosure: Nothing to disclose

P1399 TRANSORAL OUTLET REDUCTION FOR WEIGHT REGAIN AFTER GASTRIC BYPASS: ONE-YEAR FOLLOW-UP

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Introduction: Enlargement of gastrojejunal anastomosis is associated with weight regain in patients with Roux-en-Y gastric bypass (RYGB). Endoscopic transoral outlet reduction (TORe) has proven safe and effective for treatment of weight regain. The objective of this study was to evaluate the safety and the efficacy in weight loss and quality of life after TORe.

Aims and Methods: Patients with at least 50% of weight regain and enlarged gastric outlet after RYGB treated at our centre were retrospectively identified from a prospectively collected database. Endoscopic outlet reduction was performed with Overstitch (Apollo Endosurgery), a full-thickness endoscopic suturing device. Before suturing the outlet rims were cauterized with pulsed Argon Plasma Coagulation on 40 Watts, 1l/min (VIO 300D, ERBE Elektromedizin GmbH). Telephonic follow-up was done at 1, 3, 6 and 12 months. The quality of life was evaluated according to the Quality Of Life Scale (QOLS).

Results: Thirty-three patients (29 female, mean age 43.7) underwent TORe from January 2015 to April 2017. Baseline mean BMI was 37.9 (range 31–50) and weight was 107.9 kg (range 77–132). Mean procedure time was 34 minutes (range 15–60) and a mean number of 2.3 stitches per patient were placed (range 2–4) on the level of the gastric outlet. After suturing the patency of the redone outlet was tested with a standard gastroscope. There were 2 (6%) complications: one patient developed fever due to a small retrogastric collection and was treated with antibiotics, while one patient had a gastric perforation that required urgent surgery. Mean hospital stay was 2.4 days (range 1–10).

Thirty patients completed the follow up at 1, 3, 6 and 12 months. Three patients were lost during the follow-up. Mean weight loss at 1-month was 8.7 kg, at 3 months was 11.7 kg, at 6 months was 14.1 kg while at 12 months was 14.8 kg. Mean BMI was 32 and the %EWL was 34.5 at 1 year. Only two patients regained weight compared to baseline during the follow up. All the patients reported satiety after 1 month, which was confirmed by 56% of patients after 6 months and by 37.5% after 12 months of follow-up. In addition, over 50% of the study population had an improvement quality of life in terms of physical activity, relationships and dietary habits at 1 year follow-up.

Conclusion: In our experience TORe was a safe and effective procedure in patients with weight regain after RYGB, with stable promising results even in the long-term follow-up.

Moreover, our study showed an improvement in patients' quality of life, in terms of satiety, relationships, dietary habits and aerobic physical exercise.

Further clinical trials are needed to confirm these results and to establish the role and correct timing of TORe after RYGB in the multidisciplinary strategy.

Disclosure: Nothing to disclose

P1400 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR UNDIFFERENTIATED EARLY GASTRIC CANCER, BEYOND EXPANDED CRITERIA

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Introduction: Expanded indication of endoscopic submucosal dissection (ESD) for intramucosal undifferentiated early gastric cancer (EGC) up to 2 cm without lymphovascular invasion have been accepted because of negligible lymph node metastasis.
However, preoperative measurement of the tumor was completely not as same as postoperative one and if the postoperative tumor size would be a little more than 2 cm with R0 resection, additional surgery recommaded.
Aims and Methods: The aim of this retrospective study was to analyze the long-term outcomes of ESD carried out to treat undifferentiated EGC in two groups (group A: up to 2 cm, group B: 2–3 cm)
Between January 2001 and March 2015, 104 patients with undifferentiated early gastric cancer (EGC) including poorly differentiated adenocarcinoma (PD, $n=66$) or signet ring cell carcinoma (SG, $n=38$) on preoperative biopsy underwent ESD (group A: 71 cases, group B: 33 cases),
Total ESD speciemens were evaluated en bloc resection, R0 resection, and curative resection (CR) and to evaluate long-term outcome, annual endoscopic surveillance with biopsy and CT scan were done.
Results: M/F was 40/31 and 17/16. Mean follow-up period in group A and B were 61.10 ± 38.12, 60.79 ± 47.75. Mean age in group A and B were 52.90 ± 13.62, 57.00 ± 12.25. En bloc in group A and B were achieved in 92.9%, 90.9% of patients, respectively *(NS)*. R0 resection in were achieved in 87.3%, 51.5% of patients, respectively *($p < 0.05$)*.
Curative resection was 83.0% in group A and group B was not include this definition.
Postoperative bleeding, perforation during the procedure, and delayed perforation were no significantly different in both groups, respectively.
Recurrence rate in group A and B were 5.6%($n=4$), 18.1% ($n=6$), retrospectively *(NS)*.
Recurrence rate with R0 resection in group A and B were 1.7% (1/59), 6.25% (1/16) *(NS)*.
All cases with lateral margin positive required additional ESD ($n=2$), desctructive therapy ($n=3$), or surgery ($n=4$) and no recurrence happened.
No patient died of gastric cancer.
Conclusion: In group B, R0 resection rate was lower than group A. However, long term follow up showed en bloc resection, recurrence rate, and with R0 resection in both group were not different. Carefully, undifferented EGC with 2 to 3 cm in a size recommended ESD and long-term close follow-up.
Disclosure: Nothing to disclose

P1401 EFFICACY OF G-POEM IN REFRACTORY GASTROPARESIS: A SYSTEMATIC REVIEW

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Introduction: Gastric per-oral endoscopic myotomy (G-POEM) of the pylorus has emerged as a novel endoscopic technique for refractory gastroparesis (GP). However, limited data on the efficacy and safety of G-POEM are available. Therefore, a systematic review was conducted to evaluate the efficacy of G-POEM in refractory GP.
Aims and Methods: We performed a thorough literature search using PubMed, EMBASE, Cochrane library, Medline, Google scholar and Science citation index for studies related to G-POEM between January 2010 to January 2018. Search terms included MeSH and non-MeSH terms relating to gastroparesis, refractory gastroparesis, gastric per-oral endoscopic myotomy, endoscopic techniques in gastroparesis and delayed gastric emptying. Additional case-reports, case series, and abstracts were retrieved by searching from references of relevant studies. Pooled technical success, clinical success, and adverse events were calculated.
Results: Based on our search criteria 23 studies were identified and 7 were excluded after careful review. 16 studies which included 189 patients were analyzed. The overall technical success rate, clinical success rate, and frequency of adverse events were 88.5, 83.2, and 10.8%, respectively. The common adverse events associated with G-POEM were pneumoperitoneum (4.7%), ulcer (1.6%), bleeding (1.5%) and stricture (1.01%). Overall mean procedure duration was 61.2 +/− 11.4 minutes.
Conclusion: G-POEM is a technically feasible and effective therapeutic option for gastroparesis with good clinical responses. However, larger data is still required to determine the subgroup of patients who would benefit from this novel procedure.
Disclosure: Nothing to disclose

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P1402 FLEXIBLE ENDOSCOPY VESSEL-TISSUE SEALER ASSISTED FOR TREATMENT OF ZENKER DIVERTICULUM: AN EFFECTIVE AND SAFE PROCEDURE

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Introduction: Zenker's diverticulum (ZD) is an uncommon disorder. Therapy of symptomatic ZD has evolved from an open surgical approach to less invasive transoral endoscopic techniques.
Flexible endoscopy allows to use vessel-tissue sealer to perform diverticulotomy. An overtube protects both diverticulum and esophageal wall with a well-view of the septum. This procedure has demonstrated to be safe for high-risk surgical patients in small previous case series with a lower morbidity rates and quick patient's recovery. Very little has been published with this approach in ZD treatment.
Aims and Methods: 1. To evaluate the effectiveness and safety of flexible endoscopy treatment assisted by vessel-tissue sealer technique. 2. Describe epidemiology data of ZD patients.
One-single-centre prospective and descriptive study including ZD patients treated with flexible endoscopy, using vessel-tissue sealer technique for the resection of ZD.
Patients were included consecutively from March 2009 to April 2018. Patients were censored until the end of the follow-up or death. We analysed complications, symptoms before treatment, sex, age, type of sedation and number of interventions needed for resolve ZD. Bleeding complication was considered when cases required a second endoscopy.
Results: 46 symptomatic ZD patients were included in the final analysis. Women were 41.3%, median-age of 73.7 ± 11 years. Median follow-up period was 37.21 ± 28 months. 58.7% ZD were considered small (<3 cm). Solid or semi-solid food related dysphagia was present in 55.6% of patients, whereas liquid-food and total dysphagia were observed in 34.8% and, 6.7% respectively. There were 4.3% complications with this technique. Bleeding was the most frequent adverse event in relation to endoscopy procedure (2.2%).
Technique was successful in 76.1% in one single procedure. However, it increased until 89.1% with a second procedure. No statistically significant differences were found between complications rates according to diverticulum length, or number of interventions needed. Likewise, we did not find differences between the need of re-intervention and diverticulum length or symptoms. The majority of patients (80.7%), were managed as out-patient or short admission less than 24 hours.
Conclusion: In this large case series study, ZD treatment based on flexible endoscopy assisted by vessel-tissue sealer is an effective and safe procedure with a high successful rate in a few endoscopy sessions and low complications rate. This procedure can be recommended as a solid alternative in ZD endoscopic treatment.
Disclosure: Nothing to disclose

P1403 PRIMARILY ENDOSCOPIC MANAGEMENT OF POST-SURGICAL FISTULAE IN THE UPPER GI TRACT IS AN EFFECTIVE AND SAFE THERAPEUTIC OPTION

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Introduction: Post-surgical fistulae involving the upper digestive tract (UDT) are associated with significant morbidity and mortality. Endoscopic management is a minimally invasive alternative option to surgical repair in this situations.
Aims and Methods: We aimed to access efficacy and safety of a primarily endoscopic approach for management of post-surgical fistulae involving the UDT. Retrospective multi-centric study, involving 71 consecutive patients that were managed endoscopically for post-surgical fistulae of the UDT, between March 2009 and December 2017, in 3 endoscopic centers. Possible factors associated with fistula closure, fistula recurrence and mortality including age, indication for surgery, fistula orifice size and time to fistula diagnosis/ treatment were evaluated. Complications related to endoscopic therapy were classified as early ($\leq$1 week) or late ($>$ 1week). Statistical analysis was performed with IBM SPSS®22 and a p value <0.05 was considered significant.
Results: The mean age was 52.3 ± 16.2 years and 63.4% (45) were women. Indications for surgery were: obesity 57.7% (41); neoplasia 32.4% (23); others 9.9%(7). Median time between surgery and fistula diagnosis was 8(2–62) days. The average size of fistula orifice was 7.74 ± 5.06mm. Endoscopic interventions included: Metallic stents in 86% (61) patients (totally covered 29; partially covered 32), clips in 21.1% (15) patients (OTSC 7, TTS 8) and intraluminal drainage with plastic stents in 2.8% (2) patients.
Early complications ($\leq$1 week) occurred in 7.0%(5) patients: stent migration (n = 3); mucosal dissection (n = 1); anastomotic dehiscence (n = 1) and late complications ($>$1 week) in 29.6%(21) patients: dysphagia related to mucosal ingrowth/overgrowth (n = 8), stent fracture (n = 4), stenosis after stent removal (n = 3), migration (n = 3), other (n = 3).
Overall clinical success (fistula closure) was documented in 76.1%(54) patients. Fistula closure was obtained with a single endoscopic intervention in only 38%(27) patients. The median number of endoscopies until fistula closure was 2(1–8). Median time until confirmation of fistula closure was 8(4–63) weeks. Surgical re-intervention was performed in 21.9%(13) patients. The main reasons for surgical re-intervention were: Abdominal fluid collection drainage and peritoneal lavage (n = 7), esophageal exclusion (n = 3), fistula suture (n = 2), fistula-jejunostomy (n = 1).
After a median follow-up of 8(1–98) months, the mortality rate was 22.5% (16) being significantly higher in patients who underwent surgery for neoplastic compared to non-neoplastic etiologies (56.5% vs 8.3%, $p < 0.001$). None of the evaluated variables were found to be significantly associated with endoscopic treatment failure, fistula recurrence or mortality.
Conclusion: Endoscopic treatment of post-surgical fistulae involving the upper digestive tract is associated with high clinical success with an acceptable safety profile.
Disclosure: Nothing to disclose

P1404 SURVEILLANCE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL COLORECTAL TUMORS

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Introduction: Endoscopic mucosal resection (EMR) is currently the most used technique for resection of large colorectal polyps. However, in large lesions EMR can often only be performed in a piecemeal fashion resulting in relatively low radical (R0)-resection rates and high recurrence rates. Endoscopic submucosal dissection (ESD) is a newer procedure that is more difficult resulting in a longer procedural time, but is promising due to the high en bloc resection rates and the very low recurrence rates. There are few reports on surveillance for patients with superficial colorectal tumors after ESD. The aim of this study is to evaluate surveillance after ESD for superficial colorectal tumors.
Aims and Methods: Endoscopic submucosal dissection (ESD) was performed on 558 colorectal tumors in 500 consecutive patients at Showa University Northern Yokohama Hospital between September 2003 and March 2013. Tumors larger than 20mm were indicated for ESD. We investigated the following variables: patient characteristics, the American Society of Anesthesiologists score, tumor location, tumor size, growth type, pit pattern, histology, en bloc resection rate, achievement of curative resection, procedure time, and adverse events. Curative resection was defined when the pathological specimen had tumor-free resection margins, without submucosal deep invasion ($\geq$1000μm), lymphovascular involvement, or a poorly differentiated adenocarcinoma component.
Results: We identified 496 tumors in 446 patients who were confirmed follow-up data for more than 5 years. Based on the postprocedural pathologic reports, 17 lesions were excluded because they showed positive vertical margines and they were indicated for additional surgery. The rest of lesions were categorized as follows: lesions with piecemeal resection (n = 9), lesions with en bloc resection (n = 470). The 5-year cumulative recurrence rate was 22.2%(2/9) in piecemeal resection group and 0.6%(3/470) in en bloc resection group ($P = 0.003$). Further, En bloc resection group were divided as follows: lesions with positive lateral margins of en bloc resection (n = 15) and lesions with R0 resection (n = 455). The 5-year cumulative recurrence rate was 6.7%(1/15) in the non-R0 group and 0.4%(2/455) in the R0 group. The risk of recurrence after complete en bloc resection of ESD is definitely low, but two recurrence tumors were encountered.
Conclusion: The local recurrence rate was higher in lateral margin-positive cases than in R0 resection cases. En bloc resection of ESD could reduce recurrence. However there were a few cases to recur even if R0 resection was achieved, surveillance after ESD for superficial colorectal tumors are significant necessary for R0 resection.
Disclosure: Nothing to disclose

P1405 "DIAGNOSE-AND-LEAVE" STRATEGY FOR DIMINUTIVE LEFT COLORECTAL POLYPS

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Introduction: The "diagnose-and-leave" strategy is based on the decision of leaving in situ diminutive ($\leq$ 5mm) rectosigmoid hyperplastic polyps, based on optic chromoendoscopy assessment. ASGE recommends this strategy only if endoscopic diagnosis provides a 90% or higher negative predictive value for adenomatous histology when used with high confidence.
Aims and Methods: Our aim was to assess the feasibility of this strategy in our centre. We performed a prospective observational study of patients submitted to colonoscopy with optic chromoendoscopy (narrow-band imaging – NBI) during 2017. Pathological and endoscopic characteristics of diminutive left colorectal polyps (location, size, NICE classification and degree of confidence in this assessment) were collected. We compared NICE classification using optic chromoendoscopy and histology for each polyp.
Results: 107 colonoscopies and 199 diminutive left colorectal polyps were included: 48% from the descending/sigmoid colon and 52% from the rectum. Mean size was 3.4 ± 1mm. According to the NICE classification, 74% of polyps were type I and 26% type II. Pathology revealed that 58% were hyperplastic polyps, 33% were adenomas, 1% were sessile serrated polyps and 8% were inflammatory changes. The endoscopic diagnosis using NICE classification for adenomatous histology had an 82% accuracy, 51% sensibility, 95% specificity, 80% positive predictive value and 82% negative predictive value.
Conclusion: Optic chromoendoscopy assessment of diminutive left colorectal polyps did not reach the ASGE recommended cut-off. We will need to improve our optic chromoendoscopy performance, for instance trough the implementation of NBI training programs, before the "diagnose-and-leave" strategy can be used in our centre.
Disclosure: Nothing to disclose

P1406 SHOULD WE ASK FOR AN ILEO-COLONOSCOPY IN ALL PATIENTS WITH SPONDYLOARTHROPATHY OR ONLY IN SYMPTOMATIC PATIENTS?

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are the most common chronic inflammatory bowel disease (IBD) and may be associated with spondyloarthropathy (SPA). The aim of our work is to specify in a group of patients suffering from any form of SPA having benefited from systematic ileocolonoscopy the frequency of macroscopic lesions found at endoscopy.
Aims and Methods: This is a prospective study, during a period of 8 years and 7 months [January 2009 – July 2017]. All patients with a selected SPA according to ESSG criteria with or without gastrointestinal manifestations were included.
Results: One hundred seventy-three patients had undergone systematic ileocolonoscopy in the setting SPA, 33% had diarrhea as gastrointestinal manifestations. The average age of our patients was 38 years [16 years-76 years]. Male predominance was noted (91H/82F). The results of the endoscopy were as follows:
- Normal endoscopy without macroscopic lesions in 63% of cases, the histological study of systematic staged rectocolic biopsies confirmed these results except in 2 patients returning in favor of IBD.
- In 35% of patients endoscopy revealed an endoscopic appearance of ileal localized Crohn's disease in 34% of cases, colic in 36% of cases and ileocolic

localization in 30% of cases. However, there was no endoscopic aspect of UC. The endoscopic lesions described were: congestion with erythematic, aphtoid ulcerations, and erosions. The histological results in this group of patients were in favor of IBD in 31% of cases (N = 19) including 18 cases of CD and 1 case of UC, ileal and/or colic lesions were non-specific in 30 patients.
- Revealed the presence of colonic the presence of colonic polyps in 4 patients without lesions of the mucosa and the histological study was in favor of tubular adenoma in low-grade dysplasia in 2 cases and normal in the 2 others.
Colonoscopy was associated with a single case of complication represented by colonic perforation.
Of the patients in whom endoscopy was in favor of IBD, 49% were asymptomatic in the digestive tract.
Conclusion: In our study, systematic ileocoloscopy performed in patients with ASA revealed macroscopic and microscopic evidence of lesions in favor of IBD in 36.4%. This systematic screening is therefore recommended for early management of IBD.
Disclosure: Nothing to disclose

P1407 DO HYPERMOBILE JOINTS PREDICT A PAINFUL COLONOSCOPY?

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Introduction: Patient perception of colonoscopy varies greatly; young slender women and irritable bowel syndrome (IBS) patients appear to be at risk for peri-procedural pain. Recent evidence suggests a high prevalence of connective tissue disorders referred to as ''Hypermobility Spectrum Disorders'' (HSD) in this population. Therefore, HSD might be associated with increased pain during colonoscopy.
Aims and Methods: In this study we aimed to compare pain perception during colonoscopy between HSD and non-HSD patients. We prospectively included patients undergoing a standard colonoscopy. Patients with a history of major abdominal surgery, inflammatory bowel disease, or who were taking part in the national cancer screening program, were excluded. Subjects were assessed for HSD using the Brighton criteria, and IBS and functional dyspepsia (FD) using the ROME III criteria. After colonoscopy and recovery from sedation, patients were asked to report pain scores on a 100mm visual analogue scale (VAS). In addition, cecal intubation time was measured, and endoscopists scored the difficulty of the procedure (100mm VAS).
Results: Of 201 included patients, 22 (10.9%) met criteria for HSD. HSD patients were more often female than subjects without HSD (86.4% vs. 48.6%, $p = 0.001$). A crude linear regression model demonstrated that pain scores were 13.30mm higher (95%-CI 0.07–26.53, $p = 0.049$) in HSD vs. non-HSD patients. When subsequently correcting for possible confounding factors, however, this difference in pain scores could be explained by a confounding effect of female gender. Indeed, female gender was the strongest predictor of a higher pain score (B: 18.51mm, 95%-CI 10.56–26.47, $p < 0.001$). No other factors were found to be associated with patient pain score. Cecal intubation time and perceived procedural difficulty did not differ significantly between HSD and non-HSD subjects.
Conclusion: HSD is not an independent predictor of painful colonoscopy, since female gender as a confounding factor explains the higher pain scores in HSD patients compared to non-HSD patients. In addition, performing colonoscopy is not more complicated in HSD vs. non-HSD. Endoscopists should consider offering higher dose sedo-analgesia to female patients, but not to HSD patients per se.
Disclosure: Nothing to disclose

P1408 ROBOTIC FLEXIBLE ENDOSCOPY ALLOWING INTRALUMINAL SURGICAL TRIANGULATION FOR COMPLEX ENDOSCOPIC PROCEDURES: PRECLINICAL EXPERIENCE WITH 20 COLONIC ENDOSCOPIC MUCOSAL DISSECTIONS

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Introduction: Interventional procedures performed by means of flexible endoscopy have been considerably increasing thanks to recent technical and technological advances. Endoscopic submucosal dissection (ESD) is as effective as technically demanding. Robotic assistance and endoscopic translation of surgical principles could shorten the learning curve of existing endoluminal interventions and help establish innovative procedures. Our group previously described a master-slave robotic flexible endoscopic platform allowing for intraluminal surgical triangulation[1].
Aims and Methods: The aim of this study was to evaluate preclinical feasibility of robotic colonic ESD in a porcine model.
A mobile robotic cart and a detachable flexible endoscope compose the slave unit. The endoscope has 2 working channels for telemanipulated flexible instruments (graspers, a hook, and an isolated tip knife) and a third working channel for conventional endoscopic instruments. The jaw-like opening of the tip of the scope allows for the spacing of operative instruments offering surgical triangulation. The whole system has 10 degrees of freedom. The ergonomic master unit allows a single operator to control all movements of the endoscope and instruments through two control handles.
A surgeon without prior exposure to ESD had to perform 20 robotic colonic ESD in 6 pigs. Pseudotumors were delineated with coagulation marks on the bottom, lateral, and upper walls of the colon at a distance from the anal verge ranging between 15 and 35 cm. The assistant at the patient's side performed a lifting submucosal injection when required by the operator. Total time (from mucosal marking to complete excision), ESD time (from the first incision to complete excision), ''en bloc'' resection of the marked area, specimen size, excision speed (specimen size/ESD time) and complications were recorded.
Results: All 20 pseudotumors, with the mean size of $15.18 \pm 8.66 cm^2$, were resected ''en bloc''. One perforation (5%) occurred during the first experimental session and was managed intraoperatively, without interference with the planned procedure. Mean total time, ESD time, and excision speed accounted for 33.36 ± 14.20 min, 29.42 ± 14.29 min and $57.05 \pm 29.42 mm^2$/min respectively, regardless of the ESD location. Comparative analysis between the first 10 and the second 10 ESDs showed a significant increase in dissection speed (43.72 ± 30.74 vs. 70.37 ± 22.09; $p = 0.007$).
Conclusion: Robotic colonic ESD is feasible in a preclinical model. The robotic platform and flexible instruments responded well to the stress test. Comparing current results with previous studies performed by our group, robotic assistance outperforms conventional and mechanical platforms while carrying out colonic ESD[2]. These preclinical results suggest that robotic assistance could be a shortcut to endoscopic expertise. The described robotic flexible endoscopic platform is ready for the first clinical case.
Disclosure: Nothing to disclose

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P1409 I-SCAN OPTICAL ENHANCEMENT IN COMBINATION WITH MAGNIFICATION ENDOSCOPY FOR THE *IN VIVO* ASSESSMENT OF HISTOLOGIC INFLAMMATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Apart from mucosal healing as an established treatment goal in inflammatory bowel diseases (IBD), recent evidence suggests that histologic healing is another key prognostic parameter in IBD patients. I-scan optical enhancement (OE) is a novel endoscopic pre-processing optical filter technology, in which the spectrum of the emitted wavelengths is reduced, thereby leading to enhanced visualization of the mucosal and vascular pattern and first studies suggest that magnification endoscopy in combination with virtual chromoendoscopy can render the endoscopic diagnosis in IBD more precisely.
Aims and Methods: Our aim was to evaluate whether i-scan OE in combination with high-resolution optical magnification endoscopy can accurately assess histologic inflammation in IBD patients. The *in vivo* assessment of histologic inflammation was made with optical magnification endoscopy in conjunction with i-scan OE by a total of four endoscopists. Targeted biopsies of the imaged areas were obtained and results were compared against established and validated histology scoring. Moreover, interobserver agreement was calculated.
Results: 82 IBD patients (29 CU, 53 MC) were consecutively enrolled (40 men, median age 43, range 19–72). A newly developed I-scan OE magnification score showed high accuracy, sensitivity and specificity for assessing the histologic level of inflammation and correlated strongly with histopathologic scoring ($r \geq 0.7$, $p \leq 0.05$). Further, a prevailing amount of patients with mucosal healing on standard endoscopy showed signs of microinflammation on optical magnification endoscopy in combination with i-scan OE. Interobserver agreement for assessing microscopic inflammation with optical magnification endoscopy and i-scan OE with Cohen's kappa was substantial (≥ 0.7).
Conclusion: Optical magnification in combination with i-scan OE allows for a precise assessment of histologic inflammation during real-time endoscopy in IBD patients. Therefore, this approach holds the potential to reduce the need of physical biopsies for monitoring of inflammatory activity in patients with IBD during colonoscopy.
Disclosure: Nothing to disclose

P1410 BARRIERS, BREAKTHROUGHS AND PREDICTORS OF SUCCESS IN IMPLEMENTING SPLIT REGIMEN OVER SINGLE DOSE (IMPROVES): A MULTICENTER STUDY USING A PLAN-DO-STUDY-ACT APPROACH

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Introduction: Even if Split-dose regimen (SpD) [and Same-day regimen (SaD) for afternoon colonoscopies] is recommended by international guidelines[1,2], its adoption is still suboptimal.

Aims and Methods: Our aim was to survey and improve adhesion to SpD through a Plan-Do-Study-Act (PDSA) approach and to identify factors predicting its adoption.

This multicenter cross-sectional study consisted of 3 phases. Cycle1: survey of current practice; Interventional phase: local spontaneous corrective measures after analysis of Cycle1 data; Cycle2: survey of modified practice. Every outpatient or inpatient scheduled for a complete colonoscopy was eligible.

Differences were compared using a Student's T or a Chi Square test as appropriate. Multiple stepwise selection logistic regression models were built.

Results: 8213 patients (mean age 60.29 (SD 13.58), men 54%, outpatients 88.4%) were enrolled in 74 Endoscopy Units between 2013 and 2016 (4189 in Cycle1 and 4024 in Cycle2; no difference except a slightly higher rate of comorbidities in Cycle2). The SpD and SaD adoption raised from 29.1 and 3.1% of Cycle1 to 51.1 and 4.4% of Cycle2 ($p < .0001$ and.0039) respectively, while the Day-before regimen adoption declined from 67.8% to 44.5% ($p < .0001$). SpD advanced in all time slots ($p < .0001$ for each, including colonoscopies scheduled <9:30 am), but it became the preferred regimen only after 11:30 am (reaching 66.3% of late morning and 73.5% of afternoon colonoscopies); improvement in SaD adoption was detected only for afternoon colonoscopies ($p < .0001$), reaching 19% in Cycle2.

Significant changes detected in Cycle2 were: a higher use of 4L polyethylene glycol and a lower use of sodium picosulfate/magnesium citrate or sodium phosphate ($p < .0001$); a higher use of private transportations to reach the hospital ($p < .0001$); median delay between the end of bowel preparation and colonoscopy reducing from 12.42 to 7 hours ($p < .0001$), this delay being >6 hours in 75.3% of Cycle1 versus 56.4% of Cycle2 patients ($p < .0001$); fewer colonoscopies scheduled under deep sedation ($p = .0005$) and before 9:30 am ($p = .0019$); a higher rate of 100% product drinkers ($p = .007$). In Cycle2 adequacy of bowel cleansing was higher both in right ($p = .0274$) and left colon ($p < .0001$) and more patients would like to repeat the same regimen for future colonoscopies (83.1 vs 80.4%; $p = .021$).

At multivariate analyses, variables predicting SpD adoption (afternoon colonoscopies excluded) were: the colonoscopy scheduled 9:30–11:30 (OR 2.66) and after 11:30 am (OR 7.08; $p < .0001$); regimen communicated by the Endoscopy Unit and by more than one modality ($p < .0001$); colonoscopy being the first (OR 1.28, $p < .0001$), prescribed for screening instead of surveillance (OR 1.27, $p = .007$) and by a gastroenterologist instead of a general practitioner (OR 1.3, $p = .0001$). Colonoscopy planned under deep sedation (OR 0.51, $p < .0001$), a higher patient educational level ($p = .0063$) and being enrolled in Cycle1 vs 2 (OR 0.359; $p < .0001$) were negatively associated with SpD adoption.

SpD adoption independently predicted the willingness to repeat the same preparation ($p = .0001$), endoscopist satisfaction ($p = .0175$) and an adequate preparation of left ($p < .0001$) and right colon ($p < .0001$).

Conclusion: Notwithstanding barriers limiting the spread of Split-dose regimens (e.g. early morning colonoscopies, anesthesiological concerns, information providers, patient characteristics), corrective measures through a PDSA approach result in higher adoption of SpD (even in early morning colonoscopies), higher colonoscopy quality and higher patient and physician satisfaction.

Disclosure: Nothing to disclose

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P1411 A PROSPECTIVE EVALUATION OF STUDY OF FOCUSED IMAGE ACQUISITION FOR COLORECTAL ENDOCYTOSCOPY

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Introduction: Endocytoscopy (EC) is a brand-new contact-type endoscope commercially available in Japan and the European Union. It allows in vivo evaluation of cellular atypia with 520-fold magnification. Thus, EC provides diagnostic accuracy comparable to pathological diagnosis[1]. However, it is uncertain whether the EC image can be easily obtained, compared with conventional magnifying endoscopy.

Aims and Methods: The aim of this prospective study was to determine whether EC images can be acquired as easily as images in conventional magnifying endoscopy. This was a single-arm, prospective study conducted at Showa University Northern Yokohama Hospital. Consecutive 278 diminutive polyps (≤5 mm), all of which were observed by endocytoscope (CF-H290ECI, Olympus Corp.), were enrolled between June and December 2017. Inclusion criteria were follows: i) patients >18 years old, ii) patients who were not treated with anticoagulants, iii) patients who agreed with study participation. Exclusion criteria were histories of inflammatory bowel disease, chemotherapy, or radiation therapy for colorectal cancer. CF-H290ECI can acquire both conventional power magnification image (100×) and ultra-magnifying image (520×) by adjusting the zoom lever of the endoscope. During examination, detected polyps were observed by both narrow band imaging with conventional magnification (NBI-ME) and NBI with ultra-magnification (EC-NBI). To evaluate the degree of difficulty for obtaining an EC image, we measured the time that the physician could maintain an image in focus, by using both NBI-ME and EC-NBI as surrogate markers. We defined the image acquisition rate as the rate of lesions that the physician keeps continuously in focus for more than 3 seconds. In this study, physicians were told to maintain in-focus images, in both NBI-ME and EC-NBI, as long as possible. All procedures were recorded as movies and the in-focus times were measured by a research assistant and a single expert endoscopist in the recorded movies.

Results: Consecutive 278 polyps were analysed. Mean size was 3.4 ± 1.0 mm and the subsets of polyp locations were as follows: right sided, 119 polyps; left sided, 93 polyps; rectum 63 polyps. One-hundred and seventy-eight polyps were diagnosed as tubular adenoma, while the remaining 100 polyps were diagnosed as hyperplastic polyps. The image acquisition rate (the rate of lesion that physician maintain the image in focus more than three seconds) of EC-NBI was 94% (261/278), whereas NBI was 41% (113/278) ($P < 0.001$, Fisher's exact test).

Conclusion: This study showed that EC-NBI was able to take focused images for longer periods than NBI-ME. Thus, we conclude that EC-NBI images can be taken easily. We suspect that this is because EC is a contact-type endoscope. Once the physician can contact the polyps, a contact-type endoscope allows the physician to fix a focused image for longer than a conventional endoscope.

Disclosure: Nothing to disclose

Reference

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P1412 OPTICAL CLASSIFICATION OF NEOPLASTIC COLORECTAL POLYPS – A COMPUTER-ASSISTED APPROACH (THE COACH STUDY)

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Introduction: The aim of endoscopic polyp characterization is to predict histopathological diagnoses on the basis of optical polyp features. Clinical data suggest that the quality of optical diagnoses of colorectal polyps differs markedly among users. Technical support is therefore demanded in order to improve accuracy of optical predictions. Computer-assisted optical biopsy (CAOB) approaches have recently been published but these apporaches have focussed on high-magnification endoscopy techniques [1–2]. The latter endoscopes and processors are not available in Europe. An automated computer-based decision suppurt based on standard solution picturer is not avialable until now.

Aims and Methods: The aim of this study was to develop a computer program that was able to differentiate neoplastic from non-neoplastic polyps using unmagnified endoscopic pictures.

During 250 colonoscopy procedures polyp photographies were performed using the unmagnified high-definition white light (HDWL) and Narrow Band Image (NBI) mode. All detected polyps (n = 275) were resected and sent to pathology. Histopathological diagnoses served as the ground truth. Machine learning was used in order to generate a computer-assisted optical biopsy (CAOB) approach (machine learning phase). In the test phase pictures of 100 polyps were presented to CAOB in order to obtain optical diagnoses. Altogether 788 pictures were available (602 for training the machine learning algorithm and 186 for CAOB testing. All test pictures were also presented to two experts in optical polyp characterization. The primary endpoint of the study was the accuracy of CAOB diagnoses in the test phase.

Results: A computer program for automated optical polyp characterization was sufficiently developed. Accuracy of the CAOB approach was 78.0%. Sensitivity and negative predictive value (NPV) were 92.3% and 88.2%. In the high

confidence setting (n = 89) accuracy of CAOB predictions was 80.9%. High confidence CAOB predictions showed a sensitivity of 93.9% and a NPV of 89.7%. Overall accuracy obtained by two expert endoscopists was 84.0% and 77.0%. Regarding accuracy of optical diagnoses CAOB predictions did not differ significantly compared to experts (p = 0.307 and p = 1.000 respectively).
Conclusion: Computer-assisted optical biopsy showed good accuracy on the basis of unmagnified endoscopic pictures. Performance of CAOB predictions did not differ significantly from experts' decisions. The concept of computer assistance for colorectal polyp characterization needs to evolve towards a real time application prior of being used in a broader setup.
Disclosure: Nothing to disclose

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P1413 EFFICACY AND SAFETY OF ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL LESIONS IN THE ELDERLY

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Introduction: Endoscopic mucosal resection (EMR) is a minimally invasive technique used for the treatment of superficial neoplasms of the gastrointestinal tract, including early carcinomas. There is limited data on the safety and efficacy of this technique for large colorectal lesions in elderly patients.
Aims and Methods: The aim of this study was to evaluate the efficacy and safety of EMR of large colorectal lesions (≥20 mm) in the elderly (≥75 years) and to compare the outcomes with those of younger patients (<75 years).
Retrospective study of all patients who underwent EMR of colorectal lesions ≥20mm at our institution between January 2013 and December 2016. Patients were divided in two age groups considering 75 years as cut-off: ≥75 years (Group 1) *vs* <75 years (Group 2). The demographics of the patients, size and location of the lesions, technical aspects of the procedure, rate of endoscopic recurrence and complications were considered.
Results: A total of 136 colorectal lesions were removed in 123 patients. Fifty-one EMR were performed on 44 patients ≥75 years and 85 EMR were performed on 79 patients <75 years. The median age in Group 1 was 80 years (range 75–89 years) and 67 years in Group 2 (range 47–74 years). There was no significant difference in sex ratio, lesion size and lesion distribution between the two groups. En bloc resection was performed in 29.4% (15/51) of the lesions in Group 1 *vs* 31.8% (27/85) in Group 2 ($p = 0.774$). There were 2 cases (3.9%) of perforation in Group 1 and 3 cases (3.5%) in Group 2 ($p = 1.00$). There were no cases of delayed bleeding. The rate of endoscopic recurrence was 21.3% (10/47) in Group 1 and 23.6% (17/72) in Group 2 ($p = 0.766$). The overall endoscopic success rate was 84.3% (43/51) in Group 1 and 84.7% (72/85) in Group 2 ($p = 0.951$).
Conclusion: EMR is a safe and effective procedure for the treatment of large colorectal neoplasms in the elderly, with outcomes similar to those obtained in younger patients.
Disclosure: Nothing to disclose

P1414 UNDERWATER ENDOSCOPIC MUCOSAL RESECTION (UEMR) FOR COLORECTAL (CR) LESIONS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Underwater endoscopic mucosal resection (UEMR) for colorectal (CR) lesions has been described for overcoming the technical drawbacks of standard mucosectomy (EMR). This approach takes advantage of the behavior of mucosal lesions floating away from the muscular layer, once immersed in liquid. Thus, luminal water infusion allows to achieve an alternative way to have the lesion lifted before being resected, without any submucosal injection. We performed a systematic review with meta-analysis to evaluate the efficacy of UEMR for the resection of CR lesions.
Aims and Methods: Electronic databases (Medline, Scopus, EMBASE) were searched up to March 2018. The search was restricted to english language full articles. Studies including patients with CR lesions resected by the UEMR technique were eligible. The complete resection (primary outcome), en-bloc resection, recurrence and adverse event rates were pooled by means of a random- or fixed-effect model according to the degree of heterogeneity to obtain a proportion with a 95% confidence interval (CI).
Results: Ten studies were eligible for inclusion providing data on 508 lesions endoscopically removed in 433 patients (m/f = 239/194; means ages ranging from 62.2 to 75 years). Six studies were performed in United States and the other in Europe; seven studies were prospective. The specific indications for performing UEMR, instead of standard EMR, varied widely across the studies: large (defined as above 20 mm in 2 studies, above 15 mm in 1 and above 10 mm in the others) lesions (5/10 studies, 248 lesions), recurrence after EMR (1/10, 36 lesions), scarce accessibility (1/10, 27 lesions). Three studies included mixed cases and aimed either to evaluate the feasibility of the new technique (2/10, 124 lesions) or to compare it to the standard approach (1/10, 73 lesions). Most of the lesions were located proximally to the splenic flexure (309 lesions, 61%). The means of the lesion size ranged from 15 mm to 33.8 mm.
Complete resection rate was 96.36% (CI:91.77–98.44) with a rate of en-bloc resection of 57.07% (CI:43.20–69.91%). The recurrence rate was 8.82% (CI:5.78–13.25) in a mean endoscopic surveillance period of 7.7 months (range 4–15 months). The intra and post-procedural bleeding rates were 3.14% (1.65–5.88%) and 2.85%(CI:1.64–4.90), respectively and were always endoscopically managed. Intra procedural bleeding were always mild and were considered as part of the procedure in all series. The overall adverse events rate was 3.31% (CI: 43.20–69.91%). No cases of perforation were reported.
Conclusion: Underwater endoscopic mucosal resection (UEMR) is an effective and safe technique for resecting colorectal lesions. The rates of complete resection, recurrence and adverse events are at least comparable to the ones recorded in literature for standard EMR. These data are even more relevant considering that most of the studies aimed to remove recurrent, large or difficulty accessible lesions.
Disclosure: Nothing to disclose

P1416 DOES ENDOSCOPIC SUBMUCOSAL DISSECTION REALLY DIFFER BETWEEN COLONIC AND RECTAL LESIONS? A WESTERN EXPERIENCE BY A SINGLE ENDOSCOPIST ON 505 PROCEDURES

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Introduction: In the treatment of early stage malignant and pre-malignant lesions, endoscopic submucosal dissection (ESD) is an effective, minimally invasive treatment modality which can provide en bloc and complete resection, when compared to other treatment modalities such as endoscopic mucosal resection and polypectomy.
Aims and Methods: In this study, we aimed to compare the effect of localization on ESD treatment success, in patients with pre-malignant and early-stage malignant colorectal lesions. Up to date, the number of lesions included in this study is higher than any single-institutional publications in the Western literature.
Between April 2012 and April 2018, patients with a total of 2458 colorectal lesions were referred to our clinical unite to be treated with advanced endoscopic techniques. Colorectal ESD was performed on 541 lesions. Data were recorded prospectively and analyzed retrospectively by utilizing t-test and chi-square methods. 8 patients with subepithelial lesions, 7 patients with tumors located on anastomosis line and 21 patients who didn't have post-operative evaluation were excluded from the study. According to the localization of the lesions, ESD procedures were categorized as rectum (R-ESD) and colon (C-ESD). The perioperative results of these two groups were compared.
Results: For pre-malignant and early-malignant lesions, 505 colorectal ESD procedures were performed in 486 patients. The overall en bloc and complete resection rates were 95.1% and 92.3% respectively for colorectal lesions. Numbers of lesions localized to rectum and colon were, 253 and 252 respectively. Between two groups, no differences were observed for age, gender, en bloc and complete resection rates, severity of dysplasia, rate of invasive carcinoma, utilization of snare or other knife, procedure times. ($p > 0.05$).
Lesions localized to rectum were larger than lesions localized to colon. Although procedure times were similar between groups, dissection rate was faster in rectal lesions. For controlling bleeding and providing pre-coagulation during the procedure, hemostatic forceps use were utilized more in rectal lesions. There were significant differences in classifications of lesions ($p < 0.05$): Lateral spreading tumor non-granular (LST-NG) type lesions were more common in colon group, while LST granular mixed type (LST-GM) lesions were more common in rectal group. Rate of malignancy was higher in rectal lesions; however no significant differences were observed ($p > 0.05$).
During procedure, utilization of clip was required for 14 lesions with mucosal damage. Delayed perforation was observed in 1 lesion. Except for the late perforation, all complications were treated with endoscopy. Usage of clip was higher in lesions located to colon ($p < 0.05$). Patients with Sm2 invasion were referred for surgical treatment. During follow-up, no residual or relapsing lesions were identified in patients who underwent endoscopic and radiological evaluation.

Conclusion: According to the results of our study, ESD is faster and safer for lesions localized to rectum, compared to the other segments. But rectal lesions are larger and more prone to bleeding, thus more pre-coagulation is needed to control bleeding in these lesions. For lesions localized to colon, especially at the flexures, ESD is slower due to decreased maneuverability of endoscope and anatomic limitations; rate of complications is higher compared to lesions localized to rectum. With respect to our short and long-term follow-up results, we conclude that ESD can be safely and effectively used in the treatment of colorectal lesions.
Disclosure: Nothing to disclose

P1417 ENDOCYTOSCOPIC VASCULAR PATTERN OF COLORECTAL LESIONS IS USEFUL FOR PREDICTING PATHOLOGICAL DIAGNOSIS

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Introduction: Magnifying narrow band imaging (NBI) is useful for examination of colorectal lesions, for differentiating neoplasms from non-neoplasms, and for predicting the histopathological diagnosis. Endocytoscopy (EC) is performed with a new type of endoscope that is commercially available in Japan and the EU. It allows visualization of glandular structure and cellular atypia *in vivo* with ×520 magnification. EC has visualized living tumor cells *in vivo* and obtained ultra-magnified pathological images simply by applying the scope to the target mucosa during endoscopic examination. However, in order to visualize cell nuclei, dye staining (i.e., methylene blue) is mandatory. Since dye staining complicates the procedure, a new observation method without use of dye has been needed. On the other hand, EC with NBI (EC-NBI) allows ultra-magnified microvessel observation without using any dye solution.
Aims and Methods: The aim of this study was to determine whether the observation of surface microvessels using EC-NBI was useful in predicting the histopathology of colorectal lesions. The study included 460 patients who underwent complete colonoscopy and endoscopic or surgical treatment between April 2006 and February 2016. A total of 623 lesions (54 non-neoplastic polyps, 340 adenomas, 73 intramucosal cancers, 21 slightly invasive submucosal [SMs] cancers, and 135 massively invasive submucosal [SMm] cancer) were retrospectively evaluated. We defined ultra-magnified microvessel findings as an endocytoscopic vascular (ECV) pattern and classified the findings into the following 3 groups: EC-V1, surface microvessels were very fine or obscure; EC-V2, surface microvessels were more clearly seen, with a regular vessel network, and uniform caliber and arrangement; and EC-V3, surface microvessels were thick, with non-homogeneous caliber and arrangement.
Results: EC-V1 was observed in 90.7% of non-neoplastic polyps, with EC-V2 in 97.1% of adenomas. Mucosal and SMs cancers tended to present as EC-V2 (91.5%). However, most SMm cancers presented as EC-V3 (82.2%). The sensitivity, specificity, and accuracy of EC-V1 for diagnosis of hyperplastic polyps were 90.7%, 98.6%, and 98.0%, respectively. Similarly, the sensitivity, specificity, and accuracy of EC-V3 for diagnosis of SMm were 82.2%, 98.2% and 94.7%, respectively.
Conclusion: Endocytoscopic vascular pattern was useful for predicting the histopathology of colorectal lesions.
Disclosure: Nothing to disclose

P1418 LONG-TERM OUTCOME AFTER ENDOSCOPIC MUCOSAL RESECTION (EMR) FOR COLORECTAL LESIONS

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Introduction: Endoscopic mucosal resection (EMR) is a widely recognised, safe and minimally invasive technique for the removal of large, non-polypoidal colorectal lesions without resorting to surgery. In spite of high complete resection rates, local recurrence is not uncommon. Most studies have reported on short-term recurrence post EMR. We analysed our experience to determine long-term outcomes at 3 and 5 years post EMR.
Aims and Methods: A retrospective analysis was performed of all patients who underwent an EMR at lower GI endoscopy during a 2-year period, from January 2010 to January 2012, at a large non-tertiary endoscopy unit. Data was collated from endoscopy reports accessed from the hospital endoscopy reporting system (HICSS). Reports were analysed for details of the EMR performed and follow-up endoscopies for recurrence at the site of the initial EMR. The size and morphology of polyp, location and histology was recorded along with EMR details including completeness of excision and use of argon plasma coagulation (APC). Polyp recurrence at subsequent endoscopies up to 5 years was also recorded.
Results: A total of 437 patients underwent EMR during the study period. After exclusion for malignancy requiring surgery, incomplete follow-up, polyp size <1cm and index EMR outside the study period, 241 cases were analysed. Of the 241 polyps, 63% (153) were 1–2cm, 33% 2.1–5cm (79) and 4% (9) >5cm. Of the 241 polyps, 61% were located in the left colon and 39% right-sided. Most polyps irrespective of size were sessile (79%) with the remainder being flat (15%) or sub-pedunculated (6%). Duration of follow-up ranged from 3 to 60 months with a mean follow-up of 31 months (median 33 months). Residual/recurrent adenoma was successfully treated with further endoscopic resection and/or ablation. Histologically, there was no progression of severity of dysplasia/grading of adenoma in those patients who developed recurrence at long-term follow-up.
Conclusion: This study confirms EMR is a safe alternative to surgery for the management of large or difficult colonic polyps with good long-term outcomes. Our short-term recurrence rates are comparable to previous studies[1]. These low recurrence rates are maintained at long-term follow-up with good histological outcomes as well.
Disclosure: Nothing to disclose

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P1419 SCARE ENDOSCOPIC RESECTION FOR EARLY COLORECTAL CANCER IS IT AN ACCEPTABLE OPTION TO AVOID UNNECESSARY SURGERY AFTER A FIRST RESECTION WITH MICROSCOPICALLY POSITIVE DEEP MARGINS?: A MONOCENTRIC CASE SERIES OF A WESTERN CENTER

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Introduction: Endoscopic resection is usually the first-line treatment for colorectal adenomas and superficial adenocarcinomas. In case of pejorative histology: submucosal invasion >pT1 sm1 or pT1sm1 with pejorative qualitative criteria (poorly differentiated or with lymphovascular invasion or budding grade 2 or 3) a surgical resection is necessary because of the risk of lymphatic invasion despite complete resection (R0). In case of microscopically incomplete resection (R1) without any pejorative histologic criteria a surgical approach is the gold standard because the risk of lymph node metastasis is unknown. In order to try to avoid unnecessary surgeries we evaluated the efficiency and the safety of a second attempt to complete the resection in selected patients and in agreement with the surgical team. To many physicians this strategy appears to be an acceptable option; nevertheless few series studied specially this option. Indeed, second endoscopic approach is safe and effective (but less) after macroscopic incomplete resection (R2) and we wanted to prove with our case series the interest of endoscopic scare resection for R1 resection.
Aims and Methods: Between 2009 and 2018 we included retrospectively patients who underwent a second endoscopic resection in our center (Paoli-Calmettes institute Marseille) after R1 resection in another center. Macroscopic incomplete resection (R2) during the first endoscopy were excluded. The primary endpoint was the rate of avoided surgeries. Secondary endpoints concerned the morbidity rate and the recurrence rate.
Results: Between 2009 and 2018 we included 14 patients (mean age 73 years [64–88], men = 8, women = 6) who underwent a second endoscopic resection after a first resection R1 for colorectal adenocarcinomas. The technique resection was endoscopic submucosal dissection (ESD) in 6/14 patients (42%), endoscopic mucosal resection (EMR) in 7/14 patients (50%) and a hybrid method (hybridESD) in 1/14 patient. 7 patients had rectal lesion (50%) and 7 colonic lesions (50%). 10 patients (71%) had a en bloc resection (5 EMR, 5 ESD) and 4 patients had a piecemeal resection (2 EMR, 2 ESD and 1 hybrid ESD). In 12/14 patients (86%) complementary surgery has been avoided: in 8/12 cases (66%) because the lesion was less than a pT1sm1R0 on the second endoscopic resection,

in 2/12 cases (17%) because the lesion was pT1sm1R0 with no pejorative qualitative criteria and in 2/12 cases (17%) we confirm pT1sm2 lesion as on the initial resection but with negative positive deep margins on the second resection (one patient refused initially rectal surgery, rectal surgery was not possible for the second one) and we wanted avoid more than pT1sm2 lesion. In 2/14 patients (17%), surgery was recommended: 1 patient for R1 resection on the second procedure and 1 patient for pT1sm2R0 on the second procedure (pTis on the first) Regarding the secondary endpoints, only 1 patient presented a side effect which was a post polypectomy syndrome quickly controlled by an antibiotic treatment and by this time no recurrence was notified. The median follow-up time was 569 days and no local recurrence has been observed in our patients.
Conclusion: In case of R1 resection for superficial adenocarcinomas without pejorative histology a second endoscopic resection in an expert center may be a safe way to evaluate the real risk of metastatic lymph node in order to avoid unnecessary surgery.
Disclosure: Nothing to disclose

P1420 PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION OF COLORECTAL SUPERFICIAL LESIONS ≥20 MM IN SIZE: SHOULD WE TATTOO MORE?

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Introduction: Piecemeal endoscopic mucosal resection (P-EMR) of large colon superficial lesions (≥20 mm in size) raises several concerns, including the possibility of inadequate/incomplete polypectomy and future recurrence. It is desirable to locate with precision the site at which a lesion was removed in piecemeal fashion at the follow-up colonoscopy, even if the resection was apparently complete based on endoscopic criteria. However, the resection scar is not always easy/possible to locate in the surveillance colonoscopy, reason why some authors and guidelines suggest colonoscopic tattooing of the mucosa adjacent to all resection sites of lesions ≥20 mm (other than those in the cecum, adjacent to the ileocecal valve or in the low rectum) to allow optimal localization of the scar at future endoscopic exams. This is important because incomplete resection rates are higher for larger lesions removed piecemeal, the risk of recurrence after P-EMR of >20 mm lesions has been described as so high as 50% and some interval cancers may develop as a result of incompletely resected neoplastic lesions.
Aims and Methods: Evaluation of the scar identification rate post P-EMR at the first follow-up colonoscopy.
Retrospective unicenter analysis of all colorectal lesions ≥20 mm removed by P-EMR during the previous 7 years. Lesions located in the cecum, adjacent to ileocecal valve or in the low rectum were excluded, as well as pedunculated and semipedunculated lesions, lesions whose resection was considered incomplete at the moment of resection, invasive carcinomas and which didn't have follow-up colonoscopy in ≤12 months. All the remaining were included and divided in 2 groups: lesions in which tattooing of the mucosa adjacent to the resection site was not performed (group 1) and lesions in which tattooing was performed (group 2).
Results: In total, 177 P-EMR were included (group 1: n = 132; group 2: n = 45). The scar identification rate post P-EMR at first follow-up colonoscopy was 70.5% and 100% in group 1 and 2, respectively ($p = 0.000$). In group 1, lesions ≥30 mm and adequate bowel preparation were predictive factors of scar identification in the surveillance colonoscopy. In group 2, the colonic tattoo enabled precise scar location at all cases independently of factors as: lesion size, bowel preparation and timing of first follow-up colonoscopy. Globally, considering the cases in which the resection site was identified, the incomplete resection/recurrence rate (after P-EMR) was 31.2% (48/138).
Conclusion: Tattooing the mucosa adjacent to resection sites of large colonic lesions (other than those located in the cecum, adjacent to the ileocecal valve or in the low rectum) promotes accurate and efficient surveillance after P-EMR. The high rate of incomplete resection/recurrence observed in this study and described in the literature reinforces the conclusion of our analysis. Tattooing more after P-EMR may prevent some interval colorectal cancers.
Disclosure: Nothing to disclose

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P1421 LONG-TERM OUTCOMES OF INITIALLY ENDOSCOPICALLY RESECTED MALIGNANT POLYPS WITHIN THE UK BOWEL CANCER SCREENING PROGRAMME

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Introduction: Literature supports that endoscopic resection and surveillance of malignant polyps is feasible and with low short term local recurrence rates and metastasis especially in patients with well/moderately differentiated cancer with invasion depth >1mm and no lymphovascular invasion, but data are limited.[1,2]
Aims and Methods: Aim of our study was to evaluate short and long-term clinical outcomes of malignant polyps that underwent endoscopic resection as the initial intervention under the Bowel Cancer Screening (BCS) programme during 2006–2011.
We performed a retrospective analysis of all patients attending BCS in Wolverhampton bowel cancer screening hub. Cases were identified after interrogation of BCS software database and verified using endoscopy and histology databases. Long-term outcomes were derived from patient case notes. Recurrence was defined as no mucosal, local lymhnode disease or metastatic spread.
Results: 34 polyps were identified initially in 33 patients. 32 patients were analysed due to missing follow up data. Mean age was 64.5 and 26 were male. Post endoscopic resection, follow-up was endoscopic surveillance (28%, n = 9), surgery (69%, n = 22) but 2 declined, palliation (3%, n = 1). One of the surgically managed patients had transanal endoscopic microsurgery. 30-day mortality rates were 10% (n = 2) in surgical group vs. 0% in others. No complications were reported in the endoscopy group.
Table 1 presents the number and type of polyps identified, mode of endoscopic removal, mean polyp size as assessed in endoscopy, histological clearance margins and follow-up pathway for each group.
In the endoscopic surveillance group, 1-year recurrence was 0%. 22.2% of (n = 2) patients had recurrence at 5 years (3 years and 4 years). In the surgical cohort, 15% (n = 3) of patients were found to have residual cancer in the resected specimen. No patients were found to have positive lymph nodes. 5-year recurrence in the surgical group was 0%.
Two patients declined surgery. One underwent endoscopic surveillance with no 5-year recurrence. The other received chemoradiation and died within a year. One patient had metastatic disease on staging after endoscopic resection and followed a palliative approach.
6 patients had a poorly differentiated adenocarcinoma on histology with 2 following endoscopic follow up and 4 having subsequent surgery. The 5-year recurrence was 0%. Mucinous adenocarcinoma was seen in 2 patients in 3 pedunculated polyps. At 1 year the recurrence rate was 0% but 100% at 5 years. Lymphovascular invasion was seen in 5 patients and associated with local or metastatic spread on initial staging in 40%. One further patient died post operatively (day 3). 40% of patients had no recurrence at 5 years.
Conclusion: Patients undergoing surgical follow up had lower recurrence rates compared with endoscopic follow up although no recurrent disease was found in the surgical cohort at resection. Patients with mucinous adenocarcinoma and lymphovascular invasion at initial histology appeared to have poorer outcomes. There was no difference in prognosis between en block and piecemeal endoscopic resection but margin clearance was not accurately identified in piecemeal polypectomies. Further data from the 2012–2016 cohort will follow.
Disclosure: Nothing to disclose

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Table 1: Characteristics and information about the malignant polyps of the study cohort

				Margin clearance			Follow up		
	Type of resection	Sample size (n)	Mean polyp size (mm)	positive margin or <1mm (R1)	>1mm clearance (R0)	unable to assess	Endoscopy	Surgery	Declined surgery/palliative
Sessile	En bloc	9	13.8	6	3	0	3	6	0
	Piecemeal	10	22.7	6	0	4	2	7	1
Pedunculated	En bloc	9	15.5	3	5	1	4	3	2
	Piecemeal	5	22.2	1	2	2	0	4	0

P1422 QUALITY ASSURANCE IN ENDOSCOPY: ABOVE AND BEYOND PROCEDURE-RELATED PERFORMANCE

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Introduction: In recent years considerable progress has been made to establish formal frameworks to ensure that quality services are delivered safely to patients. This was accompanied by considerable progress of the equipment available to deliver endoscopic services. While there are some studies assessing the procedural performance of specific equipment innovations, very little is known about the reliability of equipment and subsequent changes of reliability over time as well as the availability of equipment when time between repairs and repair time were taken into considerations.

Aims and Methods: We reviewed endoscopic service records of endoscopic equipment for a seven year time-period of a large tertiary teaching hospital delivering annually >12.000 endoscopic procedures. We aimed to capture the number of procedures done per scope, the number of repairs, costs per repair and time required for repair.

Results: In total 56 scopes (all from one supplier) were in use at the time of data capturing. While in 2011 on average scopes had a useability of 453 days until next repair (95% CI 312–593), this dropped to 80 days (95% CI 56–103) in 2017. This was associated with a significant increase of repair costs per 1000 procedures. At the same time the number of procedures per scope or the average age of the endoscopes did not significantly change. Moreover the time required for repairs provided by the manufacturer increased from an average of 27 days (±23 SD) to 75 days (±35 SD). Interestingly, repair times of a third party supplier engaged for some of the repairs since 2015 remained consistently below 40 days. There were significant differences in the number of repairs per 1000 procedures if the two most recent generations of scopes were compared. It appears that the mean failure rate per 1000 procedures has substantially increased with the latest scope generation, from 4.10 (±1.73 SD) to 5.47 (±4.46 SD).

Conclusion: Over a seven-year time period the reliability of standard endoscopic equipment appears to have substantially deteriorated. At the same time the turnaround time for repairs of a major supplier has doubled. In combination this substantially impacts on the availability of endoscopic equipment and equipment costs. Appropriate monitoring of the reliability of endoscopic equipment and the performance of service partners should be part of the quality framework of endoscopic providers.

Disclosure: Nothing to disclose

P1423 DEVELOPMENT AND INITIAL VALIDATION OF A UNIVERSAL CLASSIFICATION FOR COLO-RECTAL POLYPS AND NEOPLASIA (UNICORN)

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Introduction: Identification and accurate characterisation of colonic polyps is important in the prevention of colo-rectal cancer. Currently, the well validated classifications for colon polyps are based on image enhancement technology (IEE). Magnification endoscopy is also required for some of the proposed algorithms. The uptake of such technology is not universal and learning curves are variable. High-definition white light endoscopy (HD-WLE) is used routinely by endoscopists. We developed a new classification and clinical algorithm using HD-WLE and proceeded to an initial validation.

Aims and Methods: The aim of our study was to develop and validate a classification and algorithm for colonic polyps using HD-WLE. In the first step, 10 experts developed the UNICORN classification by a series of consensus statements. Polyps were divided into Type 1a or hyperplastic polyps (HP),Type 1b or Sessile serrated polyps (SSP)),Type 2a or low-risk adenomas, Type 2b or high-risk adenomas and Type 3 or deep submucosal invasive cancer. In the next step, participants in 9 Endoscopy centres underwent training with a specially designed tutorial. Subsequently, 35 polyp images collected on HD-WLE from the 3 major endoscopic systems were provided. These included 16 images of Type 1, 18 images of type 2 polyps and 1 type 3. Participants were divided into experts and non-experts based on their level of experience and were asked to predict polyp type. Level of confidence of prediction was also recorded. Accuracy of prediction was calculated by measuring sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) as well as diagnostic effectiveness or accuracy.

Results: 12 experts and 15 non-experts participated in the validation using polyp images. Both groups achieved negative predictive values (NPV) >90% for HP, SSP and high risk adenomas. NPV was 86 and 81% respectively for low-risk adenomas. The expert group achieved diagnostic accuracy of 0.92 for HP, 0.93 for SSP, 0.87 for low risk adenomas and 0.92 for high-risk adenomas. The corresponding values for the non-experts were 0.91 for HP, 0.90 for SSP, 0.84 for low risk adenomas and 0.90 for high-risk adenomas. PPV was low for high-risk adenomas in the expert and non-expert group.
Detailed results are in the table.

Conclusion: HD-WLE is used routinely by endoscopists for detection and initial decision making on the management of colo-rectal polyps. Existing classifications based on IEE are associated with challenges in translation to routine clinical practice. The newly proposed UNICORN classification is based on HD-WLE. The classification proposes the use of IEE and or chromoendoscopy and magnification endoscopy for low certainty and for high-risk adenomas. Our initial results suggest that HD-WLE can be used for initial characterisation of a majority of polyps with use of IEE in specific scenarios. In our study, non-experts were able to achieve similar results to experts after a brief tutorial. High specificity and NPV for SSPs was also achieved in both groups using newly proposed criteria. Further analysis is planned looking at levels of confidence of prediction and polyp sizes. Further validation of the UNICORN classification in real-time endoscopy and involving community based endoscopists is also planned.

Disclosure: Nothing to disclose

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Table 1: UNICORN validation results.

UNICORN validation Results in % with 95% CI	HP Experts	HP Non-experts	SSP Experts	SSP Non-experts	Low risk adenoma Experts	Low risk adenoma Non-experts	High risk adenoma Experts	High risk adenoma Non-experts
Sensitivity	83(75–89)	77(69–83)	86(75–92)	84(74–90)	81(74–86)	72(65–77)	69(51–83)	68(53–81)
Specificity	96(92–97)	96(94–98)	95(92–97)	91(88–93)	91(87–94)	93(90–96)	94(91–96)	92(89–94)
PPV	89(81–94)	90(83–94)	78(67–86)	67(57–75)	87(81–92)	89(83–93)	54(39–68)	45(33–58)
NPV	93(89–95)	91(88–93)	97(94–98)	96(94–98)	86(81–90)	81(77–85)	97(94–98)	96(94–98)

P1424 A SIMPLIFIED TABLE MIXING VALIDATED DIAGNOSTIC CRITERIA IS EFFECTIVE TO IMPROVE CHARACTERIZATION OF COLORECTAL LESIONS BY FELLOWS: THE CONECCT CLASSIFICATION

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Introduction: Endoscopic characterization of colorectal neoplasia is a key point to choose in real time the best therapeutic option to treat effectively and safely each lesion. This characterization is based on 5 classifications, difficult to combine and to learn for non-experts. Thus, we mixed all the validated criteria in a single classification called CONECCT to facilitate prediction and therapeutic choice. This study aimed to evaluate CONECCT benefits in endoscopic characterization of colorectal neoplasia.

Aims and Methods: It is a prospective multicenter study involving all French gastroenterology interns and seniors who participated to usual bi-annual teaching session. Each participant performed a pre-test with 20 colorectal neoplasia (High quality pictures with chromoendoscopy) with 2 questions for each about histology prediction and adequate treatment to propose. Then, they followed a 30 min teaching session about CONECCT and repeated a post-test with same 20 lesions in different order. In order to check that their progressions are sustainable in long time, we asked them to participate in a second session, 3–6 months later, during which they performed a test (T3M) with 40 colorectal (the last 20 lesions and 20 news) neoplasia with the 2 same questions.

Results: 419 persons (280 interns and 139 seniors) participated at first session and we analyzed 206 participants for T3M (96 persons were excluded because of matching problems). Mean rate of good answers progressed from 60.6% at pre-test versus 76.4% at post-test ($p < 0.05$) versus 70.5% at T3M ($p < 0.05$).
Between pre Test and post Test, 345 (86.9%) participants progressed and mean progression per participant was 21.0%. Depending on histology, prediction results were significantly improved ($p < 0.05$) with 61.0% at pre Test and 78.5% at post Test. After the teaching program, overtreated patients reduced significantly from 30.1% to 15.4% ($p < 0.05$).
Between pre Test and T3M, 121 (76.6%) participants progressed and mean progression per participant was 12.9%. Depending on histology, prediction results were significantly improved ($p < 0.05$) with 61.0% at pre Test and 70.5% at T3M. Overtreated patients reduced significantly from 30.1% to 20.0% ($p < 0.05$).
Other interesting results are that among all french participants, 86.4% considered CONECCT as helpful for prediction and 88.5% for treatment. 51.3% already used that classification.

Conclusion: CONECCT classification teaching is effective to improve histology prediction and treatment choice regardless of lesion histology in gastroenterology interns and seniors. Overrated patients reduced significantly thanks to CONECCT.

Disclosure: Nothing to disclose

P1425 META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS SHOWS THAT ENDOCUFF INCREASES COLONOSCOPY ADENOMA DETECTION RATE

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Introduction: Endocuff -a plastic device with flexible projections- mounted on the distal tip of the colonoscope, promises improved colonic mucosa inspection

Aims and Methods: Since data from individual studies are controversial, we aimed to elucidate the effect of Endocuff on adenoma detection rate (ADR) and on advanced ADR (AADR). We performed literature searches in MEDLINE and Cochrane Library for randomized-controlled trials (RCTs) published as full papers in English language evaluating Endocuff-assisted (EAC) versus conventional colonoscopy (CC) in terms of ADR and AADR. The effect size on study outcomes was calculated using fixed or random effect model, as appropriate, and it is shown as OR[95%CI].

Results: We identified 6 studies; five parallel groups design and one tandem. Five studies evaluated the first-generation and the sixth one the Endocuff-Vision device. One study included screening examinations, another one evaluated FOBT-positive screening and surveillance examinations and four studies evaluated colonoscopies with mixed indications (screening, surveillance and symptomatic). ADR was reported in all 6 studies (3460 examinations). As compared to CC, EAC significantly increased ADR [OR(95%CI) = 1.30(1.00–1.69); $I^2 = 67\%$]. Meta-analysis of data from 5 studies (2971 examinations) did not detect any difference between EAC and CC regarding AADR [OR(95%CI) = 0.92(0.74–1.16); $I^2 = 0\%$]. There was no evidence of publication bias.

Conclusion: Meta-analysis of RCTs data provide evidence that EAC increases ADR compared to CC, without increasing AADR. Heterogeneity among the included studies calls for cautious interpretation of the results

Disclosure: Nothing to disclose

P1426 COMPARISON OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING THE POCKET CREATION METHOD AND THE CONVENTIONAL METHOD FOR COLORECTAL LESIONS

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Introduction: Endoscopic submucosal dissection (ESD) is a widely used procedure for colorectal neoplasms. However, especially for fibrotic colorectal lesions or flat colorectal lesions, it is still technically difficult because of the lack of counter-traction. Recently, the pocket creation method (PCM) was developed to overcome these technical difficulties, which facilitating ESD for such colorectal lesions by creating a large submucosal pocket under the lesion. However, it is still unclear whether the PCM is superior to the conventional method (CM) for colorectal lesions.

Aims and Methods: The aim of this study was to compare the clinical results of the PCM and CM for colorectal lesions. Between January 2016 and October 2017, a total of 87 colorectal ESD cases were performed at our institution. Retrospectively, they were divided into the PCM group (n = 40) and CM group (n = 47). All procedures were conducted using a water-jet colonoscope (PCF-290ZI; Olympus, Tokyo, Japan) and DualKnifeJ (KD-655; Olympus, Tokyo, Japan). A small-caliber tip transparent hood (DH-29CR, Fujifilm, Tokyo, Japan) were appropriately used so as to keep nice visualization between PCM. MucoUp (Seikagaku, Tokyo, Japan) was used as the injection solution.
For PCM, initial mucosal incision is made approximately 20mm in length at the distal side of the tumor after submucosal injection. Then, submucosal pocket under most of the tumor was created with Dual-J knife. The lower side of the pocket was opened in a step-by-step manner toward the proximal side, and the tumor is resected.
For conventional method, mucosal incision and submucosal dissection was performed from the proximal edge of the tumor. Then, additional mucosal incision was performed circumferentially, and submucosal dissection was made in the same manner.
For both groups, lesion size, procedure time, total amounts of midazolam, and ESD-related complications (hypotension, hypertension, hypoxia, and arrhythmia) were compared. SPSS version 14 (IBM, Armonk, NY, USA) was used for statistical analysis.

Results: Forty patients in the PCM group (16 male; 24 female; age range, 44–87 years; mean age, 75.5 years) and 47 patients in the CM group (21 male; 26 female; age range, 65–98 years; mean age, 77.3 years) were treated with ESD and analyzed. The mean resected size was 33.7 mm in the PCM group and 33.3 mm in the CM group ($p < 0.05$). ESD times for the PCM and CM groups were 51.7 and 54.6 minutes ($p = 0.14$), respectively. Midazolam doses for the PCM and CM groups were 2.87 and 2.5 mg ($p = 0.23$), respectively. En bloc resection rates for the PCM and CM groups were 97.5% and 97.9% ($p = 0.45$), and R0 resection rates were 88.2% and 75.0% ($p = 0.17$), respectively. Complications occurred in the PCM and CM groups as follows: hypoxia, 5.0% and 10.6% ($p = 0.31$); bradycardia, 2.5% and 10.6% ($p = 0.17$); tachycardia, 0% and 2.1% ($p = 0.17$); hypotension, 37.5% and 70.2% ($p < 0.05$); and hypertension, 32.5% and 23.4% ($p = 0.18$). Postoperative bleeding occurred in one case (1/40; 2.5%) of the PCM group; however, no perforations occurred in either group. Of note, even if the

lesion had submucosal fibrosis caused by a previous biopsy, en bloc resection was possible for four cases without any difficulty in the PCM group.
Conclusion: PCM is feasible, safe, and simple compared with the CM for colorectal lesions. Furthermore, it might be hugely advantageous during ESD for patients with fibrotic/scarred colorectal lesions. However, further studies using updated devices to perform the PCM are needed.
Disclosure: Nothing to disclose

P1427 LABEL-FREE MULTIPHOTON IMAGING AS A REAL-TIME DIAGNOSTIC TOOL FOR DISCRIMINATING COLORECTAL DISEASES

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Introduction: Accurate diagnosis of colorectal precancerosis and early carcinoma is crucial for cancer prevention and prognostic improvement. Various endoscopic technologies were developed to increase the diagnostic accuracy, and the biopsy-dependent pathology remains the golden standard. During routine endoscopy, real-time optical biopsy diagnosis is desired as the new imaging technology. Without fluorescent label, multiphoton microscopic (MPM) imaging directly reveals live cellular morphology and tissue microenvironment based on intrinsic two-photon excited fluorescence (TPEF) and second harmonic generation (SHG) signal. As reported, its resolution and performance *in vivo* are comparable to the *ex vivo* histopathology. We thus aimed to initially investigate the original features of colorectal diseases under MPM, and evaluate its potential for real-time diagnosis in vivo.
Aims and Methods: Experimental and diagnostic cohorts were designed in this study. The multiphoton images of 40 fresh tissues were collected and confirmed pathological performance of colorectal normal tissues, hyperplastic polyps, adenomas and adenocarcinomas. Both morphological and quantitative features were recorded and analyzed to establish diagnostic standards with MPM. For the second cohort with 86 tissues, we distinguished the various colorectal diseases with conclusive MPM features.
Results: Through the investigation, the colorectal normal, hyperplastic polyps, adenoma and adenocarcinoma were presented difference in the crypt opening, gland structure, epithelial cells and collagen fibers. The epithelial nuclear area of normal cases were similar to hyperplastic tissues ($31.36 \pm 3.18\mu m^2$ and $32.14 \pm 3.12\mu m^2$, respectively, $P = 0.062$) but apparently smaller than adenoma and cancer ($57.41 \pm 4.88\mu m^2$ and $86.62 \pm 10.61\mu m^2$, $P < 0.001$). Cellular asymmetry were 0.79 ± 0.08, 0.77 ± 0.09, 0.39 ± 0.07 and 0.76 ± 0.10, respectively, indicating the nuclear elongation of adenoma evidently, while relative round in normal, hyperplastic and cancerous cells. Compared with normal tissues, the TPEF/SHG intensity ratio for collagen content was also similar in hyperplastic cases (0.27 ± 0.04 and 0.26 ± 0.02, $P = 0.736$) but decreased in adenoma and adenocarcinoma samples (0.22 ± 0.01 and 0.17 ± 0.02, $P < 0.001$). With the typical features, we preliminarily tested the diagnostic efficiency of real-time MPM, and found its sensitivity for distinguishing normal, hyperplastic polyps, adenoma and adenocarcinoma was 90.63%, 75%, 85.94%, 97.92%, while the specificity was 99.29%, 95.14%, 95.37%, 94.36%, respectively.
Conclusion: The real-time multiphoton microscopic imaging can be effective to identify colorectal diseases with high resolution. Via integrating with the endoscopes in the future, it could promote optical precise diagnosis in clinics.
Disclosure: Nothing to disclose

P1428 TWO LITERS OF POLYETHYLENE GLYCOL (PEG) WITH 15 MG OF BISACODYL VERSUS 4 LITERS OF PEG FOR BOWEL PREPARATION TO COLONOSCOPY: PROSPECTIVE RANDOMIZED STUDY

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Introduction: Bowel preparation is an essential step for successful colonoscopy in order to achieve complete visualization the whole colonic mucosa, detection of abnormalities. four liters of polyethylene glycol (PEG) is widely used, associated with a poor tolerance of the patients seen the drink of a large amount of liquid, the reduction of this quantity associated with others agent is better accepted and tolerated by the patients, however its effectiveness on the quality of the preparation necessitates studies.
Aims and Methods: A prospective comparative randomized study comparing the tolerance, acceptability and efficacy of bowel preparation using four liters of PEG (Group A) versus two Liters of PEG plus 15 mg of Bisacodyl (Group B) as bowel-cleansing agents, Using the Boston Bowel Preparation Scale (BBPS) to evaluate the bowel-cleansing efficacy.
Results: One hundred and thirty-three patients were included (68 in group A and 65 in group B), with a sex ratio = 0.85. The average age of patients was 52 +/−14.2 years [18–75]. The indication of colonoscopy was gastrointestinal bleeding or anemia in 50.3%, constipation in 17.2% of cases.two groups were comparable for sex, history of constipation, taking all of the preparation**.** the duration after the last taking. but there was a significant difference for age classes and adherence to the Low-residue diet.
There was significant difference in the rates of side effect (Group A: 49.5%, Group B: 23.1%) (p:0.008) and acceptability (70.5% Versus 90.7% respectively) (p:0.01).
In term of effectiveness, the Group B had a better mean BBPS compared with Group A (7.05 +/− 1.5 versus 6.43 +-1.8.) (p:0.039), the BBSP greater than or equal to 6 was recorded in 89.2% versus 70.6% of patient respectively (p = 0.008). After adjustment for age classes and adherence to Low-residue diet, BBSP at Group B remained better than Group A.
Conclusion: According to our study, the efficacy of bowel preparation for colonoscopy can be improved by reducing the volume of Polyethylene glycol to two liters associated with Bisacodyl, this protocol is best tolerated and tolerated by the patients
Disclosure: Nothing to disclose

P1429 WATER-AIDED COLONOSCOPY IS AS EFFECTIVE AS CONSCIOUS SEDATION IN CONTROLLING PAIN

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Introduction: Colonoscopy is gold standard of colorectal cancer screening by detecting precancerous lesions. Air insufflation to distend lumen can cause pain and discomfort to the patient that often requires sedation. Indeed, colonoscopy is an invasive "operator-dependent" technique requiring a learning curve and the rate of missed lesions is still not satisfying. Sedation increases quality and tolerability but also costs and timing of the procedures.
The use of water infusion in lieu of gas insufflation seems to improve colonoscopy performance decreasing insertion pain and the need for sedation, increasing cecal intubation rate and facilitating completion of difficult colonoscopy without reducing the adenoma detection rates.
Aims and Methods: Aim of the study was to evaluate tolerability of warm water infusion technique (WWI) compared to carbon dioxide (CO_2) insufflation in terms of pain and need for sedation. Secondary aim was to compare the performance of the two techniques.
Prospective randomized controlled trial in which consecutive patients referred to undergo colonoscopy over a 4-month period were recruited. Pregnancy, age <18 yrs, bowel resection, malignant stenosis, emergency were exclusion criteria. After the inform consent, patients were randomized into two arms: a) warm water infusion with no sedation b) CO_2 insufflation with minimal patient's weight based sedation. Patients completed a questionnaire regarding tolerability of the procedures and the level of pain after the colonoscopy expressed on a visual scale. Cecal Intubation Rate (CIR), Cecal Intubation Time (CIT), Total Procedure Time (TPT), Adenoma Detection Rate (ADR), Adverse Events (AEs) and bowel preparation and amount of sedation required were assessed. Procedures were performed by one doctor in training under supervision.
Results: One-hundred sixty-four patients were enrolled in the study (101F, 63 M; age 63 range 21–92; BMI 24.5, range 15.5–39.5): 82 in the WWI group (44F, 38M; age 64 yrs, 21–92; BMI 24.8 15.5–39.5) and 82 in the CO_2+sedation group (57F, 25M; age 62, 21–82; BMI 24, 16–34). There was no difference in terms of pain perception, CIR, CIT, TPT and bowel cleansing between the two groups (Tab. 1). Higher ADR was achieved in the WWI arm (p 0.02). Moreover, adverse events were significantly lower with water infusion compared to CO_2+sedation (p 0.03). Finally, 3 patients required sedation during WWI to complete the procedure.

	WWI	CO_2 + sedation	P value
Cecal Intubation Rate n (%)	78/82 (95.1%)	81/82 (98.8%)	0.99
Cecal Intubation Time min means (SD)	8.67 (3.59)	8.46 (3.47)	0.66
Total Procedure Time min means (SD)	18.31 (4.9)	18.21 (6)	0.89
Bowel Preparation BBPS	7	7	0.2
Adenoma Detection Rate n (%)	20/82 (24.4%)	8/82 (9.8%)	0.02
Pain means (SD)	2.33 (2.02)	2.74 (2.71)	0.12
Sedation adjustment n (%)	3 (3.7%)	13 (15.9%)	0.01
Adverse events n (%)	1/82 (1.2%)	8/82 (9.8%)	0.03

[Table 1. Results]
Conclusion: Water Infusion colonoscopy was well tolerated and equally to intravenous sedation in terms of pain perception, procedure time and cecal intubation rate. Moreover, underwater colonoscopy in our study provided lower occurrence of adverse events and higher Adenoma Detection Rate (ADR).

The WWI technique seems to be a valid alternative to colonoscopy with sedation to achieve quality and painless colonoscopy when sedation is not available or executable and is a valuable aid to endoscopy trainees.
Disclosure: Nothing to disclose

P1430 SCREENING COLONOSCOPY IN YOUNGER ADULTS-WHEN SHOULD WE START?

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Introduction: As 90% of Colorectal cancer (CRC) cases occur in individuals over 50, screening programs have focused on this population. However more often adenomas and colorectal carcinomas were detected within younger (<50y), averaged risk adults, especially in the rectum. A study by Brenner et al reported rates of progression from advanced adenomas (AA) to CRC of approximately 2–5% per year. Therefore our aim is to assess incidence rates of adenomas, advanced adenomas and CRC according to age to determine when we should start screening colonoscopy.
Aims and Methods: 246,857 screening colonoscopies within the Austrian quality assurance program were retrospective analyzed between November 2007 and February 2018. Patients were categorized according to age and we determined ADR, AADR and CRC-rate for each group, also comparing male and female sex.
Results: Overall in 22.40% (n = 55381) of all patients, adenomas were detected, 27.8% within men and 17.2% (n = 33789) within women. Advanced adenoma detection rate (AADR) was 4.6% (n = 11266), Male-AADR (MAADR) was 5.7% and female-AADR (FAADR) 3.5%. In 0.77% (n = 1894) colorectal carcinomas were detected, 0.98% within male and 0.56% within female patients
According to age, ADR was 5.6% (♀: 3.3%; ♂: 7.5%) within group of 30–34 year old individuals; 7.0% [(♀: 8.4%; ♂: 5.8%) 35–39y], 11.7% [(♀: 14.5%; ♂ :9.2%); 40–44y], 15.0% [(♀: 17.8%; ♂ :12.1%); 45–49y] and 17.1% (♀: 21.2%; ♂ :12.9%) in patients aged 50–54, where screening is already recommended.
AADR was 1.2% [(♀: 1.0% ♂: 1.4%) 30–34y], 1.2% [(♀: 1.0%; ♂: 1.4%) 35–39y], 2.6% [(♀: 3.3% ♂: 1.8%) 40–44y], 2.8% [(♀: 2.6% ♂: 2.9%) 45–49y] and 3.1% [(♀: 3.8% ♂: 2.4%) 50–54y]. Incidence of CRC was 0.30% [(♀ :0.33%; ♂: 0.29%);30–34y], 0.37% [(♀: 0.19% ♂: 0.53%);35–39y], 0.54% [(♀ :0.77%; ♂: 0.32%);40–44y], 0.38% [(♀ :0.32%; ♂: 0.45%); 45–49y] and 0.33% [(♀ :0.40%; ♂: 0.25%); 50–54y]. Regarding localization, 50% of CRC in the group 30–34 years, 50% (35–39y), 47% (40–44y) and 44% (45–49y) were located in the rectum, compared to 0.38% in patients older than 50.
From 2008 to 2017, the overall incidence rates of adenomas in adults age 45–49 increased from 15.9% in 2008 to 20.9% in 2017; AADR 2.3% to 4.9% and incidence rate of CRC increases from 0.39% to 0.65%. In female patients, ADR was 12.6% vs. 20.7% (2008 vs. 2017); AADR 1.4% vs. 7.6% and incidences of CRC 0.70% vs. 1.38%. Within male individuals, ADR changes from 20.0% to 21.1%; AADR 3.5% to 2.5% and no cases of CRC were documented in 2008 as well as in 2017.
Conclusion: In this large cohort of screening colonoscopies, we noticed quite similar incidence rates in patients aged 45–49, compared to those, whom screening colonoscopy is already recommended (50–54years): Incidences of adenomas (15.0% vs. 17.1%), advanced adenomas (2.8% vs. 3.1%) and colorectal carcinomas (0.38% vs. 0.33%). Compared to 2008, higher incidence rates of adenomas, advanced adenomas and colorectal carcinomas were documented in 2017, especially in female patients from 45 to 49, while we found no big changes within male individuals at the same age comparing 2008 and 2017.
Regarding this and to prevent more cases of colorectal cancer we should start screening colonoscopy at the age of 45, especially in female patients.
Disclosure: Nothing to disclose

P1431 USEFULNESS AND EFFICACY OF RETROFLEXION IN THE ASCENDING COLON DURING COLONOSCOPY FOR POLYP AND ADENOMA DETECTION

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Introduction: Missing polyps in the ascending colon during colonoscopy is considered to be an important factor for interval cancer.
Aims and Methods: The aim of our study was to evaluate the feasibility of retroflexion in the ascending colon and its contribution to polyp and adenoma detection. Patients-Methods: 440 consecutive patients with a complete colonoscopy under conscious sedation (midazolam and/or propofol) were prospectively evaluated for retroflexion achievement after reaching the caecum – (only 3 attempts were permitted for achieving retroflexion). Polyp detection was divided in 3 phases: Insertion into the caecum (1st phase), withdrawal up to the hepatic flexure and then reinsertion into the caecum with forward view (2nd phase) and then retroflexion in the caecum and inspection of the ascending colon up to the right flexure and reinsertion into the caecum (3rd phase). Phases 1 and 2 were considered as forward view while phase 3 as retroflexion. Polyps were removed after the whole mapping of the ascending colon when the 3 phases were completed according to the protocol.
Results: 440 patients with complete colonoscopy, 218 (48.6%) men, mean age = 62.6 ± 11.2 years, BMI = 26.8 ± 4.4. Indication for colonoscopy: Screening (32.3%), Follow-up (31.1%), Diagnostic assessment (36.6%). Mean colonoscope length to the caecum: 89.9 ± 14.6 cm. Only 1% had poor cleaning preparation. Retroflexion was successful in 97.73% [1st attempt (78.18%), 2nd (12.95%) and 3rd (6.59%)]. No major adverse events were reported during the study. Adenoma detection rate (ADR) for the entire colon was 51% [Screening (39%), Follow-up (59%), Diagnostic (55%)]. Mean time for forward view (phases 1+2) was 69.7 ± 21.4s and for retroflexion (phase 3) 60.4 ± 16.7s. In total 199 polyps and 151 adenomas were detected in the ascending colon. Forward view (phases 1+2) identified 104 polyps and 84 adenomas yielding a polyp and adenoma detection rate (ADR) in the ascending colon of 16.7% (95% CI: 13.2–20.3) and 13.7% (95% CI: 10.5–17.0) respectively. Retroflexion identified a further 95 polyps and 67 adenomas improving the polyp and ADR in the ascending colon to 29.1% (95% CI: 24.8.2–33.3) and 22.5% (95% CI: 18.6–26.5) respectively, ($p < 0.01$). Adenoma miss rate was 44.4% (67/151) and per patient adenoma miss rate was 8.8%. Multivariate analysis showed that factors influencing the detection of adenomas with retroflexion were age >60 years (OR: 2.63, 95% CI: 1.25–5.50 p = 0.011), male gender (OR: 1.88, 95% CI :0.99–3.58 p = 0.055), previous surgery (OR: 2.74, 95% CI:1.42–5.27 $p < 0.01$), the existence of adenomas in forward view (OR: 3.06, 95% CI:1.48–6.30 $p < 0.01$) and indication ''Follow-up'' (OR: 2.12, 95% CI:0.94–4.8 p = 0.07).
Conclusion: 1) Retroflexion in the ascending colon is safe and feasible in the vast majority of patients 2) It has an added value for polyp and adenoma detection in the ascending colon provided that forward view missed an important number of lesions. Retroflexion, a simple maneuver during colonoscopy, without additional cost, may decrease interval cancers in the right colon if added in the standard practice.
Disclosure: Nothing to disclose

P1432 DOES THE ENDOSCOPIST'S GENDER INFLUENCE QUALITY PARAMETERS OF SCREENING COLONOSCOPY?

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Introduction: Gender differences were shown in relation to less career satisfaction and lower career advancement for female gastroenterologists (Gerson LB et al, *Gastroenterology* 2007).
Not much association was found so far between gender of endoscopists and outcome of their performance. Thus, the aim of the study was to assess differences in quality measures and incidence of complications according to endoscopist's gender.
Aims and Methods: Data from 174 848 screening colonoscopies between 2007 and 2018 from private practices were analyzed within Austrian Certificate in Quality for Colorectal Cancer Screening. We evaluated the adenoma detection rate (ADR), advanced adenoma detection rate (AADR) and cecal intubation rate (CIR), sedation rate (SR), complication rate and compared these quality measures between male and female endoscopists.
Results: From 189 endoscopists included in this study, 18.52% were female (27 370 screening colonoscopies, mean patient's age = 61.07) and 81.48% were male (n = 147 478, mean patient's age = 61.3). Female endoscopists had significantly more female patients (57, 56% (SD = 6.39) vs. 49, 43% (SD = 5.16), $p < 0.001$) while male endoscopists more male patients (50.57% (SD = 5.16) vs. 42, 44% (SD = 6.39), $p < 0.001$).
No statistical significance was found in median ADR among female and male participants (25.68% (IQR = 17.06) vs. 21, 41% (IQR = 13.55), U = 2 277, p = 0.152). Median male ADR and female ADR did not show significant difference in relation to endoscopist's gender (male ADR: 32.15% (IQR = 17.31) vs. 27, 47% (IQR = 14.75), U = 2 297.5, p = 0.174; female ADR: 20.0% (IQR = 13.65) vs. 15.87% (IQR = 10.92),: U = 2 240, 5, p = 0.120).
There was no statistical significance in median AADR among both groups of endoscopists (6.98% (IQR = 6.26) vs. 6.90% (IQR = 5.28), U = 2 443, p = 0.388). According to the CIR, SR and complication rate no significant difference was found (median CIR: 97, 54% (IQR = 4.08) vs. 97.47% (IQR = 4.27), U = 2 824, p = 0.659; median SR: 97, 37% (IQR = 10.33) vs. 95.45% (IQR = 13.58), U = 2 499, p = 0.502; median complication rate: 0.05% (IQR = 0.35) vs. 0.02% (IQR = 0.3) U = 2 554, p = 0.607).
Conclusion: The study showed that more female patients were examined by female endoscopists while more male patients were examined by male endoscopists but it did not show any significant difference in the quality parameters in

relation to gender of participants. Both female and male endoscopists participating in the Austrian quality certificate performed screening colonoscopy with high quality.
Disclosure: Nothing to disclose

P1433 UNDERWATER ENDOSCOPIC MUCOSAL RESECTION SHOWS TO BE MORE EFFECTIVE THAN EMR IN WORSE SCENARIOS WITH LESS ADVERSE EVENTS

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Introduction: Nowadays, endoscopic mucosal resection (EMR) is the usual technique for treatment of flat colorrectal polyps, however underwater-EMR (U-EMR) has appeared as an atractive alternative. Despite its preliminar suitability, the real indication of U-EMR remains unclear. The aim of this study is to compare the feasibility, adverse events and recurrences of both techniques in a multicentric fashion.
Aims and Methods: We performed a prospective cross-sectional study in two referral hospitals from December 2016 to November 2017 in which lesions >15 mm resected by EMR or U-EMR were included. Both cohorts were matched using a propensity matching score (ratio 2:1) to avoid a selection bias using as reference the score in SMSA score. The margins of the scars were assessed to detect residual adenomatous tissue. A follow-up colonoscopy in 3–6 months and 12 months was scheduled.
Results: A total of 162 lesions were resected and analysed from 137 patients (59% male, 66% y.o), with an average size of 25 mm and 60% of them located in proximal colon. Histological assessment revealed carcinoma in 33/162 (20%), detecting in 8 of them (5%) deep mucosal invasive cancer (referred to surgery). Regarding to the procedures, en bloc resection was achieved in 68% U-EMR versus 49% EMR ($p > 0.05$), and less number of slides to reach complete resection were detected in U-EMR (2.59+/− 2.43 vs 1.74 +/− 1.10, $p < 0.001$). There were no significant differences between efficacy comparing size of the lesions, however U-EMR might trend to be more feassible in achieving en bloc and complete resection compared to EMR, in addition to more efficient (less time spent per procedure). In terms of adverse events, post procedural bleeding (10% EMR vs 2% U-EMR; $p > 0.05$) and one perforation (EMR group) were described. In the follow up endoscopies (early-3-6moths and late-12months), no differencies were described between both techniques.
Conclusion: In real clinical practice U-EMR showed to be as effective and safer than traditional EMR especially in difficult cases. Furthermore, U-EMR yielded a feasible approach to prevent cautery artefact, allowing an accurate pathologic assessment.
Disclosure: Nothing to disclose

P1434 CHROMOENDOSCOPY WITH INDIGO CARMINE VERSUS ENDOCUFF FOR ADENOMA DETECTION RATE IN COLONOSCOPY: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Colorectal cancer (CCR) is one of the leading causes of death in the world. These deaths could be avoided by early detection of adenomas. There are some techniques to increase the adenoma detection rate (ADR) during colonoscopy, such as the chromoendoscopy with indigo carmine or the use of endocuff device. Indigo carmine highlights the surface topography of the mucosa while endocuff is a flexible long cap that is integrated into the tip of the colonoscope to flat the folds of colon. Both techniques seem to increase the ADR, but there is not direct comparison between the two methods.
Aims and Methods: The aim was to compare ADR of chromoendoscopy with indigo carmine versus endocuff. This is a randomized controlled trial performed in a single center from March 2016 to November 2017. The Institutional Ethical Committee approved the study and written informed consent was obtained in all cases. The inclusion criteria were patients over 50 years old with average risk for colorectal cancer and adequate Boston bowel preparation (≥6). Patients were randomly selected in a 1:1 ratio by a computer generator in blocks of four. Colonoscopies were performed using 10 mL of indigo carmine 0.8% in 250 mL of water or endocuff™ (Arc Medical Desing Ltd). ADR was defined as the proportion of patients with at least one adenoma (per-patient analysis). Mean adenomas per patient (MAP) was also calculated as the total number of detected adenomas in each group divided by the total number of patients in that group (per-adenoma analysis). ADR and MAP were compared for both groups using chi^2 test and Student's T-test respectively; $P < 0.05$ was considered statistically significant. The preliminary results of the 30% of the total calculated sample size (n = 150 per group) are shown here.
Results: A total of 92 patients were included but 6 were eliminated because they did not meet inclusion criteria. The selected 86 patients were randomized into the two groups, chromoendoscopy (n = 44) vs endocuff (n = 42). There were no differences in gender, age or quality of colonic preparation. The withdrawal time for chromoendoscopy was 15 ± 4 minutes whereas for endocuff was 12 ± 4 minutes ($p = 0.002$). Ileocecal valve cannulation was 91% in chromoendoscopy versus 89% in endocuff without statistical differences. The results of ADR and MAP analysis are described in the table below.

	Indigo carmine n = 44	Endocuff n = 42	P value
Adenoma detection rate, ADR (%[95% CI])			
Total	50 (35–65)	31 (16–45)	0.07
Right	32 (18–46)	10 (0.7–19)	**0.02**
Transverse	16 (5–27)	13 (2–23)	0.69
Left	25 (12–38)	15 (4–27)	0.28
Rectum	11 (2–21)	5 (1–12)	0.31
Mean Adenomas per Patient, MAP (mean [95% CI])			
Total	1.20 (0.56–1.84)	0.51 (0.19–0.83)	0.07
Right	0.40 (0.19–0.62)	0.10 (0.00–0.20)	**0.01**
Transverse	0.25 (0.05–0.45)	0.12 (0.01–0.24)	0.29
Left	0.39 (0.11–0.66)	0.23 (0.00–0.46)	0.39
Rectum	0.16 (0.01–0.30)	0.05 (0.00–0.12)	0.20

[Table1]
There were no significant differences between chromoendoscopy with indigo carmine versus endocuff for ADR (50 vs 31, $p = 0.07$) or MAP (1.20 vs 0.51, $p = 0.07$) in total colonoscopy. ADR and MAP were significantly higher in the chromoendoscopy group for the right colon segment (32 vs 10, $p = 0.02$ and 0.40 vs 0.10, $p = 0.01$, respectively). There were not complications in any of the two groups.
Conclusion: Chromoendoscopy with indigo carmine was superior to endocuff for ADR and MAP for the right colon. We did not find statistical significant differences in the total colon evaluation.
Disclosure: Nothing to disclose

P1435 "LEAVE-IN-SITU STRATEGY" FOR DIMINUTIVE COLORECTAL ADENOMAS

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Introduction: Colonoscopy with polypectomy of adenomas reduces the incidence and mortality of colorectal cancers (1). With recent increment of the number of screening colonoscopies, it is reported that eradication of adenomas during colonoscopy can be a big burden for endoscopists (2). According to the Japanese Society of Gastroenterology guidelines (3), diminutive adenomas which has no evidence of carcinoma in their appearance are allowed to be left in situ, provided strict surveillance colonoscopies within 3 years (="leave-in-situ strategy") are conducted, which is different initiative from the European or American guidelines (4,5). However, the safety and efficacy of the "leave-in-situ strategy" of diminutive adenomas are unknown.
Aims and Methods: The aim was to retrospectively assess the safety and compliance of the "leave-in-situ strategy" of diminutive adenomas. Patients whose diminutive adenomas were not resected at the initial colonoscopies between April 2001 and November 2014 at a referral center were chosen as the subjects. All the subjects were asked to receive surveillance colonoscopies within 3 years. The primary outcome measure is the incidence rate of index lesions (ILs) at the surveillance colonoscopy within 3 years. The ILs were defined as follows: adenomas ≧10 mm, high grade dysplasias, villous adenomas, and invasive cancers. The secondary outcome measures included the rate of patients who received the 3-year surveillance colonoscopies and the number of the diminutive polyps which were detected at both the initial and surveillance colonoscopies.
Results: A total of 4816 patients were left untreated of diminutive adenomas (n = 2502) at the initial colonoscopies. The incidence rate of index lesions at the surveillance colonoscopies was 2.3%(36/1543; 12 adenomas ≧10 mm, 22 high-grade dysplasias, and 2 invasive cancers). The rate of patients who underwent 3-year surveillance colonoscopies was 32.0% (1543/4816). The same

diminutive adenomas were detected in the surveillance colonoscopies in 63.2% (1582/2502).
Conclusion: "Leave-in-situ strategy" of diminutive adenomas can be acceptable whose rate of ILs in the surveillance colonoscopies is limited to 2.3% which is similar to those in the National Polyp Study (6). However, strict instruction to the patients is indispensable considering the low receiving rate of surveillance colonoscopies.
Disclosure: Nothing to disclose

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P1438 LONG-TERM COLORECTAL CANCER INCIDENCE AND MORTALITY IN RELATION TO QUALITY OF A SINGLE NEGATIVE SCREENING COLONOSCOPY

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Introduction: The predictive effect of a quality of a single negative screening colonoscopy on long-term risk of colorectal cancer (CRC) remains uncertain.
Aims and Methods: This study aims to determine the predictive effect of quality of negative screening colonoscopy on long term CRC incidence and mortality. We retrospectively analysed subjects with a single negative screening colonoscopy defined as absence of any neoplastic lesions. Data was obtained from the Polish CRC screening program database. All colonoscopies performed between October 1st 2000, and December 31st 2011 were included. Analysed subjects were followed for CRC occurrence and death through the National Cancer Registry over median of 9.2 years up to 16.4 years. High-quality colonoscopy was defined as examination with cecal intubation, adequate bowel preparation ('very good, good or suficientaccording to Aronchick scale) performed by an endoscopist with an adenoma detection rate $\geq$20%. Standardized incidence and mortality ratios (SIRs and SMRs) were calculated by comparison with values for general Polish population according to sex and 5-years age groups.
Results: Of the 156.633 individuals included into analysis, 365 CRC after 1,449,733 person-years of follow up were observed (25.2 per 100,000 person years). CRC related deaths totalled 96 over 1,450,761 person-years (6.6 per 100,000 person years). SIRs and SMRs for individuals after single negative colonoscopy, irrespective of its quality, were 0.41 (95% CI, 0.37–0.46) and 0.22 (95% CI, 0.18–0.27), respectively. Negative high-quality colonoscopy was associated with SIR of 0.22 (95% CI, 0.16–0.28) and SMR of 0.1 (95% CI, 0.05–0.17), whereas low-quality colonoscopy yielded SIR of 0.49 (95% CI, 0.44–0.55) and SMR of 0.28 (95% CI, 0.22–0.34). Table 1 shows SIRs and SMRs after single negative colonoscopy according to the duration of follow-up. Individuals observed longer than 10 years after single negative colonoscopy had still significantly reduced risk of CRC and CRC mortality compared to general population (SIRs and SMRs were 0.53 (95% CI, 0.39–0.71) and 0.40 (95% CI, 0.23–0.63), respectively). High-quality single negative colonoscopy yielded SIR of 0.35 (95% CI, 0.13–0.77) and SMR of 0.13 (95% CI, 0.0–0.7) after more than 10 years of follow-up.

Quality of screening colonoscopy	Time from screening colonoscopy (years)	SIR (95% CI)	SMR (95% CI)
Low	0.1–3.0	0.30 (0.23–0.39)	0.11 (0.05–0.21)
	3.1–5.0	0.46 (0.35–0.60)	0.12 (0.05–0.24)
	5.1–10.0	0.62 (0.52–0.72)	0.42 (0.31–0.55)
	>10	0.58 (0.41–0.78)	0.46 (0.26–0.74)
High	0.1–3.0	0.12 (0.06–0.22)	0.05 (0.01–0.18)
	3.1–5.0	0.23 (0.12–0.39)	0.07 (0.01–0.26)
	5.1–10.0	0.28 (0.18–0.40)	0.15 (0.06–0.31)
	>10	0.35 (0.13–0.77)	0.13 (0.00–0.70)

[Table 1. SIRs and SMRs of colorectal cancer after negative screening colonoscopy according to quality according to time from screening colonoscopy.]

Conclusion: Single high-quality negative colonoscopy was associated with significantly lower CRC incidence and mortality as compared to low-quality negative colonoscopy. The predictive effect of single negative high-quality colonoscopy extended beyond 10 years of follow up.
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P1439 SEDOANALGESIA COMPLICATIONS DURING A COLONOSCOPY. WHICH FACTORS ARE INVOLVED?

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Introduction: Colorectal cancer ranks third among the most commonly diagnosed cancers worldwide. Colonoscopy has been shown to reduce morbidity and mortality in screening programs. Colonoscopy due to sedation procedure has several complications being the most frequent the cardiorespiratory complications. The overall complication rate ranges from 0.1 to 0.2%, with a mortality of 0.0014%.
Aims and Methods: To determine which factors are related to the risk of developing a sedoanalgesia complication (SAC) during a colonoscopy with the objective of reduces the post-colonoscopy complications. All screening colonoscopies after a positive faecal immunochemical test were analyzed related to 2009–2018 invitations. 87 SAC were identified. SAC was considered: chest pain, bradycardia, tachycardia, hypoxia, reflex reactions, respiratory distress, hypo-hypertension. SAC were classified in mild and serious. Considering mild as complication that obligate the interruption of the colonoscopy and serious if a hospitalization is required. A multivariate model was performed and Independent Predictors (IP) of SAC after a colonoscopy were identified through a logistic regression.
Results: After 67,946 colonoscopies, SAC rate was 0.12%. 64.4% were men. Most of the patients had 2 points in the Charlson Index (49.4%) and ASA II (42.1%). 65–69 range age was which presents he highest rate of complications. 79 mild and 8 serious SAC were identified.
Mild SAC: 30.4% was smoker and 24.1% had a moderate consumption of alcohol. The 14.1% and the 20.5% of the cases had cardiopathy and neumopathy history respectively. The 16.9% of patient were treated with benzodiazepines, 6.4% with antipsychotic and 2.6% with opioids. 49.3% of the patients had polypectomy. Serious SAC: 50% had a moderate consumption of alcohol and the 12.5% were smoker. 25% had cardiopathy and neumopathy history. 25% were treated with benzodiazepines and the 12.5% with antipsychotics. 49.3% of the patients had polypectomy.
Firstly we made a univariate analysis. Patients-variables for the analysis were: age, sex, ASA, cardiopathy and neumopathy history, patient's toxic habits (tobacco and alcohol), IMC, Charlson Index, chronicity index, polypectomy and antipsychotic, benzodiazepine or opioids therapies. Colonoscopy technique variables: patient position, type of insufflation, type of sedation, type of oxygenation, colonoscopy assist or not by an anesthetist, hours until the patient recuperation, nurse's sedation training and type of hospital. The variables with a significant result in the univariate analysis were; tobacco, alcohol, neumopathy history, polypectomy, colonoscopy assist or not by an anesthetist, hours until the patient recuperation and nurse's sedation training.
After a multivariate analysis SAC IP were: tobacco (OR:2.8; 95%CI:1.1–7.4), alcohol (OR:8.0; 95%CI:2.1–30.0), polypectomy (OR:0.4; 95%CI:0.2–0.8) and nurse's sedation training (OR:0.4; 95%CI:0.2–0.9). The logistic model explained 73% of the complications (CI95% 0.65–0.80, $p < 0.001$).
Conclusion: The colonoscopy is a procedure with a small but not insignificant risk of SAC, so it is crucial to know which factors predict the risk of those complications in order to implement countermeasures. The study that we present shows that both variables related to the patient (toxic habits and polypectomy) and related with colonoscopy technique (nurse's sedation training) are independent factors to consider while performing a colonoscopy.
Disclosure: Nothing to disclose

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P1440 IMPACT OF AN EDUCATIONAL INTERVENTION ON THE IMPROVEMENT OF QUALITY INDICATORS OF COLORECTAL CANCER SCREENING COLONOSCOPIES

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Introduction: The diagnostic accuracy of colorectal cancer screening colonoscopies (CRCSCs) depends on the adherence to quality indicators.
Aims and Methods: We aimed at evaluating the effects of an educational intervention on quality indicators of CRCSCs at a tertiary center.
CRCSCs performed between 2005 and 2009 at a tertiary center were analyzed and an educational intervention regarding the results of CRCSCs evaluation and optimal quality indicators was given to the team of gastroenterologists and nursing staff in January 2011. 2118 CRCSCs performed between 2011 and 2015 were evaluated and compared to 1545 CRCSCs performed between 2005 and 2009. Descriptive statistical analysis was performed and Chi-Square test was applied to compare quality indicators of CRCSCs between 2005 to 2009 and 2011 to 2015.
Results: 2118 CRCSCs were performed between 2011 and 2015. The mean age was 62.5 ± 10.7 years and 57% (1205) were women. Sedation was performed in 77% (1634) of the procedures. The cecal intubation rate (CIR) was 85.5% (1833). Most common reasons for incomplete CRCSCs were: patient intolerance 46.3% (132), inadequate bowel preparation 20.4% (58) and technical difficulties 15.1% (43). Good or adequate bowel preparation was noted in 1786 (84%) patients. Photodocumentation of cecal landmarks (PCL) was performed in 97.3% (1783) of the cases. Polyp detection rate (PDR) was 34.3% (726) and polyps ≥1cm were detected in 13.4% (97) patients. Colorectal cancer (CRC) was detected in 0.5% (11) patients.
1545 CRCSCs were performed between 2005 and 2009. The mean age was 60.4 ± 10.7 years and 62% (958) were women. Sedation was performed in 32% (499) of the exams. The CIR rate was 91% (1336). Most common reasons for incomplete CRCSCs were: patient intolerance 40% (84), inadequate bowel preparation 35% (73) technical difficulties 18% (37).
Good or adequate bowel preparation was noted in 1345 (87%) patients.
PCL was performed in 93% (1248) of the cases. PDR was 33% (503) and polyps ≥1cm were detected in 16% (82) patients. CRC was detected in 0.3% (5) patients.
Conclusion: Although there was a significant improvement in the quality of the PCL indicator after the educational intervention, there was no improvement in cecal intubation rates despite a significant increase in use of sedation during colonoscopy. Additionally, our results suggest a need for better patient educational programs to improve the quality of bowel preparation.

Indicator	2005–2009	2011–2015	P
CIR	1336 (91%)	1833 (87%)	0.950
Incomplete SC:			
– Intolerance	84 (40%)	132 (46%)	0.175
– Inadequate bowel preparation	73 (35%)	58 (20%)	<0.001
– Technical difficulties	37 (18%)	43 (15%)	0.436
PCL	1248 (93%)	1783 (97%)	0.001
PDR	503 (33%)	726 (34%)	0.276
Polyp measuring ≥ 1cm	82 (16%)	97 (13%)	0.313
Colorectal cancer	5 (0.3%)	11 (0.5%)	0.375
Good/reasonable bowel preparation	1345 (87%)	1786 (84%)	0.021
Poor preparation	200 (13%)	332 (15.7%)	0.02
Sedation	499 (32%)	1634 (77%)	<0.001

[Comparison of quality indicators during the two study periods]
Disclosure: Nothing to disclose

P1441 UTILITY OF 3D ENDOSCOPY IN MEASUREMENT OF COLON POLYP SIZE

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Introduction: Measuring colon polyp size is crucial in choosing an appropriate therapeutic option. However, currently available measurement procedures are not necessarily accurate. Depth and spatial information, which is lacking in conventional two-dimensional (2D) endoscopy, has become available with the use of 3D technology. In collaboration with a medical device company, by using a flexible three-dimensional (3D) endoscope currently in development, we conducted an ex vivo study to evaluate the utility of 3D endoscopy in measurement of colon polyp size.
Aims and Methods: We prepared models of colon polyps (protruding and flat lesions) ranging in size from 2 mm to 10 mm in 1-mm increments. A total of 220 measurements were made among 10 doctors (6 specialists and 4 non-specialists). A prototype 3D endoscope was used to measure polyp size either in 3D mode in combination with 3D glasses or in 2D mode. Randomization was performed by using envelopes containing the size of a model polyp and the mode of measurement to be used. Accuracy rate and measurement error (i.e., actual polyp size minus measured size) were compared between 3D and 2D endoscopy.
Results: Among the 220 measurements, 103 were by 2D endoscopy and 117 by 3D endoscopy. Accuracy rate was 23.3% (24/103) by 2D endoscopy and 25.6% by 3D endoscopy (30/117); the difference was not significant. On the other hand, measurement error by 2D endoscopy (1.81 ± 1.88 mm) was significantly larger ($p < 0.05$) than that by 3D endoscopy (0.92 ± 2.27 mm). Errors in measurements of flat polyps and protruding polyps were 2.25 ± 1.97 mm and 1.34 ± 1.69 mm, respectively, by 2D endoscopy, and 1.68 ± 1.62 mm and 0.2 ± 2.56 mm, respectively, by 3D endoscopy. Accuracy rate was 33.8% (27/80) with a measurement error of 0.96 ± 2.10 mm among non-specialists, and 19.3% (27/140) with a measurement error of 1.55 ± 2.14 mm among specialists; accuracy rate was significantly higher and measurement error was significantly smaller among non-specialists than among specialists.
Conclusion: Accuracy rate of colon polyp size measurement was not high, and there was no significant difference between 2D and 3D endoscopy. Measurements tended to be larger and measurement errors were significantly smaller in 3D endoscopy than in 2D endoscopy. Also, measurement of protruding polyps tended to be large and have smaller error than those of flat polyps. Accuracy rate was significantly higher and measurement error was significantly smaller among non-specialists than among specialists.
Disclosure: Nothing to disclose

P1442 SCREENING COLONOSCOPY: DOES THE ADR VARIATES WITHIN A TRAINING CENTER? AN EXPERIENCE AT A LATIN AMERICAN TRAINING CENTER

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Introduction: Colonoscopy is considered the gold standard screening method for colorectal cancer (CRC), it allows the detection and resection of the adenomatous lesions. There are different markers which define colonoscopy-quality indicators, these have shown to decrease the CRC incidence. One of the most important is the adenoma detection rate (ADR).
Aims and Methods: We aimed to know the ADR in colorectal cancer screening colonoscopy in an average risk population for CRC, at the Gastroenterology Service of HIGA San Martin La Plata, WGO advanced endoscopy training center, from January 2012 to December 2017.
This was an observational study. The global ADR was analyzed, adjusted to sex, morphological features, lesions topography and high-risk adenoma frequency. Colonoscopy were performed by fellows and supervised by experts. Fellows ADR was evaluated at different training stages. Statistical analysis was performed by using the $\chi 2$ test. Patients with Boston Bowel Preparation Scale ≥5 and cecal checkpoint were included.
Results: 12,106 procedure were performed, 1,111 (9.2%) of which were CRC-screening. 935 procedures met the inclusion criteria, with a mean age of 60 years (range 50 to 75y). In 256 at least one adenoma was found; 98(38.3%) showed some high-risk features. Global ADR was 27.4% and, adjusted to sex, 23.3% in women and 34.3% in men. During the first formation stage (1 to 150 procedure), ADR was of 27.8% while during the second stage (150 to 300 procedure) was 26.8% ($p = 0.78$). 398 adenomas in total were resected, corresponding to a 42.6% adenoma detection index (ADI). 337 (84.6%) were polypoid lesions. When analyzed by segments, it was found that 114 patients showed at least an adenoma in the right colon, 107 in the left colon, 57 in the transverse colon and 38 in rectum.

In the left colon, 55 (51.4%) showed at least one high risk characteristic, 26 (22.8%) in the right colon, 11 (19.3%) in the transverse colon and 17 (44.7%) in rectum. A statistically significant difference was found between the adenoma location and their high risk findings. Compared and corrected by the p-value through the Bonferroni method, statistically significant differences were found in the high-risk adenoma proportions found in the left colon compared with the transverse colon ($p = 0.0024$) and the right colon ($p = 0.0013$).
Left colon and rectum localization of adenomas, increases by 3 ($p < 0.0001$, OR = 3.73, IC 95%: 2.19–6.34) and 2 ($p < 0.0001$, OR = 1.99, IC 95%: 0.99–3.99) times respectively the possibilities that the adenomas found at any other segment of the colon or rectum may have at least a high-risk characteristic. No significative association between risk adenomas and sex was found ($\chi 2 = 1.971$, $p = 0.160$).
Conclusion: Our global and adjusted by sex ADR are comparable to those recommended by the international guidelines. Formative stages under the supervision of an experienced observer do not influence on ADR. Despite right-sided adenomas were the most frequent, left colon and rectum adenomas showed a significant association with the presence of at least one high-risk features in the adenomas founded. Therefore, the measurement of colonoscopy quality indicators in the colorectal cancer screening programs must be a goal from the earliest formative stages.
Disclosure: Nothing to disclose

P1443 WHO HAS MORE INCOMPLETE COLONOSCOPIES: SURGEONS, INTERNISTS OR GASTROENTEROLOGISTS?

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Introduction:. Intubation of caecum is foundation for general impression of colon. Cecal intubation rate (CIR) <80% correlates with higher risk of post colonoscopy colorectal cancer (PCCRC), (Baxter et al., *Gastroenterology* 2011).
Aims and Methods: Aim of the study was to investigate if surgeons, internists or gastroenterologists have higher rates of incomplete colonoscopies. Further to identify reasons for incomplete colonoscopy (complication, stenosis, pain, inadequate bowl preparation, others) and analyze the quality of bowel preparation (data collected since 2012). Therefore 264,116 screening colonoscopies performed by 294 physicans between 2007–2018, within the Austrian certificate of screening colonoscopywere analysed within the study.
Results: 32% of endoscopists were surgeons, 52% internists 16% gastroenterologists. Mean CIR was 96.45% (SD = 4.12). 3.81% (SD = 4.17) of colonoscopies within surgeons, 3.31% (SD = 4.06) within internists ($p = 0.4616$) and 3.79% (SD = 4.19) within gastroenterologists were incomplete (compared to surgeons $p = 0.9821$, compared to internists $p = 0.4772$). Mean age of patients who had incomplete procedure was 63.13 (SD = 10.23) vs. age of 61.12 (SD = 9.17) in patients who had complete procedure ($p = 0.0001$).
In group of internists adequate rate for bowel preparation was 95.52% (SD = 4.30), in surgeons rate was 96.70% (SD = 3.09) ($p = 0.0297$) and 96.20% (SD = 4.02) in group of gastroenterologists (compared to surgeons $p = 0.4281$, compared to internists $p = 0.3416$).
Conclusion: There was no significant difference between surgeons, specialists for internal medicine and gastroenterologists according rate of incomplete colonoscopies. Regarding reasons for termination of examination, surgeons claimed stenosis more often than specialists for internal medicine or gastroenterologists. Patients who underwent colonoscopy performed by surgeons had a better bowel preparation than patients of internists and gastroenterologists. Patients in which caecum was not intubated were older than patients in which caecum was intubated.
Disclosure: Nothing To disclose

P1444 SECOND EVALUATION OF RIGHT COLON. DOES THE ADENOMA DETECTION RATE INCREASE?

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Introduction: Videocolonoscopy (VCC) is the gold standard for colorectal cancer (CCR) screening. Removal of adenomatous polyps during VCC decreases CCR mortality by 50%. CCR incidence occupies the third place worldwide. Although the screening VCC efficiently prevents distal colon cancers, its efficacy to prevent right colon cancers is less clear. Interval cancer is associated with injuries lost in the right colon.
Our aim was to decide whether the performance of a second evaluation of the right colon would increase the adenoma rate (TDA)
Aims and Methods: A prospective study from September 2016 to May 2017 was performed.
All patients who underwent a CCR screening videocolonoscopy were included, with prior informed consent.
Every patient having a Boston Scale store of 2 or 3 in the right colon segment underwent a second evaluation of the right colon[C1].
Injuries found in the right colon were described according to location, size and Paris Classification; they were resected during the procedure.
The time required to perform the second evaluation of the right colon was evaluated
Results: A total of 130 patients were included in the study between September 2016 and May 2017. 21 patients (16%) were excluded according to the Boston Scale <than 2 in the right colon; and 109 patients (84%) met the inclusion criteria, 69 (63%) men and 40 (36%) women, with an age range of 45–75 years. A total of 42 (38%) patients had an injury in their right colon, 27 of them (24%) during the first evaluation and 15 (13%) during the second one.
Injuries found were 23 (21%) <5 mm, 12 (11%) of 5–9 mm and 7 (6%) >to 10 mm. According to the Paris Classification, there were 16 (14%) 0-Is, 24 (22%) 0-IIa and 2 (1%) 0-IIb injuries. Histopathological examination showed 36 (32%) adenomatous injuries and 6 (5%) corresponded to sawing injuries.
TDA during the first evaluation was 22% and increased around 7.3% during the second evaluation, thus reaching a 29.3% TDA, with a statistically significant difference according to the Chi square Test.
Average time before a second evaluation in the right colon was 1.36 minutes (1.15- 2 min)
Conclusion: The performance of a second evaluation of the right colon increases the adenoma detection rate (TDA). It consists of a simple technique, which is carried out within a period of less than 2 minutes, with favourable results for the patient
Disclosure: Nothing to disclose

P1445 DOUBLE BALLOON-ASSISTED ESD VERSUS STANDARD ESD FOR SIGMOID LESIONS

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Introduction: Endoscopic submucosal dissection (ESD) for colorectal lesions requires a higher skill level to complete. In particular, sigmoid colon lesions are thought to be amongst the hardest anatomical location for ESD. This is due to the sigmoid colon being more mobile with lack of peritoneal fixation. From this standpoint, we hypothesized that a double balloon-assisted technique could facilitate sigmoid colon ESD through stabilizing of the sigmoid colon.
Aims and Methods: A bespoke 3D-printed abdomino-pelvic anatomical housing was developed and an ex-vivo colon model mounted within it. A commercially available double balloon sheath on endoscope was used in this study. A 3.0cm pseudo-polyp was created on the fresh porcine distal colon mucosa with electrocautery. Six ESDs were performed against this 3.0cm pseudo-polyp without the double balloon sheath as control group, and with the double balloon sheath on the scope as intervention group. The total procedure time, the number of perforation and the number of muscle layer damage were collected and compared. A single operator performed every procedure.
Results: There were no perforation in all of the procedures. The total procedure time and the number of the muscle layer damage in each ESD were shown in the table. The mean total procedure time in Double balloon ESD group was 23.29 minutes and this was significantly shorter than 46.45 minutes in control group ($p = 0.007$). There was no significant difference in the number of the muscle layer damage (1.5 vs 1.0, $p = 0.599$).
Conclusion: Double balloon technique may facilitate sigmoid colon ESD by reducing the procedure time and difficulty. We postulate that this is performed by 'splinting' that section of the sigmoid intestine reducing movement and increasing stability.
Disclosure: J. Milsom – Olympus research grant and Lumendi CAB member

P1446 DIAGNOSTIC YIELD OF SPYGLASSDS FOR BILIARY TRACT LESIONS

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Introduction: SpyGlassDS has been used as diagnostic or therapeutic tool for biliary tract lesions, and the feasibility of this device was reported in several studies. We investigated the utility of the SpyGlassDS for patients with biliary tract lesions.
Aims and Methods: We evaluated success rates of observation and sampling using SpyGlassDS for 34 patients who were performed cholangioscopy for the purpose of examine the biliary tract lesions at our hospital between November 2015 and December 2017. Successful observation was defined as the case in which SpyGlassDS reached the biliary tract lesion and obtained high-quality images

enough to evaluate. Successful sampling was defined as the case in which sufficient amount of specimen was collected by SpyBite biopsy forceps. For 18 patients with cholangiocarcinoma who had undergone surgical treatment, we evaluated the concordance rate of horizontal extension of cancer between diagnosis using SpyGlass and SpyBite, and resected specimens. Horizontal extent of cholangiocarcinoma was diagnosed by SpyGlass as the presence of irregular papillary or granular mucosa or irregularly dilated and tortuous microvasculature that continuously spread from the main lesion.
Results: The rates of successful observation and successful sampling were 97.5% (119/122) and 88.5% (69/78), respectively. Biopsy using SpyBite were not informative due to insufficient amount for pathological review in 9 cases. To evaluate horizontal extension in 18 (?) cholangiocarcinoma patients, 91 checkpoints were observed using SpyGlass and 50 samples were obtained using SpyBite. Comparison between the SpyGlass images and the histological diagnosis in resected specimens revealed the diagnostic accuracy of 86.8% (79/91). The false positive rate was 11.0% (10/91), and the main cause of false positive was misdiagnosis for the inflammatory mucosa as carcinoma. Comparison between the SpyBite biopsy specimen and the resected specimen revealed the accuracy of 90.0% (45/50) and the false-positive rate of 6% (3/50), namely the diagnostic ability of the biopsy specimen was higher than that of visual images.
Conclusion: The ability to approach for the biliary tract lesion which we aimed to evaluate was good and feasible, especially in the advanced technique, evaluation for the second branch of the intrahepatic biliary tract was possible. That was very meaningful to decide the therapeutic option or the surgical form. Considering the results of visual images or the biopsy specimen, the accuracy was mostly satisfactory.
Disclosure: Nothing to disclose

P1447 AMPULLARY RADIO FREQUENCY ABLATION: A NEW MINIMALLY INVASIVE APPROACH TO AVOID SURGERY?

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Introduction: Recently ERCP Guided RF probes were designed. This device has been already used in cholangiocarcinoma and pancreatic cancer with biliary obstruction.
This new treatment induces local coagulative necrosis by delivering thermal energy from high frequency current via bipolar probes and induced an immunomodulation.
We report our experience in ampullomas treated by combination of endoscopic resection and radio frequency ablation (RFA).
We aim to evaluate the feasibility, clinical efficacy and safety of biliairy RFA a new minimally invasive approach.
Aims and Methods: In this study 9 patients (2 males and 7 females) average 70 (41–93) underwent prior endoscopic ampullectomy. Indications of biliary RFA were deep margins not free in 8/9 patients and a relapse in 1 case. Surgery was contra indicated due to comorbidities in 3/9 patients, but mainly because the residual tissue was adenoma with low-grade dysplasia (n = 5). We used dedicated RFA probe manufactured by Taewong Compagny (ELRA^{TM}) of 18 mm length and 7 F. From July 2015 to September 2017 we performed 12 sessions of ampullary RFA (7 patients with a single session 1 patient with 2 sessions and 1 patient with 3 sessions for recurrence).
Technique: Finally a cholangiogram was obtained to clearly determine the location of the lesion and to access its length. The most often there was none defect or stricture visible. The RFA probe was then introduced over the guide wire on the low part of common bile duct.
RFA energy was delivered over the selected period by the device usually 2 mn 10W; We used selected power and time settings recommended by manufacturers based on the results of preclinical studies After withdrawing the probe a biliary stent fully covered metallic stent (n = 8) or accessory plastic stent (n = 4) was placed to ensure biliary drainage and avoid a delayed stricture. The most often a small plastic pancreatic stent (5F) was also placed to avoid acute pancreatitis and migrated spontaneously a few days after (X ray control checked their spontaneous migration after 1 month). Biliary stents were usually removed after 2.5 months (1–5 months) on average during a new ERCP to control the result and perform new biopsies on site.
Results: Feasiblity: technical success was 100%. No complication such as angiocholitis or pancreatitis occured immediatly after RFA ablation. All patients, except two, were discharged one day after procedure. Regarding late complications 2 biliary benign strictures in 2 patients at 4 and 7 months easily treated by a new stent. None pancreatic stricture with an average follow up of 12 month occurred. All patients are alive at the end of this study.
Clinical efficacy was accessed on absence of reccurence of ampuloma on biopsy with an average follow up of 11 months in 6/9 patients. 1/9 patient was lost because was very old (93 years old). 2 patients presented recurrence. 1 with a recurrence after 22 months treated by a second RFA ablation and actually free of disease for 17 months. Last patient presented 2 recurrences after 2 and 7 months treated by RFA ablation with a good result for 4 months.
Conclusion: ERCP with RFA ampullary is safe and seems to be an effective alternative in patients with a high risk for surgery (important co-morbidities) or patients who refuse surgery.
Further studies are mandatory to confirm these preliminary results.
Disclosure: Nothing to disclose

P1448 POST-ERCP PANCREATITIS (PEP): MINIMIZING ROLE OF PANCREATIC DUCT (PD) STENTING WITH NON-INVASIVE COMBINATION THERAPY IN DIFFICULT CASES

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Introduction: Selective biliary cannulation can be challenging during endoscopic retrograde cholangiopancreatography (ERCP). Double-guidewire technique (DGT) is one of the various salvage techniques utilized to improve success rate of selective deep biliary cannulation. Instrumentation of the PD has been associated with increased risk of PEP. Safety of DGT in difficult ERCP access needs to be better defined to determine if it truly affects PEP.
Aims and Methods: ERCP data was retrospectively retrieved from our electronic database between July to December 2017. Approval of the local review board was sought. A total of 258 ERCP cases were reviewed with regards to patient demography, successful standard biliary cannulation (SBC), cases requiring DGT, periprocedural rectal non-steroidal anti inflammatory drug (NSAID), intravenous hydration with lactated Ringer's (LR), PD stenting and common complication rates including PEP, infection, bleeding and perforation. Aim was to determine PEP rates in DGT cases and role of PD stenting in these situations. Data was analyzed using SPSS v20.
Results: From a total of 258 ERCP cases conducted, 13.5% (35 cases) failed SBC and required DGT to facilitate successful biliary access. Of all DGT cases, rectal NSAID was administered in 65%, PD stenting was performed in 23%, and hydration with intravenous LR was initiated in 83% as PEP prophylaxis. DGT cannulation rate following failed SBC was 83%. The incidence of PEP, infection, significant bleeding and perforation were 2.9%, 17.1%, 0% and 0% respectively. The rate of PEP in the subgroup without PD stent placed was only 3.7%. Impact of PEP prophylaxis was found to be significant for rectal NSAID ($p < 0.01$), PD stenting ($p = 0.039$) and LR hydration ($p < 0.01$). There was no PEP witnessed when at least 2 PEP prophylactic measures were instituted (either rectal NSAID and/or PD stent and/or LR drip).
Conclusion: Our data demonstrated PEP rates remained low despite performing DGT for difficult biliary access and PEP risk may be minimized even without PD stenting if at least 2 other PEP prophylactic measures are undertaken such as using rectal NSAID and LR drip. This suggests PD stenting may not be critical in the setting of DGT if deemed challenging. A larger prospective study is indicated to evaluate this finding.
Disclosure: Nothing to disclose

P1449 COMPARISON OF THE DIAGNOSTIC SENSITIVITY OF A NOVEL PERORAL CHOLANGIOSCOPY-GUIDED TARGET BIOPSY TO THAT OF CONVENTIONAL ENDOSCOPIC TRANSPAPILLARY FORCEPS BIOPSY IN PATIENTS WITH SUSPECTED BILE DUCT CANCER

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Introduction: Endoscopic transpapillary forceps biopsy has been used for the histopathological confirmation of bile duct cancer. However, its sensitivity has been reported to be around 50%. To improve the sensitivity, peroral cholangioscopy (POCS)-guided target biopsy has been attempted as an alternative. However, its fragility and impaired maneuverability have hindered its popularity. Recently, a new disposable-type peroral cholangioscope with better maneuverability, SpyGlass DS^{TM}, was developed. Some studies have shown that this cholangioscope has a high sensitivity.
Aims and Methods: To compare the diagnostic sensitivities of POCS-guided target biopsy and conventional endoscopic transpapillary forceps biopsy in patients with suspected bile duct cancer.
This retrospective cohort study included 1) patients with suspected bile duct cancer and 2) patients who underwent both the biopsy methods at our institutions between November 2010 and November 2017. The primary endpoint of this study was the diagnostic sensitivity for malignancy. The specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and sample size of both methods were also compared.
Results: A total of 40 patients were included. Their final diagnoses were bile duct cancer (n = 32), gallbladder cancer (n = 2), and benign or inflammation stricture (n = 6). The sensitivity, specificity, PPV, NPV, and accuracy of the conventional method were 71%, 100%, 0%, 32%, and 80% and the SpyGlass-guided targeted biopsy were 50%, 100%, 0%, 47%, and 60%, respectively. The mean sample sizes for the conventional method and for SpyGlass-guided targeted biopsy were $1.69 \pm 2.10\,mm^2$ and $0.43 \pm 0.47\,mm^2$, respectively ($P < 0.01$).
Conclusion: The diagnostic sensitivity was rather high for conventional endoscopic transpapillary biopsy compared with SpyGlass-guided target biopsy,

which was probably because of insufficient volume of the biopsy specimen for SpyGlass-guided target biopsy.
Disclosure: Nothing to disclose

P1450 ASSESSMENT OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN THE ELDERLY -IS ERCP REALLY SAFE IN THE ELDERLY?-

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is important for diagnosis and therapeutics for cholangiopancreatic disease. Several studies demonstrated its safety in the elderly. But most of those reports assessed only complication rates of ERCP.
Aims and Methods: We retrospectively analyzed the clinical records of consecutive patients (n = 299) undergoing ERCP between November 2016 and December 2017. We divided them into two groups: group A ≥75 years old and group B <75 years old. Patient attributes, ERCP success rate, complication rate, hospitalized days and changes of PS were compared between two groups using chi-square test or t-test. The multivariate regression model was applied to find the risk factors of the prolonged hospitalization and the worsening of PS.
Results: A total of 299 patients was divided into two groups: group A (n = 123, mean age: 82.5 ± 5.3), and group B (n = 176, mean age: 62.3 ± 9.6).
Patients in Group A were more likely to have hypertension, chronic kidney disease and poor PS. Findings for other characteristics were similar between two groups.
All patients underwent ERCP successfully. No significant differences were observed between two groups regarding major ERCP-related complications (pancreatitis, bleeding, cholangitis and so on), while only the rate of pneumonia was higher in group A (p = 0.037).
Hospitalization for 20 days or more was needed in 33 patients (26.8%) in group A and in 24 patients (13.6%) in group B (p = 0.0043). The worsening of PS was observed in 19 patients (15.4%) in group A and in 4 patients (2.3%) in group B (p < 0.0001).
The multivariate regression model identified that the complications (Odds Ratio [OR] :3.81, 95% Confidence Interval [CI] :1.69∼8.57, P = 0.0012) and the older age (OR:2.02, CI: 1.09∼3.72, P = 0.024) were independent risk factors for the prolonged hospitalized days, and it also identified that the older age (OR:5.86, CI:1.89∼18.2, P = 0.0022), complications (OR:3.33, CI:1.03∼10.8, P = 0.045) and malignancy (OR:2.75, CI:1.03∼7.32, P = 0.043) were independent risk factors for the worsening of PS. Especially, Combinations of the older age and complications placed patients at increasingly higher risk of the prolonged hospitalization (OR:4.02, CI:1.40∼11.5, P = 0.0097) and the worsening of PS (OR:9.89, CI:2.81∼34.8, P = 0.00036).
Conclusion: We found that the risk of pneumonia, the prolonged hospitalization and the worsening of PS after ERCP are significantly higher in the elderly. We should perform ERCP carefully in the elderly.

	Over 75 years old	Under 75 years old	p-value
Character	123	176	
Male/Female	79/44	122/54	0.36
Benign/Malignancy	90/33	122/54	0.47
ASA1-2/3-4	95/27	143/33	0.50
Heart disease	25	36	0.98
Pulmonary disease	7	5	0.22
Diabetes mellitus	31	47	0.77
Hypertension	59	61	**0.021**
Liver cirrhosis	3	6	0.63
Chronic kidney disease	45	19	**P < 0.0001**
PS on admission (0–4)	67/22/23/9/2	118/37/7/13/1	**P < 0.0001**
Complications	16	16	0.37
Pneumonia	3	0	**0.037**
Pancreatitis	5	5	0.47
Bleeding	1	4	0.33
Cholangitis	3	5	0.83
Perforation	1	1	0.80
Others	3	1	0.17
Outcome			
Prolonged hospitalization	33	24	**0.0043**
Worsening of PS	19	4	**P < 0.0001**

[Table1]
Disclosure: Nothing to disclose

P1451 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY OF ACUTE CALCULOUS CHOLANGITIS IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Endoscopic Retrograde Cholangiopancreatography (ERCP) has become standard treatment of choice for treating acute calculous cholangitis, but little is known about its outcome and safety in patients with liver cirrhosis (LC).
Aims and Methods: The objectives of this study were to analyze outcomes, efficacy and safety through a retrospective study of ERCP in patients with liver cirrhosis. A cross-sectional retrospective analysis of 59 ERCPs of 51 patients with LC performed at tertiary academic hospital over 5years period was conducted. The patients (LC group) were subdivided into two groups based on their Child-Pugh classification (CP-class): 32 with CP-class A (LC-A), 14 with CP-class B (LC-B) and 5 with CP class C (LC-C).
Results: Procedural outcomes and post-procedural complications (bleeding or perforation) did not differ significantly among three groups. The 30-day, procedure-related adverse events included post-ERCP pancreatitis (n = 5, 8.47%), hemorrhage (n = 2, 3.39%), cholangitis (n = 5, 8.47%), and death (n = 2, 3.39%). There was a higher rate of adverse events in patients with LC-C when compared with those with LC-A and LC-B (11.4%, 5.3%, and 6.1%, respectively; P = .034). There was no correlation between the risk of significant hemorrhage and CP class, even in those who underwent an endoscopic sphincterotomy. No patients experienced worsening of the CP score 1 month after ERCP compared with the baseline score. During a median observation period of 44 months, the recurrence rates of cholangitis were similar between the three groups (recurrence rates: 8.1 vs. 7.5 vs 6.4%, p = 0.625). The overall mortality rate was increased in the LC-C group (1-year mortality rates: 4.3 vs. 6.3 vs. 12.7%, p = 0.021).
Conclusion: The adverse events seen in patients with liver cirrhosis are not different from those seen in the general population of patients undergoing ERCP, although patients with Child C have higher adverse event rates compared with those with Child A and B.
Disclosure: Nothing to disclose

P1452 RADIOFREQUENCY ABLATION (RFA) FOR INTRABILIARY EXTENSION OF ADENOMA OF THE PAPILLA OF VATER: PRELIMINARY RESULTS

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Introduction: Endoscopic snare papillectomy (ESP) of adenoma of the papilla of Vater is an effective technique which can be curative in more than 85% of the cases. Intrabiliary extension of the adenoma can limit the curative intent of the endoscopic resection.
Aims and Methods: Radiofrequency ablation (RFA) of the intraductal extension was evaluated in consecutive patients with adenoma of the papilla of Vater after papillectomy.
ESP was performed with an intent for en-bloc-resection without submucosal injection and placement of a 5 french prophylactic pancreatic stent. Possible intra-biliary extension was assessed on cholangiogram and after traction with an inflated extraction balloon: in case of suspected intrabiliary extension, biopsies were performed and a biliary stent was placed. RFA was planned during a subsequent procedure 1 month later. RFA was performed with the VIVAcombo™ generator (STARmed, South Korea) and an 18 or 33 mm long bipolar catheter (ELRA), power setting 10 W, 80°, 2 minutes. A 7 french pancreatic stent was placed before RFA and 2–3 biliary plastic stents were inserted to prevent stenosis. All the stents were removed 3 months later and intrabiliary biopsies performed. In case of positive biopsies RFA was repeated.
Results: Between March 2016 and April 2018, 7 patients (6 F, mean age 67.3 years) underwent ESP for adenoma of the papilla of Vater with intrabiliary extension. Liver function tests were normal in all the cases. Final histology resulted in 1 case of adenocarcinoma; the patient refused surgery and accepted RFA. RFA was performed one month after ESP (6 cases with a pancreatic stent in place, 1 without due to failure in replacement). The patient without the pancreatic stent developed severe post-RFA pancreatitiswhich resolved with conservative treatment. After a mean follow-up 13 months, 4 patients have no evidence of residual intrabiliary adenoma on biopsies, 2 patient are under treatment, while the patient with adenocarcinoma accepted duodenopancreatectomy due to repeated biopsies positive for adenocarcinoma (**table 1**).
Conclusion: RFA ablation of intrabiliary extension of adenoma of the papilla of Vater after papillectomy appears feasible and effective. According to our small experience, RFA should be performed with a pancreatic stent in place to reduce the risk of pancreatitis. Further data and extended follow-up are needed.
Disclosure: Nothing to disclose

Abstract No: P1452
Table 1: Characteristics of the 7 lesions treated by Radiofrequency ablation (RFA) after endoscopic snare papillectomy

Patient	Adenoma size (mm)	Adenoma pathology	Duct involved	Intraductal extension (mm)	Intraductal pathology	RFA sessions n	Concomitant therapies	Biliary stents n	Follow-up (months)
1	22	AdenoK	CBD	5	Adenok	1	–	2	25
2	20	LGD	CBD	10	LGD	3	APC	2	22
3	40	LGD	CBD	5	LGD	1	–	2	21
4	15	HGD	CBD	5	HGD	2	APC	2	9
5	25	HGD	CBD	10	HGD	2	–	2	–
6	15	HGD	CBD	5	LGD	1	APC	3	1
7	25	HGD	CBD	3	LGD	1	APC	3	–

P1453 ASSOCIATION BETWEEN PREDICTIVE FACTORS AND RADIATION EXPOSURE DURING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Introduction: The objectives of this study were to analyze the dose of radiation to which the physician is exposed during endoscopic retrograde cholangiopancreatography (ERCP) and to identify predictive factors of radiation exposure during the procedure. Further, we evaluated the characteristics of patients and procedural factors associated with prolonged fluoroscopy time.

Aims and Methods: A cross-sectional retrospective analysis of 780 ERCPs performed at tertiary academic hospital over 48-month period was conducted. The primary outcome of interest was the radiation exposure during ERCP as determined by fluoroscopy time and additionally to determine the association between variables and radiation exposure. And we correlated them with age, sex, body mass index (BMI), diagnosis, duration of procedure, procedure name, and procedure complexity.

Results: As a result of analysis of the 780 ERCPs performed for 2 years, the mean fluoroscopy time was 5.07 minutes (95% confidence interval (CI), 4.87–5.26). The mean radiation durations were as follows: cholelithiasis was 5.76 minutes (95% CI, 4.75–6.80); malignant biliary obstruction was 6.13minutes (95% CI, 5.91–6.35); pancreatic disease was 5.28 minutes (95% CI, 4.45–6.28); benign biliary stricture was 5.32 minutes (95% CI, 5.02–5.94). There was no significant difference between the two expert endoscopists in present study. Multivariate analysis revealed that prolonged duration of fluoroscopy was related to specific factors of patient including higher BMI (BMI > 27.5 kg/m2) (+ 4.1 minutes; 95% CI, 2.56–5.63), mechanical lithotripsy (+ 4.85 minutes; 95% CI, 0.45–9.25), needle knife (+ 4.5 minutes; 95% CI, 2.15–6.86), and malignant biliary obstruction (+ 2.34 minutes; 95% CI, 0.15–4.53).

Conclusion: ERCPs are associated with significantly higher radiation exposure of patients on the specific procedure. The endoscopists should be aware of the determinantal factors including patients who were obese, mechanical lithotripsy, malignant biliary obstruction and the use of a needle-knife, affected the fluoroscopy time during ERCP.

Disclosure: Nothing to disclose

P1454 ENDOSCOPIC RESECTION MAY BE CURATIVE FOR AMPULLARY CANCER? RESULTS OF A EUROPEAN MONOCENTRIC RETROSPECTIVE STUDY

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Introduction: The treatment of ampullary carcinomas is based on duodenopancreatectomy (DP). However, in the absence of poor prognostic factors (submucosal invasion, lymphovascular embols (LV), budding, poorly differentiated tumors), the risk of lymph node metastasis is low, justifying endoscopic local resection. However, data on the performance of endoscopic ampullectomy in the treatment of ampullary cancer remain limited. Aim of this monocentric retrospective study was to evaluate the rate of curative endoscopic resection of ampullary carcinoma.

Aims and Methods: We included all consecutive patients presenting with ampullary carcinoma treated by endoscopic resection (ER) between January 2006 and September2017 in our department. Data were retrospectively extracted from electronic medical database. Endosonography was performed before resection to exclude T2 or N+ lesions. Endoscopic ampullectomy (EA) was performed following the previously published technique. Prevention of acute pancreatitis (AP) was achieved by the placement of a 5 Fr pancreatic stent, and for 8 years in combinaison with rectal indomethacin. Tumoral invasion was staged using the Japanese classification: Du0 was defined as invasion limited to the duodenal mucosa or sphincter of Oddi, Du1 to the submucosa, Du2 to the duodenal muscularis propria. Complementary surgery was proposed in case of submucosal invasion, low differentiation, R1 resection or LV. In another situation, clinical and endoscopic follow-up was recommended.

Results: During the study period, 153 EA were performed including 29 carcinomas (7 neuroendocrine tumors, 22 adenocarcinomas). Twenty-two patients (16 males) were treated endoscopically for 22 ampullary adenocarcinomas. Mean diameter was 20 mm (7–30mm). All lesions, except one related to familial adenomatous polyposis, were sporadics. Monobloc resection was achieved in 77%. A prophylactic pancreatic stent was inserted in 72% (divisum pancreas = 2, insertion failure = 4) . Morbidity was 18% (delayed bleeding = 3, severe AP = 1). No procedure-related death was observed.
Histopathological examination showed well or moderately differentiated carcinoma in respectively 45% and 13%. LV and budding were observerd respectively in 9% (n = 2) and 4.5% (n = 1). Pathological subtype was classified into intestinal and biliopancreatic subtypes respectively in 13 (59%) and 5 (23%), 4 (18%) cases being unclassifiable. Microscopic deep margins were positive in 50%. Carcinomas was staged Du0, Du1 and Du2 respectivement in 20 (91%), 1 (4.5%) and 1 (4.5%). Eleven patients with R0 resection of Du0 cancers without lymphovascular invasion were followed-up a mean of 24 months, with only 1 local recurrence. This relapse in low grade dysplasia was successfully treated by intraductal biliary radiofrequency. Eleven resections had positive deep margins (Du0 = 9, Du1 = 1, Du2 = 1. Among these 11 patients, 3 patients had PD (pT0N0 = 1, pT1N0 = 1, pT0N1 = 1) and 8 patients were followed-up. Of these patients, 5 had local recurrence which were treated by surgery (n = 1), chemoradiotherapy (n = 1), radiofrequency (n = 1) or best supportive care (n = 2). Local recurrence rate after endoscopic resection of Du0 adenocarcinoma with negative deep margins (R0) was 9% (n = 1). Endoscopic approach provides curative treatment for adenocarcinoma in 64% in intent to treat but in 100% for R0 Du0 carcinoma.

Conclusion: EA is a validated treatment for cancers that do not invade beyond the oddi sphincter. This technique makes it possible to avoid surgery in almost 60% of cases. A positive deep margin is associated with a higher risk of local recurrence, justifying surgery.

Disclosure: Nothing to disclose

P1455 ENDOSCOPIC SNARE PAPILLECTOMY: LONG TERM RESULTS IN 173 CONSECUTIVE PATIENTS

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Introduction: Ampullary adenomas represents 5% of the neoplasia of the gastrointestinal tract. The premalignant nature of ampullary adenoma justify their radical excision.
Aim of this study is to evaluate the results and the long-term follow-up of endoscopic snare papillectomy (ESP) of ampullary tumor.

Aims and Methods: Consecutive patients undergoing ESP between October 1999 and February 2018 were identified from an electronic database.
The following data were recorded: size of the ampullary lesion, pre- and post-endoscopic resection histology, complications, local recurrence rate and survival. Endoscopic follow-up was scheduled after 1, 3, 6 and 12 months for the first year, and then yearly for the following 5 years.

Results: ESP was performed in 173 consecutive patients (89 M, mean age 60.5). En bloc resection was possible in 88% of patients. 28 patients (16.2%) had familiar adenomatous polyposis (FAP).
Biliary sphincterotomy with or without insertion of a plastic stent was performed after papillectomy in 77 patient (44.5%); a pancreatic stent or a naso-pancreatic drain, with or without pancreatic sphincterotomy was inserted in 95 (54.9%) patients, 14 had a pancreas divisum and in 8 cases pancreatic stent placement failed.
The following adverse events were recorded:
- delayed bleeding (n = 16, 9.2%) treated endoscopically except 2 cases that required angiography;

- retroperitoneal perforations (n = 5, 2.9%), successfully treated by percutaneous (n = 3) or surgical (n = 2) drainage;
- pancreatitis (n = 4, 2.3%, 3 without pancreatic stent).
There was 1 case (0.6%) of mortality due to pancreatitis.
Follow-up (mean 51.9 months, range 1 -108) was available in 146/173 patients (84.4%). Results are summarized in **table 1**.
Residual and recurrent adenomas were diagnosed in 30 (17.3%) and 29 (16.8%) cases, respectively but were successfully retreated endoscopically in all the cases except 5 patients who underwent surgery (duodenopancreatectomy) due to failed resection.
Conclusion: The present series reports the results of ESP after more than 4-year median follow-up.
ESP is effective with favorable long-term outcomes; multidisciplinary is team needed to manage complications. The high incidence of residual/recurrent adenoma is balanced by the successful endoscopic re-treatment in 91.5%. Compliance to the follow-up is important for the early detection and re-treatment of recurrences; a recall system is therefore mandatory.

	n (%)
Alive, performed endoscopic follow-up	119 (81.5)
Alive after duodenopancreatectomy	13 (8.9)
Death for unrelated reasons	14 (9.6)
Post-ESP histology in 119 pts	**Recurrence (n = 29) %**
Adenoma /Tis	23/99 (23)
Adenocarcinoma	5/13 (38)
Neuroendocrine tumor	1/7 (14)

[Table 1. Follow-up results in 146/173 (84.4%) after endoscopic snare papillectomy (ESP).]
Disclosure: Nothing to disclose

P1456 ENDOSCOPIC OR COMBINED ENDOSCOPIC/ PERCUTANEOUS MANAGEMENT IN COMPLEX BILE DUCT INJURIES

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Introduction: Bile duct injuries (BDI) occur most often after biliary tract surgery, with laparoscopic cholecystectomy representing the leading cause. Reconstructive biliary surgery is considered standard treatment for the most severe form of biliary injuries, also known as complex BDI. Recent studies have suggested a role for an endoscopic or combined endoscopic/percutaneous approach in selected patients.
Aims and Methods: We report our experience with a variety of endoscopic or combined endoscopic/percutaneous techniques to re-establish biliary drainage in patients with complex BDI and biliary exclusion.
Results: We identified 15 symptomatic patients with complex BDI and biliary exclusion who were treated by various endoscopic or combined endoscopic/percutaneous methods to recreate a communication with the excluded bile ducts. In 6 patients, BDI occurred after cholecystectomy. In 5 patients, biliary reconstruction was performed using a TIPSS-200 set, initially developed for insertion of transjugular intrahepatic portosystemic shunts (TIPSS) Successful drainage of the excluded biliary ducts with resolution of symptoms was possible in 14 patients, either through recreation of bilio-biliary continuity (10 patients) or by creating a bilio-enteric drainage tract (3 patients) or by both techniques (1 patient). Mean duration of the biliary repermeabilisaiton procedure was 107 min (range 59–180). No immediate severe complication occurred. Complete internalization of biliary drainage was possible in 14 patients. An average of 7.4 additional ERCP procedures per patient were performed after the initial repermeabilisation procedure and an average of 7.5 biliary stents were placed per patients (range 1–19). Mean duration of follow-up was 53.5 months (range 5–195). During the follow-up period, 8 patients developed a biliary stricture at the level of the initial BDI, three patients developed episodes of cholestasis and/or cholangitis secondary to biliary stent occlusion, biliary stones or sludge, and one patient developed a recurrent biloma. These late complications were all successfully treated endoscopically. All patients are free of external drainage at follow-up. Biliary surgery was necessary in 1 of the patient. During the follow-up period, 3 patients died of causes unrelated to the repermeabilisation procedures.
Conclusion: In patients with complex BDI and biliary exclusion, various endoscopic or combined endoscopic/percutaneous procedures may be successfully performed to recreate bilio-biliary or bilio-enteric continuity. In experienced hands, these techniques seem safe and can prevent reconstructive biliary surgery in the majority of the cases
Disclosure: Nothing to disclose

P1457 NATURAL HISTORY OF BILIARY CAST SYNDROME AFTER LIVER TRANSPLANTATION: A PROSPECTIVE CHOLANGIOGRAPHIC EVOLUTION STUDY

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Introduction: Biliary cast syndrome (BCS) is a rare complication after liver transplantation (LT) defined as material molded into the bile ducts and associated with ischemic cholangitis. Knowledge on cholangiographic features and endoscopic management of BCS is scarce. We sought to review the radiologic and cholangiographic features of BCS.
Aims and Methods: Records of the prospectively collected database of patients having been treated by liver transplantation in Erasme hospital from 12/2004 to 12/2014 were analyzed to identify patients having biliary complications (BC). After the exclusion of those having altered anatomy or no stricture, their cholangiograms and magnetic resonance cholangiography (MRCP) were systematically reviewed identifying patients with BCS. It was defined as intrabiliary material associated to filling defect during cholangiography in the supra-anastomotic portion of the biliary tree with features of biliary injury. Three types of BC were identified: BCS, anastomotic (AS) and non-anastomotic strictures (NAS). Clinical, endoscopic and radiological data of those patients were reviewed.
Results: BC were present in 86 (27%) of the 313 patients (70% male; mean age, 61 ± 7 years). Forteen cases (4.6%) identified to have a BCS were treated by ERCP. There was no statistical difference in patient demographics, delay between LT and BC in the three groups.
Pre-therapeutic MRCP was available in 12/14 cases with none having been described as BCS. The revision of these MRCP disclosed the following features: T1 hypersignal material filling the duct was present in 11, a "duct-in-a-duct" picture in 8 and an aneurysm-like saccular dilation of the bile duct in 3 of the 12 cases, respectively. On initial ERCP, 8 of the 14 patients had no stricture. A saccular aneurysmal or moderate biliary dilatation containing cast was present in 6 and 5 patients respectively.
It was possible to obtain a complete cast extraction by ERCP in 12 of the 14 cases in a median of 2 (1–7) ERCP sessions in a median period of 3 (1–22) months. Only one of the 12 patients with cast completely extracted presented with cast recurrence in the follow-up (8%). Eleven of the 13 patients (85%) for who ERCP follow-up was available presented an evolution with secondary biliary strictures treated with multiple plastic stents. Stricture calibration was obtained in 10 of them (90%) after a median of 5 (4–9) ERCP sessions on a median of 12 (5–19) months treatment period.
In 4 of the 10 patients, we observed stricture recurrence at 14 (1–84) months of stent retrieval. New stenting sessions for stricture recurrence calibration were performed by a median of 6 (4–10) ERCP in 22 (12–42) months for those patients with 3 of them (75%) obtaining stricture calibration and one partial hilar calibration and left excluded bile ducts without clinical counterpart.
At the end of a median follow-up of 58 months, we observed a lower overall survival (42.9% (BCS) Vs 83.3%(AS) Vs 68.8% (NAS), p value of log rank test = 0.035) and a lower re-transplant-free survival (42.9%(BCS) vs 80.6% (AS) vs 56.3%(NAS), p value of log rank test = 0.025) for patients with BCS compared to those without.
Conclusion: Biliary cast syndrome is a rare complication of liver transplantation and is associated to specific radiological features. Complete cast extraction is possible by ERCP. The prognosis of those patients is poorer compared to the overall patients presenting biliary complications after LT.
Disclosure: Nothing to disclose

P1458 HOLMIUM LASER LITHOTRIPSY TO TREAT DIFFICULT BILIARY AND PANCREATIC STONES USING PERORAL SINGLE OPERATOR CHOLANGIOPANCREATOSCOPY

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Introduction: In tertiary centres 5–10% of bile duct stones are difficult to clear with conventional ERCP techniques. Similarly, most pancreatic stones cannot be removed.
Recently it has been possible to treat complex calculi under direct vision with peroral single operator cholangiopancreatoscopy (POC) using Holmium (Ho) laser lithotripsy.

Aims and Methods: Prospective observational study of data collected between July 2015 and November 2017 from a single endoscopist's experience. In patients with difficult stones, POC was performed using Spyglass DS ® (Boston Scientific) in all procedures.
Stone lithotripsy was performed with a VersaPulse Powersuite Holmium laser (Lumenis) and a ScopeSafe 200-µm fibre (Optical Integrity). Patients underwent standard ERCP and cholangiopancreatoscopy. Once the stone was visually confirmed, the laser fibre was placed onto the stone and short bursts of energy were applied to achieve fragmentation. Stone fragments were then removed with ERCP-directed balloon or basket. If required, treatments were repeated to achieve complete ductal clearance.
Results: 26 patients underwent POC – guided laser lithotripsy.
25 patients underwent technically successful procedures, with one unsuccessful attempt. This was for pancreatic stone lithotripsy with inability to access the stone due to pancreas divisum. The patient underwent subsequent pancreaticojejunostomy.
Patients had required a mean 1.6 (range 1–4) earlier attempts to remove stones at ERCP including preceding endoscopic sphincterotomy +/− sphincteroplasty. Five patients required multiple lithotripsy sessions to remove the stones, otherwise a mean of 1.3 sessions was required for ductal clearance. 17 patients had multiple stones at time of procedure (15 biliary and 1 pancreatic). Median number of stones per patient was 3 (range 1 -7). The mean largest biliary stone was 13mm (range 3–30mm) and pancreatic stone 9mm (range 8–10mm). Mean procedural time was 48 minutes for bile duct stones and 29 minutes for pancreatic stone cases.
Laser power settings were higher for pancreatic stones (pancreatic 8–30 and biliary 8–10 W). Complications were mild, aspiration pneumonia (2) and pancreatitis (1) from 21 procedures. There were no ductal injuries.
Stones were cleared in all patients undergoing lithotripsy.
Conclusion: Cholangiopancreatoscopy-guided Holmium laser lithotripsy appears to be safe and very effective at treating difficult biliary and pancreatic stone disease, with pancreatic stone disease being more challenging to manage. Further studies are required.
Disclosure: Nothing to disclose

P1459 BIOPSIES IN COMBINATION WITH BRUSH CYTOLOGY CAN IMPROVE THE CHARACTERIZATION OF MALIGNANT BILIARY STRICTURES DURING ERCP

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Introduction: Brush cytology is systematically performed during endoscopic retrograde cholangiopancreatography (ERCP) to characterize biliary stenosis. However, it has a low sensitivity in detection of malignant strictures.
Aims and Methods: The aim of this retrospective study was to verify if biopsies improve the characterization of malignant biliary strictures.
We reviewed 186 patients with biliary strictures who underwent endoscopic brush cytology with or without biopsies, between January 2010 and December 2017. Brush cytology was performed at the site of biliary stricture at least ten times and at least two fragments were obtained for histopathological diagnosis. Final diagnosis was based on cytology/biopsy, percutaneous biopsy, surgery, or clinical follow-up.
Results: The mean age was 69.6 ± 14.2 years and 111 (59.7%) of patients were males. Single stricture of the main bile duct was documented in 96.8% (n = 180). The majority of stenosis was located in the proximal and distal thirds of the biliary duct (51.1% e 27.4%, respectively). Malignant strictures were identified in 76.9% of patients with pancreatic cancer (n = 66) and cholangiocarcinoma (n = 61) being the most frequent aetiology. Biopsies were performed in 97 (52.2%) patients.
For detection of malignancy, brush cytology alone had a sensitivity of 34.27% (95% IC: 26.54–42.66), a specificity of 97.67% (95% IC: 87.71–99.94) and an accuracy of 48.92%. For pancreatic cancer specifically, brush cytology presented a sensitivity of 34.85% (95% IC: 23.53–47.58) and specificity of 100%, and for cholangiocarcinoma a sensitivity of 36.07% (95% IC: 24.16–49.37%) and specificity of 100%. Biopsy alone had a sensitivity of 30.43% (95% IC: 19.92–42.69), specificity of 96.43% (95% IC: 81.65–99.91) and accuracy of 49.48%. A combination of brush cytology and biopsies yielded a slight increase in sensitivity to 38.46% (95% IC: 30.45–46.96). ERCP was repeated in 72 (38.7%) patients and cytology repeated in 22 (27.3%), 6 of which detected malignant stricture that was not previously identified.
Conclusion: Combination of brush cytology and biopsies during ERCP can increase detection of malignant biliary strictures when compared to cytology alone. Cholangioscopy-guided biopsies may improve the characterization of these malignant strictures.
Disclosure: Nothing to disclose

P1460 ENDOSCOPIC MANAGEMENT OF BILE DUCT STONES IN PATIENTS WITH SURGICALLY ALTERED ANATOMY; EVALUATION OF NEWLY DEVELOPED SHORT TYPE DOUBLE BALLOON ENDOSCOPE

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Introduction: Introduction: Endoscopic retrograde cholangiography (ERC) is an endoscopic procedure that is applied worldwide for the examination and treatment of biliary stones. However, the success rates for the use of conventional endoscopic devices for the treatment of biliary stones had been unsatisfactory in patients with surgically altered gastrointestinal (GI) anatomy. Recently many papers proved that the development of the balloon-assisted endoscope (BAE) radically made endoscopic approaches feasible, however, those studies objected varieties in sizes of total number of object patients and the success rate was overall wide ranging.
Aims and Methods: The aim of this study was to evaluate a large case series of ERCP using short type DBE for common bile duct stones in postoperative patients.
From February 2006 to October 2017, ERC using short-type DBE (DB-ERC) was performed in 210 postoperative patients (325 procedures). We retrospectively studied the success rate of reaching the blind end, the mean time to reach the blind end, the success rate of complete ERC related interventions, the mean procedure time, and adverse events.
Results: The success rate of reaching the blind end was 98.5% (320/325). By type of reconstruction methods, the success rate of reaching the blind end was 98.1% (202/206) in Roux-en-Y(R-Y) reconstruction, 99.1% (106/107) in B-II gastrectomy, 100%(106/107) in jejunal interposition. The mean time to reach the blind end was 16.5 minutes. By type of reconstruction methods, the mean time to reach the blind end was 19.5 minutes in Roux-en-Y(R-Y) reconstruction, 11.4 minutes in B-II gastrectomy, 10.5 minutes in jejunal interposition. The success rate of complete ERC related interventions were 97.5% (312/320). By type of reconstruction methods, the success rate of complete ERC-related interventions was 98.5% (199/202) in Roux-en-Y(R-Y) reconstruction, 96.2% (102/106) in B-II gastrectomy, 91.7%(11/12) in jejunal interposition. The mean procedure time was 76.9 minutes. By type of reconstruction methods, the mean procedure time was 86.0 minutes in Roux-en-Y(R-Y) reconstruction, 61.6 minutes in B-II gastrectomy, 55.1 minutes in jejunal interposition. The occurrence of adverse events was 9.2% (30/325). By type of reconstruction methods, the occurrence of adverse events was 8.7% (18/206) in Roux-en-Y(R-Y) reconstruction, 10.3% (11/107) in B-II gastrectomy, 8.3%(1/12) in jejunal interposition.
Conclusion: Conclusions: ERC using a short-type DBE for biliary stones is highly effective and safe in patients with altered gastrointestinal anatomy. DB-ERC is a promising therapeutic modality in such patients and should be selected as the first-line policy.
Disclosure: Nothing to disclose

P1461 ENDOSCOPIC MANAGEMENT OF POST LIVER TRANSPLANT BILIARY ANASTOMOTIC STRICTURES: A RETROSPECTIVE ANALYSIS

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Introduction: Biliary anastomotic strictures (AS) occur in 5–15% of liver transplant (LT) recipients and cause graft dysfunction and morbidity. The main alternative to surgical reconstruction is stenting at endoscopic retrograde cholangiopancreatography (ERCP), using plastic polyethylene or fully-covered self-expanding metal stents (fcSEMS). We retrospectively reviewed outcomes after ERCP for biliary AS, aiming to assess rates of success and complications.
Aims and Methods: We retrospectively reviewed outcomes after ERCP for biliary AS, aiming to assess rates of success and complications.
Records for all patients undergoing ERCP post LT between 2013–16 were reviewed. AS were classified as early or late (<3 or ≥3mths post LT) and cases of diffuse cholangiopathy excluded. Data collected included graft characteristics, timing/nature of ERCPs and complications. Stricture resolution was determined from graft function, imaging and ERCP findings.
Results: In total 252 ERCPs were performed (median 4/patient, range 2–10) in 62 patients, 72.6% male, age at LT 54yrs (range 20–71). 48 grafts (77.4%) were donations after brain death, 13 (21.0%) after cardiac death and 1 live donor. At first endoscopy 53 (85.4%) had a native papilla. Median time from LT was 28days (4–75) in early AS (n = 29, 46.7%, 9 presenting with bile leak) vs 11.5mths (3.4–251) in late AS (n = 33, 53.2%). Biliary stents were placed in 172 ERCPs (63.4% plastic vs 36.6% fcSEMS) and AS dilated in 68 (27.0%; 60 in conjunction with stenting).
Stricture resolution was achieved endoscopically in 47/55 patients with complete outcome data (85.5%). Plastic stents were placed at index ERCP in 23/26 of early AS, in whom sequential plastic 'upstenting' was ultimately successful in 9

(39.1%) and 12 (52.2%) proceeded to fcSEMS (stricture remodelled in all). Of late AS, 9/29 were managed with fcSEMS (88.8% successfully), 8 plastic 'upstenting' (75% success), 8 fcSEMS after initial plastic stent (all successful) and 2 resolved with dilatation only.
The overall rate of post-ERCP pancreatitis (PEP) was 7.1% (none severe by Cotton criteria) and was higher after fcSEMS (15.9%) than plastic stenting (5.5%, $P = 0.024$), despite similar use of NSAID prophylaxis. Compared with plastic stents, fcSEMS were more likely to migrate (36.5% vs 12.8%, $P < 0.001$) and embed (6.3% vs 0%, $P = 0.008$) but stent occlusion was numerically lower (0% vs 4.6%, $P = 0.084$). Of 8 endoscopic failures (14.5%), 3 (5.5%) required percutaneous stenting and 2 (3.6%) biliary reconstruction, one after duodenal perforation by a migrated plastic stent.
Conclusion: Endoscopic management is effective in treating 85% of biliary AS. fcSEMS appear superior to sequential plastic 'upstenting' but are associated with higher rates of PEP and migration.
Disclosure: Nothing to disclose

P1462 BASKET VERSUS BALLOON EXTRACTION FOR CHOLEDOCHOLITHIASIS: A SINGLE-CENTER PROSPECTIVE RANDOMIZED STUDY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) has become an integral part in the therapeutic armamentarium when dealing in patients with choledocholithiasis. However, when choosing the proper extraction device, data are inconsistent, with selection being, often, a matter of the endoscopists' preference.
Aims and Methods: We conducted a single-center prospective randomized controlled study to access success rates for basket versus balloon catheters for small stones for the first time in Europe.
In our non-inferiority study, 180 patients with bile duct stones were randomized in a basket and a balloon catheter group. Inclusion criteria were fluoroscopically bile duct stones ≤10mm in diameter and a common bile duct (CBD) diameter ≤15mm. The primary endpoint was the rate of complete bile duct clearance for each extraction method used. Secondary endpoints included time completed and the amount of radiation dose recorded in each ERCP session, as well as any reported adverse events.
Results: Balloon was non-inferior to basket stone extraction (OR 3.35, 95% CI 1.12–10.05, $p = 0.031$). Complete clearance was achieved in 69 out of 82 patients (84.1%) in the basket catheter group versus complete clearance in 79 out of 84 patients (94%) in the balloon catheter group ($p = 0.047$); this seems to hold especially true for patients with few stones and of small size (≤2 stones, $p = 0.043$ and stone diameter ≤5mm, $p = 0.032$). Complete stone clearance in the basket group patients took longer than complete stone clearance in the balloon group (4.52 and 4.06 min, respectively, $p = 0.015$). Higher median radiation doses for stone clearance were recorded in the basket versus the balloon catheter group (1534.43 Gy versus 1245.45 Gy, $p < 0.015$).
Conclusion: In conclusion, our study showed that balloon was non-inferior to basket stone extraction. More prospective future studies with proper methodology will enhance our knowledge and provide us with more robust data regarding complete stone clearance and catheter type.
Disclosure: Nothing to disclose

P1463 INCIDENCE AND RISK FACTORS OF POST-ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY PANCREATITIS (PEP) ACCORDING TO THE TYPE OF PROPHYLAXIS USED OVER TIME

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Introduction: The use of rectal NSAIDs, the intravenous administration of Lactated Ringer (LR) and pancreatic duct stenting are recommended measures that demonstrated a positive impact in preventing PEP.
Aims and Methods: Our objective was to evaluate if the association of LR with NSAIDs in average-risk or high-risk patients undergoing ERCP is effective in reducing PEP when compared to the usually recommended use of NSAIDs in high-risk patients.
We conducted a retrospective, observational and cross-sectional study. Patients undergoing ERCP for biliary diseases between January 2013 to December 2017 were included. Patients diagnosed with any pancreatic disease (pancreatic cancer, chronic pancreatitis, previous acute pancreatitis) and post-surgical altered biliopancreatic anatomy were excluded. Patients were divided in three cohorts depending on the type of PEP prophylaxis used in different periods of time. Group I: rectal diclofenac 100mg in high-risk patients of PEP; group II: rectal diclofenac + LR 500 mL in high-risk patients of PEP; group III: rectal diclofenac + LR 500 mL in every patient undergoing ERCP. All patients were monitored for pain and serum pancreatic enzymes over 24h after ERCP. The incidence of PEP was analysed by ANOVA and risk factors by binomial logistic regression.
Results: A total of 613 patients were included, mean age 77 yrs, 329 females; 251 in group I, 152 in group II and 210 in group III. The global incidence of PEP was 2.6% (2.4% in group I, 2.0% in group II and 3.3% in group III; $p = 0.70$). Factors associated with a higher risk of PEP were bile duct stenting (OR 8.2, CI 95% 1.46–46.14) and incomplete biliary drainage (OR 6.4, CI 95% 1.24–33.18) in group I, the presence of cholagiocarcinoma (OR 17.87, CI 95% 1.53–208.93) and smoking (OR 12.19, CI 95% 1.06–140.28) in group II. There was no evidence of associated risk factor in group III.
Conclusion: The combination or LR with rectal NSAIDs in high-risk and average-risk patients is not associated with a lower incidence of PEP when compared to the administration of rectal NSAIDs alone in high-risk patients. While attempting to further prevent PEP in patients receiving rectal NSAIDs, some new risk factors that should be taken into consideration have been identified.
Disclosure: Nothing to disclose

P1464 SAFETY AND EFFICACY OF EUS-GUIDED GALLBLADDER DRAINAGE (EUS-GBD) COMBINED WITH ERCP IN THE SAME SESSION

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Introduction: ERCP is increasingly being combined in a single-session with other endoscopic procedures such as EUS (staging, screening for CBD stones, rendezvous for failed cannulation) duodenal stenting or cholangioscopy. EUS-guided gallbladder drainage (EUS-GBD) is an emerging option for acute cholecystitis in non-surgical candidates. Patients with acute cholecystitis often need CBD stone removal. Combination of ERCP for CBD stones and EUS-GBD might be appealing in some patient subsets, but there is virtually no objective evidence to support this combined approach to gallstone disease.
Aims and Methods: To assess the safety and efficacy of EUS-GBD combined with ERCP in the same session.
Single-center retrospective cohort study comparing outcomes of EUS-GBD alone to those of ERCP combined with EUS-GBD in the same session between June 2011 and May 2017. Lumen-apposing metal stent (LAMS, Axios®) were used in both groups. Exclusion criteria: ERCP or EUS-GBD used for salvage of one another (ie, transcystic GB drainage after failed EUS-GBD or EUS-GBD for failed biliary drainage at ERCP), EUS-guided biliary drainage (EUSBD) in the same session, and ERCP within 5 days (before/after) EUS-GBD. Epidemiologic, procedural, and clinical outcome data were analyzed with Wilcoxon, Chi-square and Fisher tests where appropriate. Primary endpoints were rates of technical success, clinical success and adverse events.
Results: Sixty four consecutive patients underwent EUS-GBD between June 2011 and May 2017. 19 Patients were excluded: in 11 the indication for either ERCP or EUS-GBD was salvage of a failed tandem procedure, 5 had EUS-guided biliary drainage in the same session and a further 3 had another ERCP within 5 days of the index procedure. Forty-five patients met inclusion/exclusion criteria: 24 EUS-GBD and 21 EUS-GBD combined with ERCP. Baseline characteristics were comparable in both groups. There were no significant differences in technical (100% vs 91.7%) and clinical success rates (90.5% vs 91.7%) of EUS-GBD in the combined versus the single procedure groups. The rate of adverse events (23.8% vs 20.9%) and the rate of technical issues (14.3% vs 37.5%; $p = 0.10$) during LAMS deployment were also comparable. Results are detailed in Table 1. Technical success of ERCP was 100% and 81% of patients required sphincterotomy and stone extraction.
Conclusion: While ERCP combined with EUS-GBD maintains similar rates of technical and clinical success to EUS-GBD alone, a combined procedure does not appear to increase adverse events. Despite the limitations of our study, these findings are encouraging and warrant further evaluation before this therapeutic approach can be generalized.

	EUS-GBD+ERCP (n = 21)	EUS-GBD (n = 24)	p
Median Age (IQR)	85.3 (78–89)	83.9 (78.6–89.9)	0.70
Male, n (%)	10 (47.6%)	13 (54.2%)	0.66
Baseline disease -Benign, n (%) -Malignant, n (%)	18 (85.7%) 3 (14.3%)	20 (83.3%) 4 (16.7%)	1
Indication – Cholecystitis, n (%) -Choledocolithiasis, n (%) -Biliary decompression, n (%)	19 (90.5%) 1 (4.8%) 1 (4.8%)	24 (100%)	0.21
Technical issues during LAMS deployment, n (%)	3 (14.3%)	9 (37.5%)	0.10
Adverse events, n (%)	5 (23.8%)	5 (20.9%)	1
Clinical success, n (%)	19 (90.5%)	22 (91.7%)	1
Technical success, n (%)	21 (100%)	22 (91.7%)	0.49

[Table 1.]

Disclosure: This abstract has been presented in ESGE days 2018 and has been accepted for DDW 2018.

P1465 EUS ANATOMY OF THE PANCREATOBILIARY SYSTEM IN A SWINE MODEL: THE WISE EXPERIENCE

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Introduction: The swine model has been described as a realistic tool for EUS training [i]. Papers extensively describing EUS swine anatomy are lacking in the current literature, though.
Aims and Methods: The aim of the article is to describe both linear and radial EUS pancreatobiliary swine anatomy.
We report the animal lab experience of the WEO (World Endoscopy Organization) International School of EUS (WISE) group at ASAN Medical Center in Seoul. 2 adult mini pigs were scoped under general anesthesia, endotracheal intubation and mechanical ventilation. Both radial and linear array echoendoscopes were used for delineation of pancreatobiliary anatomy and videos were recorded.
Results: It was possible to image aorta, crus of the diaphragm, celiac trunk, superior mesenteric artery, pancreas, common bile duct, gallbladder, portal vein, kidneys, spleen and hepatic hilum. Images obtained were comparable to human EUS findings, even if with some remarkable differences.
Conclusion: Swine model confirmed to be a highly realistic teaching model for EUS. To the best of our knowledge swine EUS anatomy has not been reported to date. We believe that this image-provided description of swine pancreatobiliary anatomy can be a useful tool for EUS training in the setting of in-vivo hands-on sessions.
Disclosure: Nothing to disclose

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P1466 PREDICTIVE FACTORS FOR THE ASSESSMENT OF THE KI-67 INDEX IN PANCREATIC NEUROENDOCRINE TUMORS DIAGNOSED BY ENDOSCOPIC ULTRASONOGRAPHY

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Introduction: Endoscopic ultrasonography (EUS)-guided puncture is the standard of care for tissue sampling of pancreatic masses. For pancreatic neuroendocrine tumors (P-NET), obtaining material that allows a complete anatomopathological examination with Ki-67 index quantification is essential for its adequate characterization. However, the factors that enable it are unclear, namely the advantage of fine needle aspiration (FNA) versus fine needle biopsy (FNB).
Aims and Methods: The aim of this study is to evaluate in patients with P-NET diagnosed by EUS the factors that potentially influence the ability to obtain adequate samples allowing complete anatomopathological examination with assessment of the Ki-67 index.
Retrospective study of all patients with P-NET with histological diagnosis by EUS at our institution between January 2013 and December 2017. The size of the lesion, location of the lesion, tissue acquisition technique (FNA vs FNB) and needle gauge were analysed.
Results: Twenty-one procedures were performed in 20 patients: 11 women (55.0%) and 9 men (45.0%) with a median age of 54 years (range 27–82 years). The median lesion size was 25mm (range 8–70 mm). In 61.9% (n = 13) of the procedures an adequate sample allowing a complete anatomopathological examination (with Ki-67 index quantification) was obtained. The Ki67 index assessment rate according to the analysed variables was: 72.7% in lesions $<$20mmm (8/11) vs 50.0% in lesions $\geq$20mm (5/10), p = 0.290; 64.3% in body/tail lesions (9/14) vs 57.1% in head/uncinate lesions (4/7), p = 0.751; 53.8% of the cases with FNA (7/13) vs 75.0% with FNB (6/8), p = 0.339; 70.0% with 22G needle (7/10) vs 54.5% with 25G needle (6/11), p = 0.469. There were no complications associated with the procedure.
Conclusion: Characteristics of the lesion and puncture technique did not significantly influence the ability to obtain material for complete anatomopathological examinations in P-TNE. However, the size of the sample does not allow a definitive conclusion. The authors recommend that this study be replicated in a larger sample of patients, possibly in a multicenter study.
Disclosure: Nothing to disclose

P1468 DIAGNOSIS AND OUTCOME OF MEDIASTINAL FOREGUT DUPLICATION CYSTS: THE ROLE OF EUS

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Introduction: Mediastinal foregut duplication cysts (FDC) are rare dysembriogenic lesions originating from the ventral portion of the endodermal primitive foregut. The diagnosis, follow-up and outcome of these lesions have been reported in only few case series and small retrospective studies.[1,2]
Aims and Methods: Aim of this study was to assess the role of endoscopic ultrasound (EUS) in the diagnosis and follow-up of FDC.
Forty-five patients who had been referred for EUS for mediastinal lesions suspected of being FDC between 01.01.2009 and 01.02.2017 were identified by using the ICD-10 code Q39.8 from the patient registry of EUS of Helsinki University Hospital. All patients' baseline characteristics (gender, age, symptoms and signs), gastroscopy, computer-tomography (CT) findings (density, localisation), EUS findings (echogenicity, localisation, final diagnosis), surgical intervention, histologic findings and complications were reviewed. Data are presented as number with percentage when categorical and as median and range when continuous.
Results: All the patients (n = 45, 17 males, median age 55 years; range: 27–79) underwent EUS for a suspected FDC after endoscopy and/or chest-CT. In 31 patients (69%) the lesion was an occasional finding. Gastroscopy was performed in 22/45 (49%) showing a submucosal lesion in 19/22 (86%). Chest-CT was performed in 36/45 (80%) and the final diagnosis was consistent with a fluid lesion in 15/36 (42%) and with a solid lesion in the remaining 19 patients; normal finding was found in 2 patients. In CT images, lesions were localized outside the oesophageal wall in 22/36 (61%) of the patients and inside in the remaining 12. After EUS, the final diagnosis was consistent with a FDC in 44/45 (98%) and normal in 1. Biopsy was not routinely performed because of the risk of infection. Thirty-four lesions (77%) were localised inside the oesophageal wall and 10 outside. Lesions were anechoic in 23 cases (52%) and hypoechoic with inner hyperechoic material in 21. Nineteen out of 45 patients (42%) underwent surgical enucleation. Finally, FDC was confirmed in 12/19 (63%) and normal finding in 1/19 (5%). Leiomyoma was diagnosed in 3 cases (in EUS 2 findings were hypoechoic and localized in the third layer and one anechoic and localized in the fourth layer), enlarged lymph node with sarcoidosis in 1 (in EUS finding was anechoic and localized in the fourth layer), mesenchymal benign tumour in 2 (in EUS one finding was hypoechoic and localized outside of the oesophagus and one was anechoic and localized in the third layer). Nine out of 45 patients (20%) underwent follow-up (median 3.4 years; 5 months–6.7 years) with EUS, being the number of controls 4 in one, 3 in one and 2 in seven. The lesion was stable in 7 patients, but two were operated because of the growth of the lesion: histology was consistent with FDC and with leiomyoma (in EUS finding was anechoic and localized in the fourth layer), respectively.
Conclusion: EUS plays still an important role for the diagnosis and the follow-up of FDC. However, differential diagnosis, mostly with leiomyoma might be difficult. No cases of malignancy occurred. FNA should be considered in selected cases to improve the diagnostic accuracy.
Disclosure: Nothing to disclose

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P1469 THE DIAGNOSTIC EFFICACY OF CONTRAST ENHANCED-ENDOSCOPIC ULTRASONOGRAPHY IN DIFFERENTIAL DIAGNOSIS OF GASTRIC GASTROINTESTINAL STROMAL TUMOR (GIST) AND NON-GASTROINTESTINAL STROMAL TUMOR

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Introduction: Gastrointestinal stromal tumors (GISTs) represent the largest group of subepithelial tumors (SETs) of the upper gastrointestinal tract. The differential diagnosis of GISTs is important because of malignant potential, in contrast to other SETs. Endoscopic ultrasound (EUS) and contrast-enhanced endoscopic ultrasound (CE-EUS) is frequently used to diagnose GISTs, however, the characteristic features to distinguish GISTs from other SETs are still unknown.

Aims and Methods: The aim of this study is to find specific features on CE-EUS in differential diagnosis of GIST with other SETs. We retrospectively reviewed the findings of CE-EUS of 25 hypoechoic tumors, located in gastric proper muscle layer in 25 patients from January 2014 to December 2016. The presence and degree of tumor vessel in the SET on CE-EUS was evaluated. In addition, the SETs were classified also according to enhancement pattern as hypo-enhancement, iso-enhancement, and hyper-enhancement. The results were compared to histological diagnosis, in which obtained by EUS-guided fine needle aspiration with biopsy or /and surgical resection.
Results: 17 of 25 SETs were diagnosed as GIST by histological results. 6 SETs were diagnosed as leiomyoma and 2 SETs were schwannoma. In 14 of 17 GISTs tumor vessel was observed and In 8 non-GISTs tumor vessels were not observed. On statistical analysis, the presence of tumor vessel was significantly related to GIST (Odds ratio, 4.250; 95% confidential interval, 1.8–10.0; $P < 0.001$); 1 or 2 tumor vessels (1+) in 5 cases, 2 or 3 tumor vessels (2+) in 6 cases,more than 3 tumor vessels (3+) in 3 cases and no tumor vessels in 3 cases. The sensitivity, specificity, accuracy and positive predictive value with vessel enhancement were about 100%, 66.7%, 77.4% and 84%. In 17 of GISTs hypoenhancement was observed in 5 cases, isoenhancement in 11 cases and hyperenhancement in 1 case. In 8 of non-GISTs, hypoenhancement was observed in 5 cases, isoinhancement in 2 cases, unenhancement in 1 case. The results showed that the tendency of correlation between iso-enhancement pattern and GISTs, but there was no statistical significance (OR, 7.78l; 95% CI 1.165–51.915; $P = 0.061$).
Conclusion: The findings of tumor vessel enhancement in CE-EUS is useful for differential diagnosis between GIST and non-GIST in gastric hypoechoic tumor of proper muscle layer. The echo patterns of contrast enhancement were insufficiency for differential diagnosis between GIST and non-GIST.
Disclosure: Nothing to disclose

P1470 SLOW-PULL TECNIQUE FINE-NEEDLE BIOPSY WITH 20-GAUGE NEEDLE (SPUTNIQ-20G STUDY) VERSUS STANDARD SUCTION OF SOLID PANCREATIC LESIONS: A MULTICENTER RANDOMIZED TRIAL

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Introduction: Standard endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) of solid pancreatic lesions involve the use of no-suction or suction aspiration techniques. A new aspiration method, the stylet slow-pull technique, consists in the slow withdrawal of the needle stylet to create minimum negative pressure. New generation of stylets could facilitate the slow-pull technique.
Aims and Methods: We compared EUS-FNB performed with the stylet slow-pull technique versus the standard suction technique in patients with solid pancreatic lesions. We evaluated blood contamination and adequacy of the samples, FNB diagnostic accuracy and complications. All EUS-FNB were performed with a 20-gauge needle (EchoTip ProCore with ReCoil Stylet^{TM}). The ReCoil Stylets has an automatic recoiling capability designed to help users to manage more easily the stylet minimising the risk of contamination.
After completion of the endosonographic examination, the pancreatic mass was evaluated with color Doppler to avoid the involvement of vessels. The needle was sharpened by withdrawing the stylet approximately 2 mm, and then was advanced into the lesion. In patients randomized to the stylet slow-pull technique, 15 to-and-fro movements within the lesion were performed, with simultaneous minimal negative pressure provided by pulling the needle stylet slowly and continuously. In patients randomized to the standard suction technique, 15 to-and-fro movements within the lesion were performed with the use of a 10-mL suction syringe. A visible core was defined as an architecturally intact-looking piece of tissue deemed sufficient for histological evaluation. Samples positive for malignancy were considered diagnostic. In patients with negative EUS-FNB, surgical specimen evaluation, results of other diagnostic investigation and/or long-term clinical follow-up (6 months) were used to establish the definitive diagnosis.
Results: In the interim analysis of the study we included 46 patients with an adequate follow-up (25 in the slow-pull group and 21 in the standard group). Patients' characteristics were reported in table 1. Among these 46 patients with an analyzable retrieved sample, blood contamination of the samples was poor in 33 patients (72%) and the final sample was adequate in the 70% of patients (32/46); no difference between the two techniques were observed. A diagnosis of malignancy was obtained in 40 cases (87%, "true positive"): 23 in the slow-pull group and 17 in the standard group. In 6 patients (2 in the slow-pull and 4 in the standard group) the suspected final diagnosis was chronic pancreatitis, but the clinical history suggested for a prudential approach, considering the final diagnosis as possible "false negative" in 4 of these patients (1 and 3 respectively). Based on these results, comparing the slow-pull group and the standard group, the sensitivity, specificity, negative likelihood ratio, positive likelihood ratio, and diagnostic accuracy were respectively of: 86 vs. 85%, 100% in both, 0.04 vs. 0.15, "infinity" in both, and 96 vs.85%. No adverse events were recorded.
Conclusion: Our preliminary data show as both slow-pull and standard suction techniques are comparable offering high diagnostic sensitivity and accuracy. Slow-pull technique seems to improve final diagnostic accuracy but it would be necessary to analyse all patients of our multicentric cohort. Up to now the endosonographer may choose either technique during FNB.
Disclosure: Nothing to disclose

P1471 DO WE NEED ENDOSCOPIC ULTRASONOGRAPHY IN THE WORKUP OF PATIENTS WITH ACHALASIA?

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Introduction: The etiology of primary achalasia of the lower esophageal sphincter is unknown. Endoscopic ultrasonography (EUS) is advised in the workup of achalasia patients to rule out secondary achalasia or pseudoachalasia, and search for a typical esophageal wall thickening. The purpose of this study was to assess the clinical contribution of EUS findings in achalasia.
Aims and Methods: We conducted a single-centre retrospective study at a tertiary referral center. We included all patients with an endoscopic ultrasonography for the workup of a suspected esophageal motility disorder from January 2012 to December 2017.
Results: Seventy-one patients were included, 54% were men, with a mean (±SD) age of 61 ± 14 years. Mean (±SD) Eckardt score at time of the EUS was 7 ± 2. EUS was strictly normal in 27 (38%) patients, and showed an esophageal wall thickening in 44 (62%) patients. The inner circular muscle layer was the most frequently affected, with a mean (±SD) thickness of 2.9 ± 2 mm. Three cases of secondary achalasia were diagnosed: 2 esophageal carcinomas and one eosinophilic esophagitis, all three diagnosed at mucosal biopsies. Sixty percent of the patients had never received a treatment at the time of EUS and 82% were treated after EUS. The most frequent treatment was an esophagogastric myotomy in 48% of the patients (per oral endoscopic myotomy in 45% and Heller myotomy in 3%), while 20% and 13%of patients were treated with pneumatic dilatation and botulinum toxin injection, respectively. The occurrence of a wall thickening was not significantly associated with the type of esophageal motility disorder or achalasia subtype, the Eckardt score, the integrated relaxation pressure at manometry, or a previous treatment. There was no statistical correlation between the presence of a wall thickening at EUS and therapeutic outcomes after any of the achalasia treatments.
Conclusion: In our work, the contribution of endoscopic ultrasound findings was limited. The presence of an esophageal wall thickening was not predictive of achalasia subtype or treatment outcome.
Disclosure: Nothing to disclose

P1472 EUS ELASTOGRAPHY STRAIN RATIO IN THE DIFFERENTIAL DIAGNOSIS OF GASTROINTESTINAL SUBEPITHELIAL LESIONS: RESULTS OF A MULTICENTER STUDY

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Introduction: Real-time endoscopic ultrasound elastography (EUS-E) allows for the quantification of tissue stiffness and has proven to be useful to better characterize lymph nodes and pancreatic masses. Strain ratio (SR) measurement has been introduced as a method to minimize the operator bias by providing semi-quantitative data. Studies on EUS-E with SR in gastrointestinal subepithelial lesions (SELs) are lacking.
Aims and Methods: Aim of this study was to assess the efficacy of EUS-E with SR in differentiating SELs. Retrospectively collected data from consecutive patients with SELs evaluated by EUS-E with SR at three centers were analyzed. EUS-E was carried out using the Olympus compact ultrasound processor EU-ME2. Two different areas were selected for SR. Area A included the biggest possible area of the lesion without surrounding tissue, while area B was selected in the peritumoral healthy gastrointestinal wall. The SR was calculated as the quotient of B/A. Every time, 3 measures of SR were recorded and the mean value for each was calculated and used as final SR. The reference standards for the final diagnosis were histology on EUS-FNB, surgical specimen or clinical follow-up.
Results: A total of 57 SELs were included. The mean lesion size was 36.4 mm (SD 20.8 mm). The lesion locations were esophagus (n = 7), stomach (n = 38), duodenum (n = 10) and rectum (n = 2). The final diagnosis of SELs included 27 (47.3%) GISTs, 14 (24.5%) leiomyomas, 7 (12.2%) lipomas, 3 (5.2%) ectopic pancreas, 2 (3.5%) schwannomas, 2 (3.5%) neuroendocrine tumors, and 2 (3.5%) cancers. The median SR was 27.2 (IQR 9.2–52.3) for GIST, and 6 (IQR 3.2–17.6) for leiomyomas. Receiver operating curve analysis of SR for the detection of GISTs vs. leiomyomas yielded an area under the curve of 0.741 (95%CI: 0.587–0.895) (Figure 1). The best cut-off level of SR to differentiate GIST from leiomyoma was 13.3 with a sensitivity of 74.1% and specificity of 71.4%.
Conclusion: The results indicate that EUS-E with SR may improve differential diagnosis of SELs, being SRs of GIST higher than those of leiomyoma. The cut-off of 13.3 may be helpful to differentiate between GIST and leiomyoma.
Disclosure: Nothing to disclose

P1473 THE IMPACT OF PANCREATIC NECROTIC CONTENTS IN FLUID COLLECTIONS ON TREATMENT STRATEGY AND SUBSEQUENT PANCREATIC DUCTAL ANATOMY

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Introduction: Acute severe pancreatitis can be necrotizing and frequently complicated by Pancreatic Fluid Collections (PFC). These PFC contains necrotic contents which has important implications on management and outcome. However, the effect of these pancreatic necrotic contents in PFC on treatment strategy and more importantly on the subsequent pancreatic ductal anatomy not clearly known.
Aims and Methods: The objective of this study is to evaluate whether the severity of necrotic contents in pancreatic fluid collections impacts the treatment strategy and pancreatic ductal anatomy
Subjects of acute pancreatitis with symptomatic PFC were included after an informed consent from Jan 2013 to December 2017. PFCs were classified into 3 distinct groups based on severity of necrotic contents, Group A) <15% SD; Group B) 15–40% SD; Group C) >40%. Subsequently EUS-guided drainage done using either short covered bi-flanged metal stent or plastic stents. After drainage, subjects were reassessed at 48–72 hours & Re-intervention including, Naso-cystic tube (NCT) placement with irrigation and Direct Endoscopic Necrosectomy were performed if required. All subjects underwent MRCP followed by ERCP between 4–8 weeks after the complete resolution of PFC to define the abnormalities in Pancreatic duct (PD) & were compared between 3 PFC subgroups. A p value <0.05 was considered statistically significant.
Results: A total of 408 subjects (350 males, median age 32 years, range 5–68 years) were included in the study group. Group A included 211 (51.7%), Group B included 155 (38%), Group C included 42 (10.3%) subjects. During EUS guided drainage, 270 underwent metal stent, 138 underwent plastic stents placement. Overall, Re-intervention was required in 110 (27%) subjects. The need for Re-intervention was significantly higher in Group C (SD >40%) compared to Group B & A (40.4% vs. 29.8% vs. 22.2%, $p = 0.03$). 340 out of 408 subjects had both MRCP and ERCP and included in final analysis. Of these, 42 (12.4%) subjects had normal PD, 35 (10.3%) had leak in PD, 20 (5.9%) had PD stricture & 11 (3.2%) had dilated PD with calculi & majority of subjects (n = 232, 68.2%) had cut-off in PD (Disconnected pancreatic duct). Normal PD was present significantly higher in Group A(SD <15%) compared to Group B & C(61.9% vs. 23.8% vs.14.2%). Similar trends were observed among Group A, B,& C for PD leak (71.4% vs. 28.5% vs. 0%), PD stricture (75% vs. 25% vs. 5%). However, PD cut off (Disconnected pancreatic duct) was observed significantly higher in Group C (SD>40%) compared to Group A (80.5% vs. 57.7%, $p = 0.001$).
Conclusion: Pancreatic necrotic contents in PFC significantly impacts management strategy and subsequent Pancreatic ductal anatomy. PFCs with severe necrotic contents require aggressive treatment strategy including Re-intervention. Normal Pancreatic duct can be seen in majority of subjects with PFC containing minimal necrotic contents. Whereas disconnected pancreatic duct is significantly higher in PFC containing severe necrotic contents.
Disclosure: Nothing to disclose

P1474 A NEW 19 G ENDOSCOPIC ULTRASOUND CORE NEEDLE FOR THE HISTOLOGICAL DIAGNOSIS OF MESENCHYMAL TUMORS: A FEASIBILITY STUDY

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Introduction: Different type and size of histological needles for Endoscopic Ultrasound guided Fine Needle Biopsies (EUS-FNB) have been developed, however the appropriated clinical setting in which they should be used has to be defined. The diagnosis of mesenchymal tumors (MT) often requires tissue for molecular studies (i.e. ISH. FISH, NGS) beside H&E and immunohistochemistry.
Aims and Methods: The aim of the study was to evaluated clinical performance of a new three points 19 G core needle with opposing bevels design in the setting of MT.
Prospectively collected data from consecutive patients who underwent EUS-FNB with a 19 G core needle characterized by a three-points design for suspected abdominal and pelvic MT at a single referral center were analyzed. Procedures were performed by a single operator between July 2017 and February 2018.
Results: Fifteen patients were managed. The procedure was technically feasible in all patients. Biopsy was performed through the rectum, the duodenum, and the stomach in 3, 2, and 10 patients, respectively. No major adverse events have been observed, although hemostatic clips were used to control mild gastric bleeding at the point of the needle passage for 2 patients. Biopsies showed in 2 cases malignancies other than MT one being a lymphoma and one a pelvic metastases from ovarian cancer. The remaining 13 patients were diagnosed MT (10 M, mean age 54 ± 16.7 years) and FNB lead to a diagnosis in 12 cases (accuracy, 92.3%); 2 sarcomas, 1 leiomyoma, 1 schwannoma, 6 GISTs, 1 glioma, and 1 desmoid-type fibromatosis. The mean size of the target lesion was 79 mm (range: 25–190). FNB was non-diagnostic in a patient with a large mass located behind the gastric wall with lipomatous radiological features. Quality of biopsy was examined showing that, although a mean number of 1.4 passes (range: 1–2) were performed based on gross visual inspection, adequate core tissue was available after the first pass for all patients. In 10 out of 12 diagnostic cases additional molecular studies were performed
Conclusion: This is the first report, to the best of our knowledge, on 19 G histological EUS needle with a novel three points design and showed both feasibility and safety of the procedure. This study showed a high rate of biopsied core tissue which was adequate for a full histological and molecular evaluations, supporting this new device as a promising tool when a pathological diagnosis is needed for patient management such as the case of MT.
Disclosure: Nothing to disclose

P1475 DIRECT ENDOSCOPIC NECROSECTOMY IN SUPER-INFECTED FLUID COLLECTIONS IN NECROTIZING PANCREATITIS USING LUMEN-APPOSING METAL STENTS: BETTER OUTCOME WITH EARLY INTERVENTION

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Introduction: In the last decade a paradigm shift in the treatment of necrotizing pancreatitis from more invasive surgical strategies toward less invasive percutaneous and endoscopic techniques took place.
Infected necrosis is a dreaded complication requiring an intervention. Nevertheless the optimal timing of first intervention is unclear and consensus data are sparse.
This retrospective two-center study evaluates immediate direct endoscopic necrosectomy using lumen-apposing metal stents in case of proven or suspected super-infection.
Aims and Methods: 60 patients with a mean age of 53.1 years were included between 6/12 and 2/18. Etiology of pancreatitis was alcoholic (n = 18), biliary (n = 23), after surgery (n = 1), hypertriglyceridemia (n = 1), post-ERCP-pancreatitis (n = 3) and unknown (n = 14). Pancreatic necrosis was diagnosed by contrast-enhanced computed tomography. Infection of necrosis was confirmed by presence of gas in the CT-scan or suspected based on clinical or biochemical markers of infection or sepsis. In case of infection a lumen apposing metal stent (hot-Axios™-Stent, Boston scientific, Marlborough, Massachusetts, USA or NAGI™-Stent, Taewoong medical, wolgot-myeon, South Korea) via transgastral or transduodenal access was implanted and sequent direct endoscopic necrosectomy was performed until resolution of the necrotic debris. The patient-cohort was divided in an early group receiving first necrosectomy within the first 30 days and a late group obtaining the intervention more than 30 days after first proof of necrosis. The C-reactive-protein as marker of inflammatory activity was recorded.
Results: The mean CRP was 219.2 ± 134.9mg/l and 56 ± 74 mg/l before and after intervention, respectively. The mean time between first proof of necrosis and first intervention was 20 ± 33.1 days, all-over mortality was 9.7%, clinical resolution was achieved in 86.7%. 4.9 ± 3.4 necrosectomies were performed per patient. The mean stay on the intensive-care-unit was 5.4 ± 11.5 days, on intermediate-care-unit 3.2 ± 6.1 days. Mean follow-up was 19 ± 12.4 months.
49 patients were assigned to an early intervention group (stent placement before 30 days after acute episode). Patients received 4.7 ± 3.2 necrosectomies after 8.9 ± 7.8 days, mortality was 8.2%, clinical resolution 87.8%. Days in intensive-care-unit were 5.0 ± 9.8, in intermediate-care-unit 4.4 ± 7.1.
11 patients were treated at least 30 days after onset of pancreatitis receiving 5.4 ± 3.3 necrosectomies after 67.6 ± 52.2 days with a mortality of 18.2%, clinical resolution of necrosis was 81.8%. ICU-days were 11.4 ± 18.3 days, stay in intermediate-care-unit was 0.8 ± 1.3 days.
Conclusion: Our retrospective data reveal an advantage of early timed endoscopic intervention over a delayed approach in necrotizing pancreatitis. Direct endoscopic necrosectomy in combination with lumen apposing metal stents shows a trend to less mortality and saving in ICU-capacity when its performed in an early stage of disease. Further randomized investigations should concretise the optimal timing of intervention.
Disclosure: Nothing to disclose

P1476 ADEQUACY AND DIAGNOSTIC YIELD OF A NOVEL CORE BIOPSY NEEDLE (SHARKCORE FNB NEEDLE) IN THE DIAGNOSIS OF SUBEPITHELIAL LESIONS: OUR SERIES

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Introduction: Subepithelial lesions of the gastrointestinal tract are commonly encountered during routine upper and lower endoscopy, diagnosticated incidentally because of their asimptomaticity. They are frequently located in the stomach, but also found in the esophagus and duodenum. Endoscopic ultrasound (EUS) plays a fundamental role in the detection and management of these

lesions, both for the ability to identify the original layer and the ultrasound pattern, but especially for the possibility to provide a histological, immunohistochemical and molecular diagnosis, through Fine Needle Biopsy (FNB).
Aims and Methods: The aim of the study is to assess adequacy and diagnostic yield of a novel core biopsy needle (Sharkcore FNB needle Medtronic). We retrospectively analized all EUS performed at our Center between September 2015 and March 2018, to further investigate suspicious subepithelial lesions found at upper and lower endoscopy.
Results: Out of 923 EUS, 123 were performed with suspicious of submucosal lesions, finally identifyng 109 (average size 16 mm, range 1–35 mm). FNB (Sharkcore FNB needle Medtronic, 22G, average of 3 passages), was performed in 22 cases (average dimension 30 mm, 12 female), only one patient experimented mild and self-limiting intralesional bleeding during FNB. The material resulted adequate in 20 cases, resulting diagnostic in 19 cases (10 GIST, 8 leiomyomas and 1 gastric splenosis). Therefore in 16 cases the sample allowed the immunohistochemical analysis, in 7 cases molecular tests. In only 4 cases surgery was performed, with a concordant diagnosis with FNB in 3 of them.
Conclusion: Our series demonstrates FNB (Sharkcore FNB needle Medtronic) adequacy of 90% and diagnostic yield of 86%.
Disclosure: Nothing to disclose

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P1477 CONNECT YOUR NEEDLE TO YOUR SMARTPHONE TO INCREASE EUS-FNA DIAGNOSTIC YIELD? ESGE RESEARCH GRANT 2016 PRELIMINARY RESULTS

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Introduction: Diagnostic yield of endoscopic ultrasound fine needle aspiration (EUS-FNA) in solid pancreatic masses depends on the lesion characteristics, needle diameter, presence of aspiration, number of passes and presence of rapid on site evaluation. We aim to prove that high needle acceleration through tissue significantly increases EUS FNA diagnostic yield.
Aims and Methods: We designed a prospective multicenter study to assess the impact of needle acceleration on the EUS FNA tissue acquisition rate, diagnostic accuracy, cellularity and quality of the acquired material (NCT03303352). Patients with larger than 20mm pancreatic solid masses with unknown histology were included. Using a 22-gauge needle, two "fast" and "slow" passes were performed, with accelerations higher and lower than 1g respectively. The two passes were performed in a randomized order, each with ten "to and fro" fanning movements. Acceleration was measured with a Pocketlab device attached to the aspiration syringe. Aspired material was fixed in alcohol and processed by the Cytoblock procedure. Slides for each pass were scored for accuracy by the Papanicolau Pancreatobiliary Terminology classification scheme and by two four-points cellularity and quality scales (minimum 0 to maximum 3). For a 25% increase in accuracy the calculated sample size was 51.
Results: 21 patients with locally advanced or metastatic pancreatic cancer on CT scan/MRI were included so far. 18 patients were evaluable, 3 patients were excluded from analysis (one withdrawn informed consent, one groove pancreatitis, one Pocketlab dysfunction). The mean acceleration values were 1.06g and 0.39g for "fast" and "slow" pass respectively ($p < 0.0001$). The tissue acquisition rate was 88%. The "fast" pass yielded a significantly better Papanicolau class ($p = 0.016$) and higher rate of positive diagnosis when compared with "slow" pass (66.6% versus 44.4%, $p = 0.638$). The mean cellularity scores were 1.56 and 1.28 for "fast" and "slow" passes ($p = 0.059$), while the mean quality scores were 2.17 and 1.67 for "fast" and "slow" pass respectively ($p = 0.083$).
Conclusion: Preliminary data proves that diagnostic accuracy was significantly influenced by a higher than 1g EUS FNA needle acceleration. There was a tendency towards better accuracy, cellularity and quality of EUS FNA specimens.
Disclosure: Nothing to disclose

P1478 THE PREVALENCE OF SMALL BOWEL AND COLONIC POLYPS IN PATIENTS WITH SPORADIC DUODENAL AND/OR AMPULLARY ADENOMAS – A PROSPECTIVE CASE CONTROL STUDY

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Introduction: Sporadic duodenal and/or ampullary adenomas are found in 1–3% of patients referred to upper endoscopy. Patients with duodenal adenomas have a 3-7-fold increased risk of colonic neoplasia above the normal population. It is unknown whether these patients have a clinically significant increased risk of small bowel neoplasia. Video capsule endoscopy (VCE) identifies Small bowel (SB) polyps in up to 75% of familial adenomatous polyposis (FAP) patients. Our aim was to investigate the prevalence of SB polyps occurring in association with large (≥10mm) sporadic duodenal or ampullary adenoma patients using VCE
Aims and Methods: A single-center, prospective case control study was performed. Patients with ≥10mm duodenal and/or ampullary adenoma were approached to participate in the study (Adenoma group). Patients with FAP were excluded. The control group comprised patients undergoing VCE for the evaluation of obscure gastrointestinal bleeding (OGIB) or Iron deficiency anemia (IDA) within the same study period.
Results: Over 20 months, 194 patients were enrolled in the study. The mean age was 65 (IQR 24–91) and 49% were male. There were 94 control patients and 99 adenoma cases (Duodenal adenomas n = 74 (75%), mean size 33mm (IQR 10–80mm); Ampullary adenomas n = 25 (25%), mean size 25mm (IQR 10–80mm)). 91% of duodenal adenomas were in the second part of the duodenum.
Five patients (adenoma group) were excluded from analysis due to inadvertent aspiration of the capsule (1), technical failure (2), inability to swallow the capsule (1) and non-adenomatous lesion (1).
There were no SB polyps in either group. One adenoma patient had an incidental finding of active bleeding, most likely from an angiodysplasia, but otherwise no significant small bowel findings were obtained.
Colonoscopy was performed in 82% and 84% (p-0.705) of the adenoma and control groups, respectively. Colonic polyps were found more frequently in the adenoma group than controls (61% vs 41%, respectively (p-0.009)). Overall, 43% of patients in the adenoma group had at least one colonic adenoma vs. 21% in the control group (p-0.002). The polyps were < 10mm in 87% and 95%, conventional adenoma in 76% and 71% (p-0.537) and sessile serrated polyps in 10% and 2%, respectively (Table-1). Advanced colonic polyps (HGD, > 10mm, Villous histology) were found in 21% of the adenoma group and 5% of the control group (p-0.02).
Conclusion: This is the first prospective case control study to show the negligible risk of synchronous SB polyps in large sporadic duodenal and/or ampullary adenoma patients. We have also confirmed the increased risk of colonic adenoma in this population, even in comparison to a control group at potentially greater risk of colonic pathology. Our data indicate that VCE for SB polyp screening in this group of patients is not necessary. However, colonoscopy is mandatory due to the high prevalence of colonic adenomas including advanced polyps.

	Adenoma (n = 106)	Controls (n = 41)	P value
1–5mm	61 (57%)	16 (39%)	
6–10mm	31 (30%)	23 (56%)	
> 11mm	14 (13%)	2 (5%)	
Conventional adenoma	81 (76%)	22 (71%)	NS
SSP	11 (10%)	1 (2%)	NS
Villous component	10 (9%)	0	
Advanced polyp	22 (21%)	2 (5%)	0.02
Patients with at least one adenoma	35 (43%)	16 (21%)	0.002
Polyps > 10mm	14 (13%)	2 (5%)	0.017
Proximal colon	51 (48%)	20 (49%)	NS
Distal colon	55 (52%)	21 (51%)	NS

[Table-1: Colonic polyp size, histology and location in both groups]
Acknowledgment: This study was supported by Medtronic
Disclosure: Nothing to disclose

P1479 VIDEO CAPSULE ENDOSCOPY HAS A HIGHER DIAGNOSTIC YIELD WITH SIMILAR TECHNICAL SUCCESS IN "OLD-ELDERLY" COMPARED TO "YOUNG-ELDERLY" PATIENTS

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Introduction: Video capsule endoscopy (VCE) is a non-invasive procedure that evaluates the small bowel (SB). The use of VCE in the elderly is rising mainly due to an increased rate of investigations for obscure gastrointestinal bleeding. While previous studies in the elderly have demonstrated delayed gastric transit time (GTT) with normal SB transit time (SBTT), detailed data is lacking regarding motility and diagnostic yield in these age groups.
Aims and Methods: To evaluate the diagnostic yield and transit times in different age categories among elderly patients.
All consecutive VCEs performed from 01/2010 to 12/2017 in a single tertiary center were reviewed. Inclusion criterion was age≥65 years. Exclusion criteria were technical malfunction or inability to swallow. The cohort was divided into two age groups: 65–79 years (young-elderly, YE) and ≥80 years (old-elderly, OE). Complete SB visualization was defined by cecal documentation. GTT and SBTT were calculated and expressed as median (range min-max). Indications, TTs and diagnostic yield were compared between groups.

Results: A total of 1765 VCEs were performed, 535 (30.3%) in patients ≥65 years including 90 (5.1%) in patients ≥80 years (12 patients were excluded). YE included 445 VCEs in 425 patients, mean age 71.3 ± 4.2 years and 51.9% male. OE included 90 VCEs in 83 patients, mean age 83.9 ± 3.2 years (range 80–93) and 47.8% male. The most common indication for referral in both groups was iron deficiency anemia (YE = 69.7% vs. OE = 73.3%, p = 0.529), followed by chronic diarrhea/suspected Crohn's disease, which was 3-fold higher in YE (17.8%) compared to OE (5.6%, p = 0.002). Complete visualization of the SB was equally achieved by both groups (YE = 96.4% vs. OE = 93.3%, p = 0.236). GTT and SBTT were comparable as well (YE = 20 (0–356) minutes vs. OE = 22 (1–184) minutes, p = 0.240 for GTT; YE = 243 (24–642) minutes vs. OE = 242 (35–581) minutes, p = 0.706 for SBTT). No correlation was found between age and GTT (p = 0.425) or age and SBTT (p = 0.334). The rate of significant visual impairment resulting from food mixing, allowed at 4 hours after capsule swallowing, with a capsule retained in the stomach for > 4 hours did not differ between groups (YE = 1.3% vs. OE = 1.1%, p = 1.000). The rate of positive VCEs was higher in OE compared to YE (68.5% vs. 51.7%, p = 0.005), as was the rate of clinically significant findings (58.4% vs. 41.1%, respectively, p = 0.003). Angioectasias were observed more frequently in OE (36.8% vs. 22.9%, p = 0.010). Active bleeding was observed in 12.8% in OE compared to 6% in YE (p = 0.037). Moreover, in sub-analysis of patients referred solely due to iron deficiency anemia, the prevalence of evident active bleeding was more than two-fold higher in OE compared to YE (14.3% vs. 6.7%, respectively, p = 0.058).
Conclusion: One third of our VCE studies are performed in the elderly while 5% are performed in patients≥80 years. "Old-elderly" patients have a higher rate of clinically-significant findings with similar rates of technical success. The high diagnostic yield in the old- and young-elderly, together with low rates of extended GTT and high SB completion rates, justify VCE studies in these populations.
Disclosure: Nothing to disclose

P1480 THE COMPARISON OF THE EFFICIENCY OF COLON CAPSULE ENDOSCOPY AND OPTICAL COLONOSCOPY IN PATIENTS WITH POSITIVE IMMUNOCHEMICAL FECAL OCCULT BLOOD TEST

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Introduction: Fecal immunochemical tests (FIT) have been used as an initial test in CRC screening programs. However, majority of patients do not have advanced neoplasia on colonoscopy. Colon capsule endoscopy (CCE) has the potential to reduce the need for optical colonoscopy (OC) in FIT positive individuals.
Aims and Methods: In this multicenter (3 tertiary referral centers) feasibility study, second generation of colon capsule endoscopy (CCE2) has been prospectively compared with OC in persons with positive semi-quantitative FIT with cut-off level 75 ng/ml. The primary outcome was negative predictive value (NPV) of the CCE2 for large polyps (≥ 10 mm). The accuracy of detection of all polyps (polyps ≥ 6 mm and ≥ 10 mm) and cancers was assessed. Colonoscopy was performed within 10 hours after capsule ingestion. CCE2 videos were viewed independently by a nurse and a physician, both blinded to the results of OC. Complications were assessed as serious (bleeding, perforation) or mild to moderate. The methods of acceptance were evaluated based on the questionnaire completed after both procedures (CCE2 and CC) were finished. The interim analysis of results is presented.
Results: From April 2016 until April 2018, 111 individuals (mean age 61 years) have been enrolled; data from 54 persons have been analyzed. During optical colonoscopy, polyps were diagnosed in 37 persons (69%), polyps ≥ 6 mm and ≥ 10 mm in 22 (41%) and 12 (22%) persons, respectively. The sensitivity of CCE2 for polyps ≥ 6 mm and ≥ 10 mm was 82% (95% confidence interval [CI]: 60–95%) and 75% (95% CI: 43–95%), respectively. The specificity for polyps ≥ 6 mm and ≥ 10 mm reached 88% (95% CI: 71–96%) and 93% (95% CI: 81–99%), respectively. Two cancers were diagnosed at both CCE2 and OC. The negative predictive value of CCE2 for polyps ≥ 10 mm was 93% (95% CI: 81–99%). Nurses identified 30 polyps of 37 (81%) found on OC compared to 36 polyps (97%) identified by physicians. A total of 40 patients (74%) preferred CCE2 as the primary screening method.
Conclusion: A second generation of colon capsule has appeared to have a high negative predictive value for clinically relevant colorectal neoplasia in screening population. This method might be considered as an adequate tool for colorectal cancer screening.
This project has been supported by the Czech Ministry of Health grant No. 16-29614A
Disclosure: Nothing to disclose

P1481 RISK OF SMALL BOWEL BLEEDING ASSOCIATED WITH USE OF ORAL ANTICOAGULANTS OR ANTIPLATELET AGENTS: A RETROSPECTIVE COHORT STUDY

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Introduction: Antiplatelet and anticoagulant therapy is increasingly being used for cardiovascular prevention. Novel direct-acting oral anticoagulants (NOAC) represent a recent, alternative, family of drugs. Rate of bleeding complications by NOAC seems to be comparable to those of warfarin but a previously assumed increase in gastrointestinal bleeding complications was meanwhile confirmed. The risk of bleeding in the setting of suspected small bowel bleeding (SSBB) in patients taking antiplatelets or anticoagulants has been poorly investigated.
Aims and Methods: Aim of this study was to evaluate diagnostic yield using video capsule endoscopy in OGIB patients taking antiplatelets or anticoagulants.
This is a retrospective review of chronic users of anticoagulants or antiplatelet agents who underwent VCE for SSBB. Small bowel findings were evaluated using Mirocam VCE (Intromedic, Korea).
Results: 264 patients (134 women, mean age 72.3 years, 55% occult SSBB) underwent VCE from January 2014 to March 2018 for SSBB. 162 out of 264 patients were taking antiplatelets or anticoagulants agents. 44 patients were taking 100 mg of enteric-coated aspirin, 24 taking thienopyridine (ticlopidine or clopidogrel), 39 taking aspirin combined with thienopyridine (combined group), 27 taking warfarin and 28 patients taking NOAC (20% dabigatran, 32% apixaban, 48% rivaroxaban). Diagnostic yield in this specific cohort was 52.5%. Relevant lesions were most frequently detected in the "combined" group (74.3%) among the five groups (aspirin group 52.2%, NOAC group 50%, warfarin group 48.1%, thienopyridine group 41.6%) (p = 0.037).
Conclusion: The risk of small bowel bleeding related to antiplatelet / anticoagulant therapy seems to be increased in patients taking the combination of aspirin and thienopyridine and preventive strategies in this group should be established. The risk related to novel oral anticoagulants seems to be similar to that for warfarin and aspirin alone.
Disclosure: Nothing to disclose

P1482 USE OF CHEWING GUM TO IMPROVE GASTRIC TRANSIT TIME IN CAPSULE ENDOSCOPY

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Introduction: The capsule endoscopy (CE) is a high yield diagnostic procedure for evaluating small bowel (SB) with low invasiveness. One of the limitations is the incomplete studies' rate, generally, due to a delay in gastric evacuation and limited useful life of the batteries. Consequently, a final segment of the SB could not be visualized and the study should be repeated. Prokinetics, laxatives, patients' position and the use of chewing gum to accelerate the transit were evaluated with discordant results.
Aims and Methods: 1. Establish if gastric transit time (GTT) and SB transit time (SBTT) were lower in patients who consume chewing gum than in those who do not. 2. Evaluate if the use of chewing gum decreases the rate of incomplete studies. 3. Describe the clinical characteristics of patients with incomplete studies. Adults referred for CE who accepted to enter the study were included. Retained CE, CE repositioning by upper endoscopy and impossibility to chew were exclusion criteria. Setting: Outpatients gastroenterology center, between 05, 2014 and 09, 2017.
Experimental, prospective, comparative, randomized, single blind and cross sectional. The patients were divided as follows: Ch group: received chewing gum (20 minutes every 2 hours from CE ingestion until the end of the procedure) and control group. Indications and procedures were performed according to usual practice, with CE. GTT and SBTT in minutes, reaching the ceccum, incomplete studies, outpatient-admitted condition, and co morbidities were registered. Ethics: the protocol was approved by the local Committee. Statistical analysis: SPSS 19, Student, $X^{2,}$ Kaplan Meier.
Results: 365 patients: 52.6% females; average age in men and women, 59.4 ± 16.13 years and 56.41 ± 15.83 years, respectively (p = 0.07);average BMI in men and women: 27.27 ± 4, 23 and 26.51 ± 5.10 kg/m2, respectively (p = 0.125); average GTT: 42.47 ± 44.86 min; average SBTT: 238.55 ± 105.16 min; Group Ch: 48, 2% (176/365), outpatients (98.5% (357/365); Co morbidities 17% (61/365) 1. a) Average GTT for Ch and control group were 46.11 ± 47.30 vs. 39.08 ± 42.31 min, respectively (T = 2.07; p = 0.13). b) Average SBTT for Ch and control group were 236.37 ± 108.70 and 240.58 ± 102 min, respectively; (T = −0.38, p = 0.70). 2. Incomplete studieś rate in Ch and control group was statistically no different (2.3% (95% CI 0.6–5.7; 4/176) vs. 1.6% (0.3–4.6; 3/189; p = 0.92) 3. Sex, hospitalization, at least one co morbidity, BMI and age were not associated with not reaching cecum.
Conclusion: GTT, SBTT and the proportion of incomplete studies were no different between consumers of chewing gum and non-consumers during CE.
Disclosure: Nothing to disclose

P1483 OMNI MODE REDUCES CAPSULE ENDOSCOPY READING TIME WHILST MAINTAINING ACCURACY

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Introduction: A typical capsule endoscopy case generates several thousand images, with abnormalities often confined to a just few frames. The use of rapid reading software has become common place in an attempt to reduce reading times. There is concern that use of such software may result in an unacceptable number of missed lesions. Omni Mode is novel EndoCapsule software algorithm, which aims to intelligently remove duplicate images whist maintaining lesion detection. Here we present the interim results of a multi-centre European study of the use of Omni Mode in daily clinical practice.
Aims and Methods: This study took place across 9 European centres, using real life cases. Patients undergoing a clinically indicated capsule endoscopy had their case read at their local centre using standard reading, with every captured frame reviewed. A pragmatic 'real life' approach was adopted, with readers using their usual viewing mode and speed. These cases were then anonymised and randomly allocated to another centre where this was read using Omni mode. Detected lesions and reading time was recorded, with findings compared between both viewing modes. All lesions were reviewed and classified according to lesion type and severity using the P- Classification. Where lesions were missed, a review of the Omni Mode reading stream was conducted at 10fps, to determine whether they were missed by the viewer or had been excluded by the software.
Results: Here we report the preliminary results for the first 210 cases analysed. The patient population undergoing capsule endoscopy had a mean age of 60.8 years (range 18- 91), with a Male to Female ratio of 1.1:1. The investigation of anaemia or overt gastro-intestinal bleeding accounted for 68% of cases. A total of 1732 lesions were identified, which were classified according to the P-Classification as P0 (927), P1 (550) and P2 (255). Lesions were identified using both reading modes in 48.3% (n = 836). 320 lesions seen in normal mode were missed using Omni Mode, of which 229 were P0, 66 were P1 and 25 were P2. When the viewing stream in Omni mode was evaluated, it was noted that only 4% (n = 13) of the missed lesions were removed from the reading stream (P0 5, P1 8, P2 0). A greater proportion of lesions were missed during standard reading, than when using Omni Mode (n = 516).
The average small bowel transit time was 4 hours and 22 mins (range: 23 mins-13h and 36 mins). Reading cases with the use of Omni Mode was significantly faster ($P < 0.0001$), with an average time saving of 29.1 mins. Cases read without the use of rapid reading software took an average reading time was 45.6 mins (6 to 181 mins), compared to 16.3 mins (3–63 mins) using Omni Mode.
Conclusion: These preliminary results suggest that Omni mode has an acceptable accuracy and is associated with a significant reduction in reading time. Missed lesions using the standard reading mode may be attributable to loss of concentration due to time spent and the tendency to use faster reading speeds.
Disclosure: Nothing to disclose

P1484 FEASIBILITY AND SAFETY OF ROBOTICALLY CONTROLLED MAGNETIC CAPSULE ENDOSCOPY IN THE VISUALIZATION OF UPPER GASTROINTESTINAL TRACT

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Introduction: The visualization of the upper gastrointestinal tract with capsule endoscopy was not possible because of the large cavity of the stomach and the lack of controlled movements. The Ankon robotically controlled magnetic capsule endoscopy (MACE) system has been developed to investigate the stomach disorders. Our current prospective study aimed to evaluate the feasibility and safety of the Ankon MACE system in the visualization of the upper gastrointestinal (GI) tract in humans.
Aims and Methods: Our current prospective study enrolled 75 consecutive patients under the age of 40, with upper GI complaints or dyspepsia, but without any alarm symptoms. All subjects swallowed the Ankon MACE after drinking of one liter of clear water for gastric distension. An external robotic system with automatic preset programs applied to maneuver the MACE in the upper GI tract and generate a targeted magnetic field. The primary outcomes were the feasibility and safety of the MACE, including the quality of gastric preparation (excellent:4 good:3, moderate:2, poor:1), the level of visualization (complete, partially complete, none) of the Z line, the entire gastric mucosa (cardia, fornix, corpus, angulus, antrum), the duodenal bulb and the Vater papilla. We also assessed the feasibility of the esophageal withhold and active pyloric passage of the MACE with the targeted magnetic field.
Results: MACE was successful in all 75 patients with good to excellent visualization (mean score: 3,37) of the stomach and the entire small bowel without any complication or capsule retention. The visualization of the Z line was possible in 67/75 patients (89%), which was assessed as complete in 23 and partially complete in 44 patients. The mean stationary time for MACE in the esophagus was 1 min and 32 sec. Complete visualization of the cardia, fundus, corpus, angulus, antrum, and duodenal bulb was 95,4%, 100%, 100%, 100%, 100% and 100%, respectively. We were able to visualize the Vater papilla in only 20 patients. The possibility of successful pyloric passage of the MACE with the targeted magnetic field without administration of intravenous metoclopramide was possible in 55 patients (73%) within 60 minutes. Following MACE 10 patients underwent upper GI endoscopy to take histology due to the following pathologies detected by MACE, such as one patient with gastric lymphoma, three patients with hyperplastic polyps, five patients with severe erosive gastritis and one patient with peptic ulcer.
Conclusion: Our present study proved that robotically controlled MACE is easy to perform, non-invasive, safe method with excellent maneuverability in the upper GI tract, and has a future potential to detect and diagnose upper gastrointestinal disorders including oesophageal, gastric and small bowel pathologies.
Disclosure: Nothing to disclose

P1485 INVESTIGATING IRON-DEFICIENCY ANEMIA WITHSMALL BOWEL CAPSULE ENDOSCOPY: IS HAEMOGLOBIN A RELIABLE PREDICTOR OF POTENTIALLY BLEEDING LESIONS?

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Introduction: Capsule endoscopy (CE) is a first-line diagnostic tool for iron-deficiency anemia (IDA) evaluation after a negative bidirectional endoscopic study. Whether haemoglobin level is a predictor of potentially bleeding lesions (P2) in small bowel capsule endoscopy (SBCE) remains controversial.
Aims and Methods: Determine the influence of haemoglobin levels on diagnostic yield of SBCE for P2 lesions in patients with IDA.
Retrospective single-center study including consecutive patients submitted to SBCE over 12 years for IDA. The minimum value of haemoglobin observed between the diagnosis of IDA and the performance of the exam was considered. The lesions were described using Saurin et al. classification[(1)]
Results: 289 patients were included, 211 females (73.0%), mean age of 61.6 ± 18.7 years. The overall diagnostic yield was 60.6%, with identification of 100 P2 lesions (34.6%)
A statistically significant association was found between the presence of P2 lesions and age (68.3 ± 17.6 vs 58.1 ± 18.3, $p < 0.001$), male gender (36.0% vs 22.2%, $p = 0.02$), haemoglobin levels (8.6 ± 2.0g/dL vs 9.3 ± 1.7g/dL, $p = 0.003$), smoking habits (23.0% vs 12.7%, $p = 0.03$), alcoholism (10.0% vs 3.7%, $p = 0.04$), Charlson index (5.2 ± 3.2 vs 3.5 ± 3.4, $p < 0.001$), arterial hypertension (70.0% vs 49.7%, $p = 0.001$), chronic kidney disease (31.0% vs 19.6%, $p = 0.04$), heart failure (39.0% vs 20.1%, $p = 0.001$), chronic obstructive pulmonary disease (16.0% vs 7.4%, $p = 0.03$) and proton pump inhibitors use (62.0% vs 48.7%, $p = 0.04$). At logistic regression analysis only haemoglobin levels ($p = 0.02$) were independently associatedwith the diagnosis of P2 lesions. Although haemoglobin levels showed a weak discriminative capacity for the diagnosis of P2 lesions ($AUC = 0.60$, $p = 0.005$), values ≤ 7.7 g/dL were associated with a higher likelihood detection of P2 lesions.
Conclusion: Haemoglobin values may help guiding the decision to study the small-bowel in patients with IDA, since values ≤ 7.7g/dL are predictive of potentially bleeding lesions.
Disclosure: Nothing to disclose

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P1486 BULKING AND LAXATIVE EFFECTS OF KIWIFRUIT DIETARY SUPPLEMENTATION: NOVEL MRI IMAGING INSIGHTS

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Introduction: Chronic constipation affects approximately 17% of the population worldwide and remains an important unmet need as patients are often dissatisfied with treatment. Kiwifruit may offer an alternative to traditional laxatives and have been shown to increase stool volume and frequency (1). Using novel validated non-invasive MRI techniques (2,3), we assessed fluid distribution in the small and large intestine and colon volumes.

Aims and Methods: A two-period crossover trial of kiwifruit versus control in adults without bowel disorders. Participants consumed two kiwifruit twice daily or an isocaloric control (28 gm maltodextrin drink) twice daily for 3 days. Participants underwent MRI scans on the third day, including a fasted scan, consumption of the two doses of test products and of two standardised test meals, altogether 9 hourly scans (baseline to 420 min after first meal). Participants attended visits 3 weeks apart.
Outcomes were small bowel water content (SBWC) and ascending colon T1 relaxation time (T1AC), volumes of the ascending, transverse and descending colon, gut transit time measured by the weighted average position score (WAPS) of markers ingested 24h before, stool frequency and Bristol stool form score and symptoms. All images were analysed blinded to intervention.
All data are reported as mean ± standard deviation. Paired tests were applied to area under the curve (AUC) summary measures.
Results: The study was completed by 14 participants, 6 male, 8 female, with a mean age of 26 (range 21–33) years.
SBWC AUC was markedly increased in participants consuming kiwifruit, 85.5 ± 34.9 l*min, as compared to control, 35.0 ± 15.6 l*min; $P < 0.001$.
T1AC was significantly higher after kiwifruit ingestion AUC (137 ± 39 s*min) as compared to control (108 ± 40 s*min, $P = 0.029$) when calculated for the period (T240-T420), representing the time period when the test product and first meal started reaching the colon.
Total colon volume AUC (baseline to T420) was increased in the kiwifruit arm (283.6 ± 59.4 l*min) as compared to the control arm of the study (243.2 ± 46.2 l*min, $P = 0.004$). This was primarily due to increased volumes of the ascending colon (kiwifruit 110.3 ± 26.1 l*min; control 92.4 ± 24.9 l*min; $P = 0.003$).
Transit time did not change ($P = 0.11$). Stool frequency was significantly increased during the kiwifruit week (1.60 ± 1.04 stools per day) compared to the control (1.22 ± 0.61 stools per day; $P = 0.02$), and baseline (1.26 ± 0.78; $P = 0.02$). The stool consistency scores were different between groups (X^2, $P = 0.005$), with looser stool consistency scores in the kiwifruit compared to both control ($P < 0.0001$) and baseline ($P = 0.002$).
There was no significant difference in scores for all symptoms (gas, nausea, abdominal pain, bloating) between the kiwifruit, control and/or baseline study periods.
Conclusion: The MRI data suggest that consumption of kiwifruit in healthy participants increases water retention in the small bowel and ascending colon, as well as increasing colonic bulk. The data is consistent with the observations of an increase in stool frequency and looser stool consistencies, suggesting that kiwifruit could be used as a dietary alternative to laxatives in mild constipation.
Disclosure: This study and Dr Dellschaft's post have been funded by Zespri, a consortium of kiwifruit growers.

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P1487 THE INCIDENTAL FINDING OF A BRANCH-DUCT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM LACKING COMPLEX FEATURES STILL REQUIRES ACTIVE LONG-TERM SURVEILLANCE

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Introduction: The optimal surveillance protocol for incidental branch-duct intraductal papillary mucinous neoplasm (BD-IPMN) remains controversial to this day. Various international authorities have produced guidelines (such as the Fukuoka guidelines in 2017 and the more recently published guideline in 2018 by the European Study Group on Cystic Tumours of the Pancreas) with differing recommendations regarding frequency and duration of repeat imaging. This is partly because the risk of growth of BD-IPMNs lacking complex features and their association with concomitant development of pancreatic adenocarcinoma (PADC) is not yet fully understood due to the paucity of data available.
Aims and Methods: This retrospective study aims to establish the risk of growth of BD-IPMNs which lack features of complexity, according to baseline size on incidental imaging. All BD-IPMNs incidentally identified on cross-sectional imaging between 2007 and 2017 in a single-centre in Malta were included and subdivided according to size according to the revised international consensus Fukuoka guidelines: <10 mm, 10–19 mm, 20–29 mm and >30 mm. For those which had follow-up imaging, size comparison was carried out and the risk of concomitant development of PADC (distinct from BD-IPMN malignant transformation) was noted and compared with the Maltese general population.
Results: A total of 328 patients with BD-IPMNs were identified and categorised according to size as detailed in the table below.

	IPMN Size (mm)			
	<10	10–19	20–29	>30
Incidental number on imaging (n)	127	151	37	13
Follow-up imaging performed (%)	41.7 (n = 53)	41.7 (n = 63)	48.7 (n = 18)	53.8 (n = 7)
Average radiological follow-up period (months)	11.9	15.4	18.3	24.9
Increase in IPMN size on follow-up imaging (%)	7.5 (n = 4)	15.9 (n = 10)	5.6 (n = 1)	28.6 (n = 2)
Development of concomitant PDAC (%)	0.0 (n = 0)	3.2 (n = 2)	5.6 (n = 1)	0.0 (n = 0)

[Radiological follow-up outcomes in BD-IPMNs lacking complex features]
BD-IPMNs measuring <10 mm on incidental imaging increased in size in 7.5% of cases to a maximum of 2 mm during an average follow-up period of 11.9 months. This did not change patient management. The rate of growth in BD-IPMNs measuring 10–19 mm was 15.9% over a 15.4 month average follow-up period. The average increase in size was of 5.2 mm, with the largest difference being of 12 mm at 24-month follow-up. 3.2% (n = 2) of those radiologically followed-up developed concomitant PADC (at 17 and 24 months respectively), whilst 1.6% (n = 1) progressed into a mixed-type IPMN. Only 5.6% of BD-IPMNs measuring 20–29 mm increased in size during an average 18.3-month follow-up period.
Concomitant development of PADC was observed in 5.6% of radiologically followed-up patients. BD-IPMNs measuring >30 mm increased in size in 28.6% of followed-up cases. The lifetime risk of developing concomitant PADC in our cohort of 141 BD-IPMN patients with surveillance imaging was of 2.1% (1 in 48) whereas the general population-matched lifetime risk in Malta is 1.5% (1 in 68), resulting in a relative risk of 1.4. The risk increases further to 3.4% (1 in 29) when BD-IPMNs measuring <10 mm are excluded, with a relative risk of 2.3.
Conclusion: BD-IPMNs lacking complex features still harbour the potential for interval growth. The risk increases further with larger BD-IPMNs. The relative risk of concomitant development of pancreatic adenocarcinoma in our patient cohort was found to be higher than the general population. Given these findings, active long-term surveillance is warranted in all incidental BD-IPMNs, even in the absence of complex features, especially if over 10 mm in size.
Disclosure: Nothing to disclose

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P1488 SIGNIFICANCE OF BOWEL WALL THICKENING ON EMERGENCY ROOM CT SCANS

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Introduction: Patients presenting to the Emergency Room with abdominal pain frequently undergo urgent CT scans, often revealing bowel wall thickening (BWT). In the absence of guidelines to address the issue, endoscopic evaluation is carried out in most of them, while only a proportion of patient have significant pathology. The study aims to evaluate the clinical relevance of such BWT and assess predictors of significant pathology on endoscopic evaluation.
Aims and Methods: Patients referred to Gastroenterology Service from the Emergency Department at Hamad General Hospital with Bowel Wall thickening on CT scans between July 2015-July 2017 were retrospectively analyzed. Apart from the CT features, correlation of endoscopic findings to clinical presentation, laboratory parameters and histopathology were studied.
Inclusion Criteria:
1. Patients who underwent endoscopic evaluation were included in final analysis.
2. In the case of a negative endoscopy, patient had follow up of at least 6 months to exclude GI Condition.
3. Age > 16 years.
Exclusion Criteria:
1. Patients who have had endoscopy or biochemical markers done after 4 weeks of CT scan reporting of LGIO thickening were excluded from the analysis.
2. Patients with known GI Pathology (IBD, malignancy).
3. Evidence of luminal obstruction, stricture or mass on CT scan.
Results: 109 of 160 referred patients satisfied criteria for study inclusion. Endoscopic appearance was normal in 37/109(33.9%). Significant findings

confirmed as chronic pathology were found in 41/109(37.6%) patients. Of these 21(19.1%) had IBD {13 Crohn's Disease (11.9%), 8 Ulcerative Colitis (7.3%)}, 9(8.3%) had Tuberculosis, 11(10.1%) had malignancy. Mucosal abnormalities but normal or acute inflammation on histopathology were observed in 31/109(28.4%) patients. Segment based diagnosis and distribution in Table 1.
Age or gender had no correlation with significant findings. Symptom duration was the strongest predictor of significant endoscopic findings (> 2 weeks 25/35, 71.4%; <2weeks 16/74, 21.6%; $P < 0.001$). Features such as blood in stool, fever and weight loss were also positively associated with having significant findings.
Laboratory parameters: WBC, Hemoglobin, ESR, Albumin and CRP were not correlated with IBD. Mean Hemoglobin (10.5 ± 2.1 vs 12.8 ± 1.9; $P = 0.001$) and Albumin (27.5 ± 6.7 vs 35.4 ± 10.8; $P = 0.008$) were significantly lower in the malignancy group. Calprotectin was done in 36/109 patients. Mean Calprotectin was significantly higher with IBD and TB (199.5 ± 299.8 vs 809.8 ± 540.8; $P < 0.001$).
Four radiologically reported parameters – fat stranding, lymphadenopathy, vascular engorgement and pelvic free fluid-were analyzed from CT reports. Of these only fat stranding was associated with IBD or TB (20/46, 44% vs 10/52, 19%; $P = 0.009$).
Conclusion: One-third of study patients had significant pathology (IBD/TB/Malignancy). Two third of patients have a negative endoscopy or acute inflammatory findings on endoscopy. Prospective data may guide patient selection for endoscopic evaluation in patients with Bowel Wall Thickening on CT scans.

	Normal or Acute pathology	Crohns Disease (CD)	Ulcerative Colitis (UC)	Tuberculosis (TB)	Malignancy	Total
Upper GI(1)	15	0	0	0	1	16
Small Bowel (2)	7	1	0	0	4	12
Ileo-caecal Junction (3)	19	6	1	3	2	31
Right Colon (4)	12	1	0	0	0	13
Left Colon (5)	10	0	4	0	3	17
2+3	0	2	0	1	0	3
3+4	5	3	2	5	1	16
4+5	0	0	1	0	0	1
Total	68	13	8	9	11	109

[Segment based diagnosis and distribution]
Disclosure: Nothing to disclose

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P1489 FLUORESCENCE IMAGING OF EARLY CARCINOMA OF THE ESOPHAGOGASTRIC JUNCTION BY TOPICALLY SPRAYING PROBE TARGETING DIPEPTIDYLPEPTIDASE-IV

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Introduction: It is difficult to detect and diagnose early carcinoma of the esophagogastric junction by conventional endoscopy or image-enhanced endoscopy. Recently, several fluorescent probes which are activated by cell surface-associated enzymes overexpressed in cancers have been developed. We have demonstrated that Glutamate-proline-hydroxymethyl rhodamine green (EP-HMRG), which can be enzymatically activated and becomes fluorescent after cleavage of a dipeptidylpeptidase (DPP)-IV-specific sequence, is useful for the detection of head and neck squamous cell carcinoma (Mizushima et al., *Head & Neck*, in press).
Aims and Methods: We investigated whether early adenocarcinoma of esophagogastric junction (EGJ) can be detected by applying EP-HMRG, using samples resected by endoscopic submucosal dissection (ESD).
Consecutive 12 patients underwent ESD for early adenocarcinoma of EGJ at 4 hospitals between May 2016 and July 2017 were recruited.
After ESD, fluorescence imaging was performed immediately after spraying EP-HMRG, and fluorescence intensity of tumor and normal mucosa regions of interest (ROI) was prospectively measured. Immunohistochemistry was also performed to investigate the expression of DPP-IV.
Results: The major histological type in the cases was differentiated type (10 differentiated type/2 undifferentiated predominant type). The lesions were located at E (4 cases), EG (2 cases), E = G (2 cases), GE (2 cases) and G (2 cases). Background mucosae around lesions were LSBE (1 case), SSBE (6 cases), normal squamous epithelium without Barrett mucosa (1 case) and gastric mucosa with atrophy and intestinal metaplasia (4 cases). In 11 out of 12 cases, tumor lesions became fluorescent within a few minutes after application of EP-HMRG. In cases with subsquamous tumor extension, point-like fluorescent lesions were observed at which cancerous glands were exposed over the squamous epithelium. Fluorescence intensity in the tumor lesions was significantly higher than that in the normal mucosa 7 min after spraying of EP-HMRG. Immunohistochemical examination demonstrated that the cancerous area, but not normal epithelium, strongly expressed DPP-IV. However, in a case with a history of previous radiotherapy, cancer legion did not become fluorescent, and did not express DPP-IV.
Conclusion: Fluorescence imaging with EP-HMRG would be useful for detection of early carcinoma of EGJ.
Disclosure: Nothing to disclose

P1490 POST-IMAGING COLORECTAL CANCER IN THE ENGLISH NATIONAL HEALTH SERVICE BOWEL CANCER SCREENING PROGRAMME

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Introduction: Computed tomography colonography (CTC) is the gold standard radiological investigation for colorectal cancer screening. The Post-Imaging Colorectal Cancer (PICRC) rate (i.e. colorectal cancers that develop after a negative CTC) is a key quality indicator of CTC; however, PICRC rates have not been previously reported in a national screening programme.
The Word Endoscopy Organisation (WEO) has, through a consensus process, agreed a standard methodology for calculating PICRC rates to enable international benchmarking of rates (1). This rate (which the WEO terms PICRC-3y) is calculated by dividing the PICRCs detected 6 months to 3 years after a negative CTC (false negatives) by the sum of the true positives (defined by CTCs with a cancer diagnosis within 6 months) and false negatives (PICRCs). This study aimed to determine the rate of PICRC-3y in the English National Health Service (NHS) Bowel Cancer Screening Programme (BCSP).
Aims and Methods: Data from each BCSP CTC is entered into a national database, the Bowel Cancer Screening System. All colorectal adenocarcinomas, within and outside the BCSP, are validated and registered by the National Cancer Registration and Analysis Service. This retrospective observational study interrogated these databases to identify BCSP true positive and false negative CTCs. CTCs were included regardless of whether they were preceded or followed by a colonoscopy within a screening episode.

	True Positive CTC	False Negative CTC	To year end	PICRC-3y Rate
2006–2008	18	1	2009–2011	5.26% (95% CI 0.1–26)
2009	45	2	2012	4.26% (95% CI 0.5–14.5)
2010	55	5	2013	8.33% (95% CI 3.6–18.1)
Total	118	8		6.35% (95% CI 2.8–12.1)

[Results]

Results: Of the 8 PICRCs, 3 were detected at subsequent BCSP procedures, one at 1 year surveillance, and 2 following re-invitation for screening at 2 years. Five were detected outside the BCSP.
Conclusion: 1. The PICRC-3y in the BCSP is 6.35%, higher than the rate in the published literature (4.4%)(2) and the corresponding rate for Post Colonoscopy Colorectal Cancer (PCCRC) over the same period (2.5%).
2. CTC is commonly reserved for patients who are either deemed unsuitable for colonoscopy, or in whom colonoscopy has failed, meaning that there are likely to be substantial differences between the populations undergoing each examination.
3. Because CTC and colonoscopy are performed in different populations, those having CTC more likely to be frailer with greater co-morbidity, the higher rate of PICRC when compared to colonoscopy may relate to the difficulty of investigating such patients, who may not be fit enough for, or refuse an intervention even if a lesion is found.
Disclosure: Nothing to disclose

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P1491 IN VIVO DIAGNOSIS OF FOOD ALLERGY WITH CONFOCAL ENDOMICROSCOPY

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Introduction: The immune-mediated adverse reaction to food is defined as food allergy, which can be divided into IgE mediated or non-IgE mediated food allergy. In the majority of cases, white light endoscopy is unremarkable in patients with food allergy and hence, obtaining several biopsies within the upper and lower GI tract is an integral part in the work-up of suspected food allergy. Within this study, we aimed to assess the potential of probe-based confocal laser endomicroscopy (pCLE) as an advanced endoscopic imaging technique allowing for in vivo microscopic imaging of the intestinal mucosa for the diagnosis of food allergy.
Aims and Methods: 29 Patients with suspected food allergy manifesting with dietary-induced abdominal pain and diarrhea were included. From all patients detailed clinical information were obtained including parameters of food allergy or intolerance and diagnostic criteria of irritable bowel syndrome. In all patients ileocolonoscopy was performed using high-definition endoscopes with digital chromoendoscopy. Intestinal lavage with quantification of a large panel of markers of food allergy or intestinal inflammation including TNF, food specific IgE and eosinophilic cationic protein was performed in the terminal ileum, the caecum and the rectosigmoid junction in all patients. At these sites real-time microscopic imaging with pCLE was performed after intravenous contrast with 10% fluorescein.
Results: Of 29 patients (mean age 53 years) with suspected food allergy manifesting with dietary induced abdominal pain and diarrhea, diagnosis of food allergy was established in 19 patients (65.5%). In both, patients with and without proven food allergy, high-definition endoscopy revealed macroscopically normal mucosa. However, in patients with food allergy and macroscopically normal mucosa, pCLE showed increased cellular infiltrates within the lamina propria with crypt distension as well as vascular alterations with dilated and tortuous vessels and increased vascular branching compared to those without proven food allergy. Further, patients with food allergy exhibited signs of barrier dysfunction with increased epithelial cell shedding, epithelial gaps and erosions with fluorescein leakage into the lumen compared to patients without food allergy.
Conclusion: Patients with food allergy exhibit signs of microscopic inflammation and structural barrier dysfunction in macroscopically intact mucosa during pCLE. Thus, pCLE holds the potential to facilitate in vivo real-time diagnosis of suspected food allergy.
Disclosure: Nothing to disclose

P1492 LABEL-FREE IMAGING FOR T STAGING OF GASTRIC CARCINOMA BY MULTIPHOTON MICROSCOPY

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Introduction: Gastric cancer is one of the most common malignancies worldwide. The accurate diagnosis of tumor invasion depth is critical for therapeutic strategy and prognosis. Without fluorescent label, multiphoton imaging (MPM) could directly reveal tissue architecture based on two-photon excited fluorescence (TPEF) and second harmonic generation (SHG). In this study, we aimed to explore the feasibility of MPM to assess the gastric tumor morphology and infiltration.
Aims and Methods: Unstained slides of 18 fresh gastric tissues with different T staging were examined by multiphoton microscopy. Morphological and quantitative analysis were studied. Nuclear area was defined as the area of nuclear boundary. Collagen content was the ratio of the SHG pixels over whole pixels.
Results: Gastric normal and tumor tissues under different T stages were visually presented with cellular and subcellular features on fluorescent imaging. Nuclear area of normal and cancerous cells were $32.01 \pm 2.89\mu m^2$ and $58.41 \pm 6.06\mu m^2$ ($P < 0.001$). Collagen contents were quantified by 0.087 ± 0.012 in normal mucosa but 0.020 ± 0.007 in cancerous mucosa ($P < 0.001$). All results were correlated well with the paired H&E stained slides.
Conclusion: Our findings suggested the convincing potential of MPM for judging T staging of gastric cancer. Without staining intervention, TPEF and SHG on MPM could objectively and quantitatively indicate the subcellular and molecular changes during carcinogenesis. With the advancement of deep penetration, self-focus imaging and 3D visualization, label-free multiphoton imaging compacted with endoscopy could be further introduced to realize a real-time in vivo assessment of tumor invasion clinically.
Disclosure: Nothing to disclose

P1493 DO WE UNDERESTIMATE THE ROLE OF HYPOTHALAMIC-PITUITARY-ADRENAL AXIS ACTIVATION BY GLP-1/GLP-1 RECEPTOR AGONIST TREATMENT? FIRST DATA FROM GLP-1 RECEPTOR POSITRON EMISSION TOMOGRAPHY OF THE HUMAN PITUITARY

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Introduction: We have developed a technology for in vivo imaging of the GLP-1 receptor (GLP-1R) using Ga-68-NODAGA-exendin for PET/CT (positron emission computed tomography / computed tomography), This technology enables non-invasive in vivo quantification of radiotracer uptake into tissues, representing a measure for GLP-1R density. During clinical studies measuring beta cell mass with this technology in patients with diabetes, we have observed a high uptake into the dorsal pituitary. Here, we analyse the first in human imaging data of the pituitary and formulate a hypothesis concerning the role of pituitary GLP-1R signalling.
Aims and Methods: Pituitary uptake in Ga-68-NODAGA-exendin for PET/CT scans obtained in prospective clinical studies in patients before and after bariatric surgery was quantified. Patients with type 2 diabetes (T2D) and morbid obesity (body mass index (BMI) >40 or BMI >35 with co-morbidity) prior to or 1 year after bariatric surgery were included. PET/CT from pelvis to skull was performed one hour after injection of 100 MBq of Ga-68-NODAGA-exendin. The maximum standardized uptake value (SUVmax) was measured in a volume of interest (VOI) placed in the sella turcica.
Results: To date, we have collected data from 4 patients after bariatric surgery (the last patients from a finalized cross sectional analysis pre/post bariatric surgery) and 9 patients before bariatric surgery (from an ongoing longitudinal study). Analysis of these data revealed a marked inter-individual difference in the pituitary uptake but also a clearly higher uptake in patients prior to bariatric surgery. The uptake ranged from 0.83 to 2.8 (average 1.81 ± 0.99) in the post bariatric surgery group and from 1.9 to 9 (average 4.5 ± 2.46) in the pre bariatric surgery group, with only a slight overlap between groups. No uptake in other areas of the central nervous system has been observed in any of the patients.
Conclusion: Although the number of patients analysed so far is limited and we have switched to whole-body scanning only during a running a cross-sectional study in order to assess the tissue distribution of GLP-1R in humans, the high radiotracer uptake indicates towards a highly relevant physiological action of GLP-1 in the pituitary. We hypothesise that the pituitary is an important target for GLP-1R signalling to the central nervous system and that in morbidly obese individuals or individuals with poorly controlled diabetes, the hypothalamic-pituitary-adrenal (HPA) axis is highly sensitive to GLP-1-mediated activation (Sharma et al 2014; Chiodinin et al 2006). The pituitary uptake may be directly related to increased cortisol levels in obese T2D patients and may predict failure or even contradictory effects of GLP-1 receptor agonist (GLP-1RA) treatment (Mikulaskov et al 2016, Diz-Chavez et al 2016). Furthermore, GLP-1R expression levels seem to decrease after bariatric surgery, which may indicate towards reduced HPA axis activity, potentially explaining in part weight loss and improved glycaemic control. Due to the close anatomical proximity and the limited spatial resolution of PET/CT, binding of Ga-68-NODAGA-exendin to the infundibular nucleus of the hypothalamus (IFN) is an alternative to neuropituitary binding. Further studies are warranted to exactly determine the role of GLP-1R signalling in the pituitary/IFN, including the correlation of pituitary/IFN uptake of Ga-68-NODAGA-exendin with cortisol production, glycaemic control, body weight (loss) and other important parameters.
Disclosure: Martin Gotthardt is patent holder for exendin analogs for imaging

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P1494 SPATIO-TEMPORAL MAPPING OF GASTROINTESTINAL MOTILITY USING MRI AND COMPUTER POST-PROCESSING: A PROOF OF CONCEPT STUDY

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Introduction: MRI is increasingly used to assess gastrointestinal motility and post-processing methods add value through objectively assessing the presence or absence of contractile activity. Such metrics often do not offer insights into the nature of contractile action, rather their presence or absence. Greater insight may be needed to determine how changes in contractile frequency, amplitude or contraction length may be associated with gastrointestinal symptoms. The objective of this study was to provide preliminary validation of an MRI based method to generate a spatio-temporal map of contractile activity in the stomach and colon.
Aims and Methods: Two cohorts of subjects were selected displaying 1) gastric ($n=24$) and 2) colonic motility ($n=20$). Subject preparation and disease status was heterogeneous to provide a spectrum of motility on which to test the spatio-temporal motility assessment technique. The technique involved delineating the bowel lumen along with inner and outer bowel wall along a chosen section of the gastrointestinal tract. A series of diameter measurements were made automatically at a 2mm interval orthogonal to the central axis of the lumen. These measurements were automatically propagated through the time series using a previously validated image registration algorithm. Contractions were quantitatively summarised with two methods measuring 1) Normalised Contraction Plot (NCP) and 2) Combined Velocity Distance (CVD). Both metrics were correlated against a three-point subjective but consensus scoring system for the gastric data and a previously validated numerical, semi-quantitative scoring system for the colonic data.
Results: Good correlation was seen between reader scores and both motility metrics (NCP, $R=0.85$, $P<0.001$, CVD, $R=0.93$, $R<0.001$) in the gastric data. Good correlation was also seen between the reader scores and the two metrics in the colonic data (NCP, $R=0.82$, $P<0.001$, CVD, $R=0.78$, $R<0.001$).
Conclusion: Spatio-temporal mapping of the stomach and colon correlates well with reader scores in a range of datasets and provides both a quantitative and qualitative means of assessing contractile activity in the gastrointestinal tract.
Disclosure: Alex Menys is the CEO of Motilent ltd.

P1495 SHORT- TERM AND LONG-TERM OUTCOMES OF SELF-EXPANDABLE METALLIC STENT PLACEMENT AS A BRIDGE TO SURGERY FOR MALIGNANT COLONIC OBSTRUCTION

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Introduction: In Japan, self-expandable metallic stent (SEMS) placement for malignant colorectal obstruction has been performed from 2012. However, SEMS placement as a bridge to surgery (BTS) is not recommended in the European Society of Gastrointestinal Endoscopy Clinical Guideline. Additionally, malignant effects of SEMS placement as BTS on long-term outcomes have not been broadly recognized. Therefore, we retrospectively reviewed the records of patients to clarify the safety and efficacy of SEMS placement and short-term and long-term outcomes of BTS.
Aims and Methods: Three-hundred-ninety-two patients who underwent surgery for colorectal cancer (pStages II, III, and IV) in our hospital from May 2012 to August 2017 were reviewed. Of the 392 patients, 54 patients with malignant colorectal obstruction underwent BTS (group A), and 338 patients without malignant colorectal obstruction underwent surgery (group B). First, we evaluated short-term outcomes of the BTS group. Second, we compared long-term outcomes between the two groups as the 3-year overall survival (3yOS) and 3-year disease-free survival (3yDFS) rates for each stage.
Results: Patients' mean ages were 70 years (group A) and 73 years (group B), and the male-to-female ratios were 25:29 (group A) and 182:156 (group B). Tumor sites (cecum/ascending/transverse/descending/sigmoid/rectum) were 2/6/5/8/32/1 (group A) and 37/58/35/16/135/57 (group B). The pStages (II/III/IV) were 21/19/14 (group A) and 153/120/65 (group B), with no significant differences between the groups. Regarding SEMS placement in group A, technical and clinical success rates were 98% (54/54) and 92% (53/54), respectively. Colonoscopy for preoperative evaluation of the proximal colon was performed in 45 patients (83.3%), and synchronous multiple cancers in the proximal colon were found in 8 patients (14.8%). The only severe complication of SEMS placement was one case of perforation due to obstructive colitis. Regarding long-term outcomes, 3yOS/3yDFS rates were 95%/83.1% (group A) and 88.0%/81.9% (group B) in pStage II, and 66.2%/57.3% (group A) and 87.2%/66.2% (group B) in pStage III. The 3yOS rates were 42.0% (group A) and 35.1% (group B) in pStageIV. No significant differences were observed between the groups in long-term outcomes (median follow-up periods were 763 days in group A and 738 days in group B), using the Kaplan-Meier method and long-rank test.
Conclusion: SEMS placement can be effectively and safely performed, and contribute to preoperative evaluation of the proximal colon. According to long-term outcomes, the BTS group was not inferior to the normal surgery group despite the higher malignant potential due to malignant colorectal obstruction. These findings suggest that the malignant effects of SEMS placement as BTS on long-term outcomes may be small in cases in which the perforation rates were low.
Disclosure: Nothing to disclose

P1496 THE BOUGIECAP: A NEW METHOD FOR TREATMENT OF OESOPHAGEAL STRICTURES

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Introduction: Non-malignant strictures in the upper GI tract are often treated endoscopically by using polyvinyl Savary-Gilliard dilators. However, the drawbacks to this technique are the lack of direct optical feedback of the bougienage and the need for fluoroscopic guidance during the procedure. A novel device, BougieCap (Ovesco, Tuebingen, Germany), allows direct optical control of bougienage.
Aims and Methods: Patients with a benign stenosis of the oesophagus and with clinical symptoms of dysphagia were recruited from two endoscopy centres for planned dilatation with the BougieCap. The device, which is a single-use transparent conical cap, is fixed to the tip of the endoscope. Different sizes for standard gastroscopes and pediatric scopes are available. For the bougienage procedure the endoscope is inserted and positioned in front of the stenosis. Under direct vision, pushing forward with the endoscope enables the conical cap to dilate the mucosa in the area of the stenosis by the conversion of longitudinal force vectors into radial force vectors. Endoscopic procedure could be repeated sequentially with a larger sized cap if necessary. Primary endpoint of the study was success of endoscopic dilatation. Secondary endpoint was improvement of symptoms of dysphagia as assessed by Dysphagia Handicap Index (DHI) before and 14 days after bougienage (dysphagia score 0: No dysphagia: able to eat normal diet; 1: Moderate passage: able to eat some solid food; 2: Poor passage: able to eat semi-solid foods; 3: Very poor passage: able to swallow liquids only; 4: No passage: unable to swallow anything).
Results: 23 patients (m/f, 11/12) underwent the procedure, mean age was 69.9 years (±18.7). Etiology of strictures was peptic (n = 9), radiation (n = 8), anastomosis (n = 3), caustic ingestion (n = 2) or unknown (n = 1). Median diameter of strictures was 9 mm (±2.3). Successful dilatation with BougieCaps was possible in 91% (n = 21). Symptoms of dysphagia decreased from a mean dysphagia score of 3.0 (±0.6) before endoscopic treatment to 1.7 (±0.7) 14 days after treatment (Mann-Whitney, $p<0.0001$). A stiff guide-wire was used in 4 cases to aid with bougienage, exclusively using a pediatric scope. In two cases with a narrow stricture and no usage of guide wire treatment failed as a result of high resistance at the site of stricture causing buckling of the endoscope in the pharynx. On average 2.3 (±0.2) BougieCaps of subsequent sizes were used per patient. No severe complications were reported. Adverse events were loss of 2 BougieCaps in the stomach causing no symptoms.
Conclusion: Endoscopic treatment of benign stenoses using the BougieCap enables direct visual control of the bougienage procedure and therefore of mucosal damage within the area of strictures. This might help to adapt endoscopic treatment even more precisely to the stricture. Symptoms of dysphagia are improved in short-term follow-up. Additional wire guidance is reasonable for selected cases (narrow lumen, pediatric scope).
Disclosure: Nothing to disclose

P1497 SHORT AND LONG-TERM RESULTS OF SELF-EXPANDABLE METAL STENTS FOR ACUTE MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metal stents (SEMS) are widely used as an alternative to surgery for palliation purposes or as bridge-to-surgery (BTS) in acute malignant colorectal obstruction (MCRO), despite concerns about the effect of stenting on adverse events (AEs) and long-term survival.
Aims and Methods: Our aim was to evaluate SEMS clinical success, AEs and impact on short and long-term outcomes.
We performed a retrospective study from 92 consecutive patients with acute MCRO that placed SEMS in a tertiary center between January 2010 and December 2017.
Results: Forty-nine patients placed SEMS as BTS and 43 for palliative purposes. The median age of the patient population was 69 years (IQR 61–79), and 55.4% of the patients were male. Most of the obstructions (96.7%) were on the left colon. At the time of the procedure, based on additional imaging studies after colonic stenting and perioperative findings, 72.8% of patients (n = 67) had lymph node invasion and 58.7% (n = 54) had metastatic disease. Long-term clinical

success was achieved in 84.8% of the patients, with no significant differences between palliation and BTS groups (81.4% vs. 87.8%; p = 0.562). Clinical success was higher when tumor location other than sigmoid (94.3% vs. 78.9%; p = 0.047) and when shorter SEMS (< 110 mm) were placed (100% vs. 64%; p = 0.002). Immediate and post-procedure AEs occurred in 6.5% and 17.3% of the patients, respectively, with no significant differences between the palliative and BTS group. The main post-procedure AEs were perforation (n = 6) and stent re-obstruction (n = 6). Nineteen percent of the palliative cohort were considered clinical failures, with 87.5% of them requiring further surgery; 11.6% of the palliative group were left with a permanent stoma; surgery-related AEs did not occur in patients with previous SEMS AEs; the occurrence of SEMS AEs did not influence overall survival. Twelve percent of the patients in the BTS group were considered clinical failures. Surgery was performed after a median time of 10 days (IQR 7–17) and was urgent in 12.2% of the patients; 16.3% of the BTS group were left with a permanent stoma. SEMS immediate (p = 0.542) and post-procedure AEs (p = 0.360) were not associated with tumor recurrence. Patients with post-procedure SEMS AEs had an inferior overall survival (median: 161 vs. 1592 days; p = 0.047). In the multivariate analysis, only SEMS-related AEs were independently associated with overall survival estimation (HR 4.06, 95% CI 1.2–13.7; p = 0.024).

Conclusion: SEMS allow relief of acute MCRO; yet, AEs are seen in almost 20% of patients. Main contributors for surgery after stent failure are perforation and stent re-obstruction. SEMS should be the first line option for palliation even in patients with longer life expectancy. In the BTS setting, SEMS-related AEs decrease survival.

Disclosure: Nothing to disclose

P1498 TWO DECADES AFTER THE FIRST, WHAT ARE THE OUTCOMES OF DUODENAL STENTING: EXPERIENCE OF A FRENCH TERTIARY CENTER ABOUT 220 CASES

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Introduction: Malignant gastric outlet obstruction (MGOO) often complicates the natural history of pancreatic adenocarcinoma but not only. However, the use of gastroduodenal self-expandable metal stents (GD-SEMS) has improved life's quality of these patients. In current practice, the effectiveness of these GD-SEMS seemed imperfect and we wanted to report our results including all neoplastic diseases.

The main aim was to evaluate patients' diets using the level of oral intake score (LOIS, 0: no oral intake, 1:liquids only, 2:soft solid, 3:full diet). The secondary endpoints were the evaluation of the complication rate, the median survival, the endoscopic duodenal reintervention rate, the endoscopic biliary reintervention rate, as well as the attempt to identify groups where the efficiency would be better or worse.

Aims and Methods: We retrospectively included all patients who underwent one or more GD-SEMS between January 2011 and December 2016 in our center (Paoli-Calmettes Institute Marseille, France). All datas was calculated using the computerized record of each patient including dietary assessments and medical observations.

Results: We included 220 patients (women = 56%, mean age = 67 [29–94]). Median time of hospitalization was 7 days [1–52]. 50% of patients had pancreatic adenocarcinoma and 50% had another malignant disease. WHO score was inferior at 3 in 122/220 cases (56%). The two most frequent locations of MGOO are second duodenum (91/220 = 41%) and genu superius (46/220 = 21%). 66% of the patients (145/220) had already undergone oncological treatment before the first stent placement and 34% (75/220) had received no treatment. Median LOIS before GS-SEMS was 0[0–2]and median LOIS after was 2[0–3]. Median increase of LOIS was 2 ($p < 0.001$). This increase of LOIS patients was more important for patients with general state preserved (WHO score < 3): 1.90 vs 1.40; $p < 0.001$. The complication rate was 2%(4/220) with 3 perforations. The median survival was 4 months. At 1 month, the duodenal reintervention rate and the biliary reintervention rate were respectively 27% and 19%. During follow-up, 150/220 (68%) patients needed only one duodenal procedure and 70/220 (32%) needed multiple duodenal procedures. The median permeability of GD-SEMS was 2.3 months and GD-SEMS was significantly more longer effective in the WHO score < 3 group versus WHO score > 2 group (3.81 vs 1.51; $p < 0.001$). Median permeability was also better significantly in the subgroup oncologic treatment post GD-SEMS than subgroup no oncologic treatment post GD-SEMS (4.76 vs 1.25; $p < 0,01$). No significantly difference was observed between subgroups pancreatic cancer and other malignant diseases (2.37 vs 2.17; p = 0.733).

Conclusion: Our study is in agreement with the data of the literature. GD-SEMS are, thought imperfect, effective on dysphagia with a low risk of complications (2%). Unlike the clinical impression we had, multiple endoscopic procedures are not systematic since they concern only 32% of patients. The duration of hospitalization is relatively long probably because it is about fragile patients whose duodenal stricture is not the only health problem. Given the very low median survival (4 months), this endoscopic treatment seems to always be adequate or even sufficient in most cases. However, the subgroup analysis makes it possible to identify a subgroup for which the efficiency is better and more durable (WHO score < 3, palliative chemotherapy post GD-SEMS). This subgroup could represent in the future the good candidates for endoscopic bypass.

Disclosure: Nothing to disclose

P1499 BARIATRIC ESOPHAGEAL STENTS AND ENDOSCOPIC SUTURING SYSTEM FOR ENDOSCOPIC MANAGEMENT OF POST-LAPAROSCOPIC SLEEVE GASTRECTOMY LEAKS: A SINGLE-CENTER EXPERIENCE

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Introduction: Sleeve leak is the most feared complication after laparoscopic sleeve gastrectomy (LSG), causing significant morbidity and mortality. Endoscopic treatment with fully covered self-expandable metal stents (FC-SEMS) may offer a useful non-invasive approach in this setting. BETA^{TM} esophageal stents (Taewoong Medical Co., Gyeonggi-do, South Korea) are FC-SEMS specifically designed for post-bariatric leaks to reduce risk of migration. Moreover, endoscopic suturing with APOLLO OverStitch^{TM} has been described as a therapeutic approach for large gastrointestinal leaks.

Aims and Methods: In this study, we aimed to report our experience in managing post- LSG leaks with BETA^{TM} esophageal stents with or without previous endoscopic suturing. We retrospectively reviewed all cases of endoscopic management of post-LSG leaks with BETA^{TM} esophageal stents and APOLLO OverStitch^{TM} suturing system referred at our institution from June 2014 to July 2017. Type of endoscopic treatment, number of procedures, outcome and complications were analyzed.

Results: Thirteen patients treated using BETA^{TM} esophageal stents for post-LSG were included in this retrospective analysis. Eight patients (61.5%) received previous unsuccessful endoscopic treatments (pig-tail plastic stent, clips, conventional FC-SEMS). Eight patients (61.5%) who presented with larger leaks underwent a combined endoscopic approach with both endoscopic suturing and BETA^{TM} stent, while 5 patients (38.5%) with smaller leak were treated using only BETA^{TM} stent. The overall success rate was 92.3% (12/13). One patient finally underwent gastrectomy after failure of multiple endoscopic procedures. A total of 16 BETA^{TM} stent were placed, which were left in place for a median of 27 days (range 16–53). No stent migration or serious adverse events were observed during a mean follow-up of 3.6 months (range 0–11).

Conclusion: In our experience, endoscopic management of post-LSG leaks with BETA^{TM} is safe and effective, with high rate of clinical success and no significant adverse events. The combined approach with APOLLO OverStich^{TM} endoscopic suturing system seems safe and effective in case of larger leaks. Further multicentric randomized controlled trial are needed to confirm these data.

Disclosure: Nothing to disclose

P1500 ETIOLOGICAL SPECTRUM AND RESPONSE TO ENDOSCOPIC BALLOON DILATION IN PATIENTS WITH BENIGN GASTRIC OUTLET OBSTRUCTION

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Introduction: Peptic ulcer disease (PUD) related gastric outlet obstruction (GOO) is known to respond favourably to endoscopic balloon dilation (EBD). However, data on efficacy of EBD for other etiologies of benign GOO is sparse.

Aims and Methods: We aimed to compare response of EBD among different etiologies of GOO.

Records of all patients with benign GOO who underwent EBD at our tertiary care centre between January 1998 to December 2017 were analysed. Dilation was done using through-the-scope balloons. Procedural and clinical success of EBD was compared amongst different etiologies.

Results: A total of 306 patients were evaluated, of whom, 264 (mean age – 37.89 ± 17.49; males – 183, females – 81) underwent dilation. Etiologically caustic ingestion was the commonest cause of GOO (53.8%) followed by drug abuse (21.6%) and PUD (12.87%). Overall procedural and clinical success was achieved in 200 (75.7%) and 243 (92.04%) patients respectively requiring a mean (SD) of 2.55 (2.81) and 5.37 (3.98) sessions respectively. Caustic related GOO responded less favourably, requiring a higher number of dilation sessions and having more refractory strictures than other etiologies. Drug induced GOO performed worse than PUD related GOO. Of the 264 patients, 9 (3.4%) had perforation during EBD, 3 of them had contained leak and were managed conservatively, while 6 patients underwent successful surgery.

Conclusion: EBD is successful in a majority of patients with benign GOO, with caustic-GOO and drug-induced GOO being more different than PUD-related GOO

Disclosure: Nothing to disclose

P1501 DILATION OF BENIGN OESOPHAGEAL STRICTURE: LONGITUDINAL STUDY IN A MOROCCAN ENDOSCOPY UNIT

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Introduction: Benign oesophageal stricture is a rare condition which can result from various causes such as peptic or caustic oesophagitis, radiation, or anastomosis. Endoscopic dilation is an effective treatment nowadays and can be performed in different manners. The aim of our work is to report the experience of our gastroenterology unit in a Moroccan university hospital concerning dilation of benign oesophageal stricture and to compare hydrostatic dilation with Savary Gillard bougie dilation.

Aims and Methods: The prospective study was led between January 2009 and January 2018 and included 130 patients with benign oesophageal strictures. We compared the outcome of two groups of patients following the method used (Group 1: bougie dilators, Group 2: balloon dilation). We studied the correlation between the number of sessions, the long-term outcome and each method. We used the chi-squared test and Fisher test for the study with a p-value <0.05. Propofol sedation was used for all the patients.

Results: Within 130 patients, 39% were male, and 61% were female. The average age was 42 years. Oesophageal strictures were from peptic origin in most of the cases (34.6%), followed by Plummer-Vincent syndrome in 31.5%, anastomotic strictures in 13%, post radiation strictures in 8.4%, and caustic strictures in 12%. One case of mycotic stenosis was reported in a HIV-positive patient. Group 1 (bougie dilators) included 111 patients (86%) and Group 2 (balloon dilation) included 19 patients (14%). 270 sessions of dilation were realized with an average of 2.2 sessions per patient (from 1 to 10). No complication was noted, and the success rate was 95% and 5% underwent surgery.

Comparing the two groups for the number of dilation sessions needed did not yield a significant correlation ($p=0.359$). The correlation between the two groups for the long term outcome was also not significant. A significant correlation was found between the type of stricture and the number of dilation sessions needed ($p=0.02$). Strictures caused by the Plummer-Vincent syndrome and peptic ones needed the least number of dilation sessions (more than 50% of patients did not need more than 2 dilation sessions) and had all a satisfying result (100%). Multivariate analysis between the type of stricture and the long term outcome yielded a significant correlation ($p < 0.05$).

Conclusion: Endoscopic dilation of benign oesophageal strictures is an efficient technique, especially in the case of Plummer-Vincent Syndrome and peptic strictures. Complications are rare if the procedure is followed properly. In our study, results confirmed that endoscopic dilation is a safe and efficient treatment for dysphagia. Bougie dilators remain also the most used technique in our experience.

Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 09:00–14:00

Surgery III – Hall X1

P1502 A NOMOGRAM TO PREDICT LYMPH NODE METASTASIS IN PATIENTS WITH EARLY GASTRIC CANCER

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Introduction: Lymph node metastasis (LNM) is the most important risk factor for endoscopic surgery in early gastric cancer (EGC) patients. We aimed to investigate the rate of LNM, analyze the endoscopic and clinicopathological features related to LNM, and investigate risk factors of EGC with LMN.

Aims and Methods: A total of 10039 patients and underwent gastrectomy with lymphadenectomy were reviewed between January 2010 and December 2015 at Jiangsu Province Hospital in China. Among them, we identified 1004 (10%) EGCs. First, endoscopic and clinicopathological features related to LNM were analyzed, then risk factors for LNM were identified using univariate and multivariate analysis. Finally, a nomogram for predicting LNM was established and validated.

Results: LNM occurred in 123 (12.3%) EGC. Most of EGCs were male ($n=720$,71.7%) and mean age was 59.65 ± 11.09 years. The rate of *H.pylori* infection was 78.0%(783/1004). LNM was significantly associated with age, sex, location, lesion size, macroscopic type, depth of invasion, differentiation type, histological morphology, lymphovascular invasion (LVI) and TMN stage. By multivariate analysis, significant independent risk factors for LNM in EGC were identified as following, male sex (OR 2.365, 95% CI 1.064–5.257, $P=0.035$), depressed type (OR 2.721, 95% CI 1.232–6.008, $P=0.013$), submucosa invasion (OR 2.987, 95% CI 1.100–8.111, $P=0.032$), LVI (OR 5.186, 95% CI 1.751–15.366, $P=0.003$), tumor located in corpora (OR 8.904, 95% CI 1.029–77.07, $P=0.047$), tumor located in angle (OR 12.998, 95% CI 1.400–120.677, $P=0.024$). Moreover, a predictive nomogram with these independent factors for LNM in EGC patients was constructed. After external validation, the AUROC curve for predicting LNM was 0.863, respectively.

Conclusion: EGC were investigated in 10.0% of gastric cancer, which LNM occurred in 12.3% of EGC. Independent risk factors of LNM included male sex, macroscopic type, the depth of invasion, LVI and tumor located in corpora or angle. A nomogram was successfully established, which may help to predict LNM in patient with EGC and evaluate endoscopic submucosal dissection feasibility in EGCs.

Disclosure: Nothing to disclose

P1503 POPULATION-BASED STUDY ON RISK FACTORS FOR TUMOR-POSITIVE RESECTION MARGINS IN PATIENTS WITH GASTRIC CANCER

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Introduction: Radical gastrectomy is the cornerstone of the treatment of locally advanced gastric cancer. An irradical resection, i.e. gastrectomy with a tumor-positive resection margin, is seen in approximately 1.8–8.4% of patients.[1]

Aims and Methods: This study aimed to evaluate factors associated with a tumor-positive resection margin after gastrectomy and to evaluate the influence of hospital volume.

In this national cohort study, patients with junctional or gastric cancer that underwent curative gastrectomy between 2011–2017 were included. The primary outcome was irradicality of the operation defined as the microscopic presence of tumor cells at the resection margin. The association of patient- and disease characteristics with irradicality was tested with multivariable regression analysis. The association of annual hospital volume with irradical resections was tested and adjusted for the patient- and disease characteristics.

Results: In total, 2799 patients were included. An irradical resection was seen in 265 (9.5%) patients. Factors associated with irradicality were: tumor located in the entire stomach (OR[95%CI]: 3.38[1.91–5.96] reference: gastro-esophageal junction), cT3, cT4, cTx (1.75[1.20–2.56], 2.63[1.47–4.70], 1.60[1.03–2.48], reference: cT0-2), pN+ (2.73[1.96–3.80], reference: pN-), and diffuse and unknown histological subtype (3.15[2.14–4.46] and 2.05[1.34–3.13], reference: intestinal). Unknown differentiation grade was associated with a decrease risk for an irradical resection (0.50[0.30–0.83], reference: poor differentiated/undifferentiated). Compared to a hospital volume of <20 resections/year, 20–29 and >39 resections was associated with lower probability for irradicality (OR 0.56[0.42–0.76] and 0.34[0.18–0.64]).

Conclusion: Tumor location, cT, pN, histological subtype and tumor differentiation are associated with irradicality. The association of irradicality with an annual hospital volume of <20 resections may underline the need for further centralization of gastric cancer care in the Netherlands.

Disclosure: Nothing to disclose

Reference

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P1504 POSTOPERATIVE OUTCOMES OF THE DUTCH UPPER GASTROINTESTINAL CANCER AUDIT ACCORDING TO THE PLATFORM OF THE ESOPHAGEAL COMPLICATIONS CONSENSUS GROUP

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Introduction: To standardize outcome reporting in esophageal surgery, the Esophageal Complications Consensus Group (ECCG) developed a standardized platform. Recently, this group published outcomes of 2704 patients that underwent an esophagectomyin 24 high-volume hospitals in the period 2015–2016.

Aims and Methods: The aim of this study was to report postoperative morbidity and mortality in the Netherlands using the definitions of the ECCG. All patients who underwent esophagectomy for cancer of the esophagus or esophagogastric junction in the Netherlands in 2016 were selected from the Dutch Upper gastrointestinal Cancer Audit (DUCA). Patient outcomes including postoperative complications, 30-day/in-hospital mortality and readmission rate were reported according to the definitions of the ECCG platform.[1] Outcomes of the DUCA were compared with the recently published outcomes of the ECCG[2] with Chi-square analysis.

Results: Some 797 patients were included from 22 hospitals. In 1 patient, the postoperative outcome was unkown. In 17 patients readmission status was unknown. Some 168 (21%) patients had an ASA score of $\geq$III and 250 (31%) patients a Charlson comorbidity score of $\geq$2. In total, 498 patients (63%) had at least one postoperative complication (versus ECCG: 57%, $p=0.07$). The most common complications were pneumonia (21% DUCA versus 15% ECCG, $p < 0.01$), anastomotic/staple-line failure or localized conduit necrosis (18% versus 11%, $p < 0.01$) and atrial dysrhythmia requiring treatment (13% versus 15%, $p=0.28$). Readmissions occurred in 105 of 780 patients (13%(ECCG 11%, $p=0.13$). The 30-day/in-hospital mortality was 2.5% for the DUCA group and 2.4% for the ECCG group ($p=0.88$).

Conclusion: The registration of complications according to the ECCG platform in the national audit promotes the use of uniform definitions and allows international comparison of outcomes. The overall complication rate, readmission

rate and mortality in the Netherlands were comparable with the outcomes of the ECGG. However, anastomotic leakage and pneumonia were more frequently reported in the Netherlands.
Disclosure: Nothing to disclose

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P1505 NATIONWIDE OUTCOME OF GASTRECTOMY WITH EN-BLOC PARTIAL PANCREATECTOMY FOR GASTRIC CANCER

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Introduction: Radical gastrectomy is the cornerstone of the treatment of gastric cancer. For tumours invading the pancreas, an en-bloc partial pancreatectomy may be needed to obtain a radical resection.
Aims and Methods: The aim of this study was to evaluate the outcome of gastrectomies combined with partial pancreatectomy for gastric cancer. Patients who underwent gastrectomy with or without a partial pancreatectomy for gastric cancer or gastro-oesophageal junction cancer between 2011–2015 for gastric were selected from the Dutch Upper GI Cancer Audit (DUCA). Outcome parameters were the pathological resection margin (pR0) and Clavien Dindo grade ^{3}III postoperative complications. The association between partial pancreatectomy and severe postoperative complications was analysed with multivariable logistic regression. Overall survival was estimated using the Kaplan Meier method and subgroups were compared using log-rank test.
Results: Of 1966 patients that underwent a gastrectomy, 55 patients (2.8 per cent) also underwent an en-bloc partial pancreatectomy. A pR0-resection was achieved in 45 of 55 patients (82 versus 85 per cent in the group with no additional resection, $p = 0.82$). Clavien Dindo grade ^{3}III complications occurred in 21 of 55 patients (38 versus 17 per cent). Pancreatectomy increased the odds of having a Clavien Dindo grade ^{3}III complication (OR: 3.13, 95 per cent c.i. 1.76–5.59). Median overall survival [95 per cent c.i.] of patients with partial pancreatectomy was 15[6.8–23.2] months, for patients with and without perioperative systemic therapy, it was 20[12.3–27.7] and 10[5.7–14.3] months, and for patients with R0 and R1/R2 resection it was 20[11.8–28.3] and 4[0.0–10.9] months.
Conclusion: Gastrectomy with partial pancreatectomy is associated with an pR0-resection rate of 82 per cent but an 3-fold increased risk for postoperative morbidity.
Disclosure: Nothing to disclose

P1506 ROOT-CAUSE ANALYSIS OF SERIOUS ADVERSE EVENTS AFTER SURGERY FOR GASTRIC CANCER

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Introduction: In the Netherlands and Rotterdam region, postoperative mortality after surgery for gastric cancer was considerably higher than for any other type of cancer surgery.
Aims and Methods: To determine modes of failure and to develop proposals for preventive measures to decrease mortality, confidential review meetings were organised and supervised by a committee of experts.
Gastric cancer patients operated between 1999 and 2008 were selected from the regional cancer registry for 16 hospitals in the south-western part of the Netherlands. Per hospital, a maximum number of 9 cases with postoperative death or prolonged hospital stay were selected for review. Chart review was performed within the regional hospitals using an incident analysis tool the so-called Prevention and Recovery Information System for Monitoring and Analysis (PRISMA methodology). The primary goal of PRISMA is to systematically identify and classify causes of errors. Causes of error were classified into technical, organisational, human, patient-related or not specified using the Eindhoven Classification Model.
Results: The review comprised 106 patients with a median age of 74 years. There was considerable heterogeneity in protocols concerning diagnostic work up, surgery, postoperative care and treatment of complications between hospitals and surgeons. The most frequent technical complication was anastomotic leakage ($n = 27$) or duodenal stump dehiscence ($n = 11$). Some 56% of the operations were classified as high-risk procedures because of patient frailty or the extent of surgery. Human error was considered contributory in 65% of the cases, mainly for not adapting the treatment plan or related to insufficient preoperative examination. Organisational failure was less important, with 'culture of overconfidence' listed as the main factor.
Conclusion: A qualitative approach is able to highlight modes of failure for gastric cancer surgery. This study shows that serious adverse events for gastric cancer surgery often tend to occur when three or more contributing causes coalesce, *i.e.* patient-, surgeon- and organisational factors. Outcome after gastrectomy for cancer could possibly be improved by regional audits that will reveal areas for improvement and stimulate standardization of (surgical) protocols.
Disclosure: Nothing to disclose

P1508 THE IMPACT OF BODY POSITION ON GASTRIC EMPTYING AFTER PANCREATICODUODENECTOMY

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Introduction: Abnormal gastric emptying velocity is a common complication after surgery of the upper intestine. Particularly after pancreaticoduodenectomy (PD), gastric emptying can be impaired (pylorus preserving procedure) or accelerated (classic Whipple procedure – pylorus resection). In this trial we aimed to study the impact of body position in gastric emptying in patients after PD and its impact on postprandial glucagon-like peptide-1 (GLP-1), insulin and glucose plasma concentrations.
Aims and Methods: 38 patients after PD, 19 subjects in sitting and 19 in supine position, were studied 2–118 (median: 19) months after the operation. Median age was 63 years, the male/female ratio 1.1, and body mass index 22.6 kg/m^2. 21 of the patients had undergone a pylorus preserving PD and 17 a classical Whipple procedure. All subjects ingested a mixed liquid test meal containing 1 g acetaminophen to measure gastric emptying. Before the meal and 10, 20, 30 and 60 minutes thereafter venous blood was drawn for the measurement of GLP-1, acetaminophen, glucose, and insulin.
Results: Fasting glucose, fasting insulin, the early integrated concentrations of acetaminophen and GLP-1 (0–30 min.) as well as integrated concentrations over 0–60 minutes of glucose and insulin are presented in Table 1. Gastric emptying speed revealed to be different between sitting and supine body position (Figure 1, Table 1). Postprandial GLP-1, insulin and glucose plasma concentrations showed no differences between the groups. Velocity of gastric emptying did not influence integrated insulin and glucose concentrations (0–60 min.). Body position had no impact on postprandial early integrated GLP-1 plasma concentrations.
Conclusion: Body position – sitting vs. supine – showed to have a significant effect on gastric emptying speed in patients after PD, sitting subjects emptied their stomachs faster. Be that as it may, no further impact of body position on postprandial glucose, insulin and GLP-1 plasma levels could be shown.

	Sitting body position	Supine body position	*p-value**
Acetaminophen			
integrated 0–30 (mg/l × min)	322.5 (251.5–486.5)	217,75 (128.9–367.8)	<0.005
Glucose			
fasting concentration (mg/dl)	98 (88–114)	96.5 (85.3–110.8)	n.s.
integrated 0–60 (mg/dl × min)	8505 (6705–9715)	8005 (6025–8475)	n.s.
Insulin			

(continued)

Continued

	Sitting body position	Supine body position	*p-value**
fasting concentration (mU/l)	3.9 (1–7.3)	5.3 (2.9–8.8)	n.s.
integrated 0–60 (mU/l × min)	1028.9 (775.1–2143.3)	1067.7 (678.2–2550.6)	n.s.
GLP-1			
fasting concentration (pmol/l)	17 (12–20)	16.5 (12.75–18.25)	n.s.
integrated 0–30 (pmol/l × min)	2270 (1405–2894)	1322.5 (767.5–3170)	n.s.

*Wilcoxon-test

[Table 1. Acetaminophen, glucose, insulin and GLP-1 plasma concentrations after PD in sitting and supine body position (median and quartiles)]

Disclosure: Nothing to disclose

P1509 GENETIC POLYMORPHISMS OF INTERFERON GAMMA (IFN-γ) IN MEXICAN-MESTIZO PATIENTS WITH ABDOMINAL SEPSIS

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Introduction: Sepsis is a common and devastating disease that contributes a significant burden to global health care. After pulmonary sepsis, abdominal sepsis is the second most common form of sepsis and requires an intensive care unit to treat affected patients. Pathogenesis of sepsis and its complications involve numerous cytokines and endothelial factors that have pro- and anti-inflammatory effects. Interferon-gamma (IFN-γ) is an important regulator of infection and inflammation. Interferon-gamma (IFN-γ) is the only member of the type IFN II family. INF-γ inhibits viral replication directly and is produced predominantly by natural killer (NK) and natural killer T (NKT) cells as part of the innate immune response. It is also produced by effector T cells. IFN-γ is regulated by cytokines secreted by antigen-presenting cells, most notably interleukin (IL)-12 and IL-18. The IFN-γ gene is located on chromosome 12q14; several single nucleotide polymorphisms (SNPs) in this gene are associated with immune and infectious diseases. Further, some polymorphisms are associated with septic processes induced by trauma and respiratory infections

Aims and Methods: The aim of the present study was to evaluate IFN-γ gene polymorphisms in Mexican-Mestizo patients with abdominal sepsis (AS) and to determine their association with disease severity and mortality.

We recruited 120 patients with AS and 120 healthy controls and identified 2 IFN-γ gene polymorphisms, one at +874 A/T (rs2430561) and another at -1616 T/C (rs2069705), by automated DNA sequencing. Disease severity of patients with AS was evaluated according to the Acute Physiology and Chronic Health Evaluation (APACHE II) scale, Mannheim index, Controlling Nutritional Status (CONUT) score, and survival.

Results: The +874T allele (Mannheim index: Odds ratio (OR) = 1.92, 95% confidence interval (CI): 1.06–3.49, P = 0.031 and CONUT score: OR = 2.10, 95% CI: 1.16–3.83, P = 0.013), **the +874AT genotype** (CONUT score: OR = 2.74, 95% CI: 1.07–7.02, P = 0.031), **the dominant model AT+TT** (CONUT score: OR = 2.81, 95% CI: 1.19–6.68, P = 0.016), **the AC haplotype** (APACHE II scale: OR = 1.22, 95% CI: 1.03–1.46, P = 0.020), **the TC haplotype** (APACHE II scale: OR = 1.41, 95% CI: 1.15–1.74, P = 0.0007; Mannheim index: OR = 1.60, 95% CI: 1.38–2.05, P = <0.0001; CONUT score: OR = 2.08, 95% CI: 1.70–2.56, P = <0.0001), **and the TT haplotype** (Mannheim index: OR = 1.74, 95% CI: 1.29–2.35, P = 0.0002; CONUT score: OR = 1.39, 95% CI: 1.03–1.89, P = 0.020) **were significant risk factors for progression to severe AS. Whereas, the AT haplotype** (APACHE II scale: OR = 0.58, 95% CI: 0.47–0.72, P = <0.001; Mannheim index: OR = 0.53, 95% CI: 0.44–0.67, P = <0.0001; CONUT score: OR = 0.40, 95% CI: 0.32–0.50, P = <0.0001) **was significantly associated with protection against severe AS. The AC haplotype** (OR = 1.80, 95% CI: 1.55–2.21, P = <0.0001), **and the TC haplotype** (OR = 1.53, 95% CI: 1.25–1.87, P = <0.0001) **were associated with increased mortality. In contrast, the -1616T allele, the dominant model CT+TT, and the AT haplotype** (OR = 0.21, 95% CI: 0.06–0.74, P = 0.007; OR = 0.20, 95% CI: 0.05–0.81, P = 0.014; OR = 0.15, 95% CI: 0.11–0.21, P = <0.0001, respectively) **were significantly protective against death.**

Conclusion: Our study suggests an important role for IFN-γ polymorphisms in the incidence, development, and outcome of abdominal sepsis in the Mexican-Mestizo population.

Disclosure: Nothing to disclose

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P1510 LONGSTANDING POSTOPERATIVE FLUID COLLECTION INFLUENCES RECURRENCE OF PANCREATOBILIARY MALIGNANCY

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Introduction: Postoperative abdominal fluid collection (PAFC) is frequently observed after surgery for pancreatobiliary malignancy. The duration of PAFC differs among patients, and little is known about the effects of the presence and duration of PAFC. The aim of this study was to evaluate the effects of PAFC on the outcomes of surgery for pancreatobiliary adenocarcinoma.

Aims and Methods: Data from 187 consecutive patients with pancreatobiliary adenocarcinoma who underwent curative surgery between August 2005 and February 2017 were analyzed retrospectively. The presence of PAFC was evaluated by computed tomography at < 1 week postoperatively; longstanding PAFC was defined as that lasting > 4 weeks.

Results: Of the 187 patients, 143 (76.5%) had PAFC and 71 (49.7%) had longstanding PAFC. The recurrence rates of pancreatobiliary adenocarcinoma in the presence and absence of PAFC were 55.9% and 43.2%, respectively. The presence of PAFC was not associated significantly with the recurrence of pancreatobiliary adenocarcinoma (p = 0.618), but longstanding PAFC was (p = 0.046). In a subgroup analysis, longstanding PAFC was related to the recurrence of only pancreatic cancer (p = 0.021). In patients with pancreatobiliary adenocarcinoma, recurrence and cancer-specific survival (CSS) were associated with high pathologic T stages (T3-4), lymph node involvement, perineural invasion (all p < 0.001), and non-receipt of adjuvant chemotherapy (p = 0.005 and p = 0.002, respectively).

Conclusion: The incidence of PAFC in patients with pancreatobiliary adenocarcinoma after surgery was 76.5%, and 49.7% had longstanding PAFC. The presence of PAFC was not associated significantly with recurrence or CSS in patients with pancreatobiliary adenocarcinoma. However, longstanding PAFC was associated with the recurrence of pancreatobiliary adenocarcinoma.

Disclosure: Nothing to disclose

P1511 EFFICACY OF ENDOSCOPIC TREATMENT OF POST-SLEEVE GASTRECTOMY FISTULAS ACCORDING TO THE RADIOLOGICAL TYPE

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Introduction: Fistulas are the main complication of sleeve gastrectomy (SG). Several types of fistulas are distinguished according to their communication with an abscess and/or an over-diaphragmatic involvement (Type I to III). Management with an endoscopic internal drainage (EID) using a double-pigtail stent has shown encouraging results. To our knowledge, the results of this approach according to the type of fistula have not been evaluated. Thus, the originality of this study rests on the evaluation of the effectiveness of the EID according to the type of fistula.

Aims and Methods: This is a retrospective analysis of a prospective unicentric cohort of patients who developed a fistula after SG. The type of fistula was always classified initially by a CT scan with oral opacification: fistula without a communicating abscess (Type I), fistula with a communicating abscess (Type II), fistula with an abscessed intra-abdominal communicating collection and susdiaphragmatic (Type III).

Our treatment algorithm consisted solely of the insertion of a naso-jejunal feeding tube (NJFT) for Type I fistulas and the placement of a NJFT with EID with or without surgical drainage depending on the septic status for type II and III fistulas.

Results: Forty-nine patients were included (13 males / 36 females), with a mean age of 41 years (18–56) and an average initial Body Mass Index (BMI) of 46 kg/m2 (38–70). 16 patients had a type I fistula (33%), 25 a type II (51%) and 8 a type III (16%).

The clinical success rate of the procedure with fistula healing was 100% (16/16) in the group I, 96% (24/25) in the group II and 12% (1/8) for group III with a statistical difference between group I, II versus III p = 0.001

Mean time for diagnosis of the fistula was significantly higher in type III, 5 (2–32) days for type I, 5.8 (2–67) days for type II and 20.7 (5–122) days for type III p = 0.04 (I, II versus III).

The mean estimated size of the defect was significantly higher in type II and III versus type I, 2.8 mm (1–4) for type I, 11.2mm (5–20) for type II and 10 mm (5–15) for type III.
The average scheduled endoscopic session required was significantly higher in type III ($p = 0.001$ I, II versus III), 2 (1–3), 2.7 (2–5) and 5.2 (2–10) for Type I and II, and III respectively. Number of unscheduled reinterventions were significantly higher in type III ($p = 0.03$). The NJFT was left in place significantly higher in type III ($p = 0.001$).
Conclusion: Our study shows that it is essential to characterize the type of fistula before the endoscopic treatment of post-sleeve fistulas to better guide the proper management. Our treatment algorithm is available for Type I and II with high clinical success rate. In addition, postoperative monitoring of patients is essential in order to detect a fistula as early as possible and avoid type III fistula requiring a complex endoscopic treatment with low success rate.
Disclosure: Nothing to disclose

P1512 EFFICACY OF ENDOSCOPIC VACUUM-ASSISTED CLOSURE COMPARE WITH SELF-EXPANDABLE METALLIC STENT FOR POSTOPERATIVE ANASTOMOTIC LEAK OF GASTRIC CANCER

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Introduction: Post-operative anastomotic leak is a life-threatening complication with a high mortality rate at gastrointestinal surgery. Endoscopic vacuum assisted closure (EVAC) has been attempted as a new non-surgical treatment option for anastomotic leakage replacing previous self-expanding metal stents (SEMS). There were many reports of EVAC treatment for post-esophagectomy anastomotic leakage, but not for post-gastrectomy.
Aims and Methods: Between Jan 2007 and Feb 2018, total 39 cases of anastomotic leak occurred in patients who underwent gastrectomy for treatment of gastric cancer. Among them, 28 patients were treated with SEMS only, 7 patients were treated with EVAC following after SEMS failure, and 4 patient was initially treated with EVAC only. We compared clinical characteristics and therapeutic outcomes between patients treatment with EVAC or EVAC after SEMS ($N = 11$) and patients treatment with only SEMS ($N = 28$). Our aims are to compare the clinical outcomes of SEMS with EVAC as treatment for anastomotic leak after gastrectomy and to discuss the efficacy of EVAC.
Results: Median follow up duration was median 17 months (range 0–48). All cases with EVAC treatment were healing successfully (11/11, 100%). Two cases of treatment failure occurred in patients who treated with SEMS (2/28, 7.1%). Median duration of EVAC treatment was shorter than SEMS treatment (15 days [range 6–47] in EVAC and 36 days [range 7–108] in SEMS). Relatively larger size leakage was treated successfully with EVAC treatment (median 2.1cm in EVAC and 1.0cm in SEMS). The anastomotic stenosis occurred in one patient of EVAC treatment (1/11, 9.1%) and in six patients with SEMS treatment (6/28, 21.4%) within 1 year.
Conclusion: As well as SEMS, EVAC can be the effective endoscopic treatment option for anastomotic leakage after gastrectomy. Considering of the size of anastomotic leakage may be important in determining treatment options. Further large number randomized controlled trials are needed to define efficacy and benefit of EVAC.

Characteristic	Total (n = 39)	EVAC (n = 11)	SEMS (n = 28)	P-value
Age	66.0(39–82)	68.0(55–81)	63.5(39–82)	0.450
ASA 1 or 2, n (%)	24(61.5)	6(54.5)	18(64.3)	0.718
ASA 3 or 4, n (%)	15(38.5)	5(45.5)	10(35.7)	0.718
Cardiovascular disease, n (%)	23(59.0)	9(81.8)	14(50.0)	0.086
Diabetes mellitus, n (%)	10(25.6)	4(36.4)	6(21.4)	0.424
Use of anticoagulant or antiplatelet agent, n (%)	14(35.9)	6(54.5)	8(28.6)	0.156
Total gastrectomy, n (%)	28(73.7)	6(54.5)	22(78.6)	0.234
Billoth I or II, n (%)	11(28.2)	5(45.5)	6(21.4)	0.234
Tumor staging (TNM) 1 or 2, n (%)	27(69.2)	9(81.8)	18(64.3)	0.446
Tumor staging (TNM) 3 or 4, n (%)	12(30.8)	2(18.2)	10(35.7)	0.446
Preoperative BMI	24.5(15.4–47.9)	23.8(19.0–26.6)	24.6(15.4–47.9)	0.363
Size of leak (cm)	1.5(0.2–3.3)	2.1(1.5–3.3)	1.0(0.2–2.5)	<0.001
Duration of treatment (days)	31.0(6–108)	15.0(6–47)	36.0(7–108)	<0.001
Duration of hospitalization (days)	23.0(10–88)	23.0(10–88)	21.5(10–84)	0.569
Device reposition or change, n (%)	12(30.8)	5(45.5)	7(25.0)	0.262
Success to closure, n (%)	37(94.9)	11(100.0)	26(92.9)	>0.999
Leak related mortality, n (%)	1(2.6)	0(0.0)	1(3.6)	>0.999
Incidence rate of stricture within 1 year, n (%)	7(17.9)	1(9.1)	6(21.4)	0.649

[Comparison of clinical characteristics and therapeutic outcomes of patients treated with EVAC or SEMS for anastomotic leakage.]
Disclosure: Nothing to disclose

P1513 SURGICAL RESECTION FOR TREATMENT OF COLORECTAL POLYPS: A SINGLE CENTRE RETROSPECTIVE COHORT STUDY

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Introduction: In January 2014, the Dutch bowel screening program was introduced to reduce the mortality rate of colorectal cancer. Because of this programme a rise in endoscopically found colorectal polyps is expected, which in turn will increase the number of surgical resections.
Aims and Methods: The aim of this study was to evaluate complications of surgically resected colorectal polyps and compare the amount of surgical resections and encountered malignancies before and after implementation of the Dutch bowel screening program.
This retrospective cohort study included patients who underwent surgical removal of colorectal polyps between January 2012 and December 2017. Patients with preoperatively established malignancy and polyposis were excluded.
Results: 143 patients were included. The surgical procedure was a segmental colectomy in 115 patients (80.4%). The procedures were performed laparoscopically in 79.7% ($n = 114$). Major complications (Clavien-Dindo $\geq$ 3b) occurred in 7 patients (4.9%), without mortality. The anastomotic leakage rate was 3.5% ($n = 4$).
In 2012, 3.2‰ of all conducted colonoscopies resulted in surgery ($n = 18$), compared to 5.8‰ in 2016 ($n = 30$). The overall malignancy rate before the implementation of the screening program was 28.9%, compared to 22.4% after the implementation ($p = .406$). High-grade dysplasia was seen in 77.4% of encountered adenomas before the implementation compared to 42.5% after implementation ($p = .001$).
Conclusion: After the implementation of the screening program the amount of surgically resected colorectal polyps almost doubled. Nevertheless the malignancy and high-grade dysplasia rate decreased.
Disclosure: Nothing to disclose

P1515 NAVIGATION SURGERY FOR LATERAL LYMPH NODE DISSECTION USING THREE-DIMENSIONAL PELVIC MODEL PRODUCED BY 3D PRINTER

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Introduction: Recent prevalence of three-dimensional (3D) printer has enabled to produce 3D model of internal organs easily. Although the usefulness of 3D model has been demonstrated in regard to parenchyma organ such as liver[1] and kidney[2], there are few reports as to the intestine.
Total mesenteric excision (TME) with lateral lymph node dissection (LLND) is the standard treatment for locally advanced lower rectal cancer in Japan[3]. The branching patterns of iliac arteries and veins vary among individuals. Therefore, it is important to understand individual variations in advance of LLND. The anatomy of pelvic vessels is being evaluated using reconstructed 3D image of iliac arteries and its branches in selected patients in our institution[4].
Here, we aimed to address the usefulness of pelvic 3D model as a navigation modality in LLND.
Aims and Methods: We selected patients who underwent resection of the rectum with LLND from June 2017 to March 2018. First, we made 3D images from enhanced computer tomography (CT). Arteries and bones were reconstructed using volume rendering technique. Vessels, nerves, ureters, muscle, and metastasized lymph nodes were reconstructed by defining as region of interest. Then, a pelvic 3D model was produced using the reconstructed 3D image.

The usefulness of the pelvic 3D model was evaluated by questionnaire (1 = disagree strongly; 2 = disagree; 3 = not decided; 4 = agree; 5 = agree strongly) for surgeons.
Results: 3D models were created in a total of nine patients; seven underwent laparoscopic surgery and two open surgery. LLND of the left side was performed in two patients, LLND of the right side in five, and bilateral LLND in two. According to the Adachi-classification[5], types of arterial variation were determined as follows; Type Ia in seven sides, Type Ib in one, Type III in two, Type IVa in one.
A total of eleven sides of hemipelvic models were produced in nine patients. Superior gluteal artery, inferior gluteal artery, internal pudendal artery and obturator artery were all depicted. Furthermore, we were also able to reproduce obturator and sciatic nerves and levator ani, piriformis, coccygeus and internal obturator muscle. The mean time and cost for producing a hemipelvic model were about 26 hours (18.5–60) and 150 euros (130–200).
The average score of the questionnaire was 4.8. There were some favorable comments as follows: 1) the pelvic 3D model is superior to a reconstructed 3D image presented on screen in understanding of pelvic anatomy. 2) it may be useful in educating residents and students who are unfamiliar with lateral lymph nodes and their surrounding structure.
Conclusion: A pelvic 3D model appeared useful to understand pelvic anatomy. Although it needs a long time and expensive cost to produce the current pelvic 3D model, the tool may be useful as navigation in LLND and teaching residents and students pelvic anatomy.
Disclosure: Nothing to disclose

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P1516 FEASIBILITY OF 2-TEAM TATME FOR LOWER RECTAL CANCER: SHORT-TERM OUTCOMES OF INITIAL TEN CASES

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Introduction: Transanal total mesorectal excision (taTME) seems to be a novel down-to-up approach for benign and malignant rectal disease. In addition, laparoscopic and taTME simultaneously (2-team taTME) against lower rectal cancer might be more promising approach. The aim of this study was to evaluate the short-term outcomes of 2-team taTME for lower rectal cancer.
Aims and Methods: A retrospective review was conducted on initial ten patients who underwent 2-team taTME from November 2017 to April 2018 in our single institution. All information was carefully reviewed and collected, including patient demographics, operative details, and surgical outcome. The primary endpoint was the quality of TME, and the secondary endpoint was short-term adverse event in the patient treated with 2-team taTME against lower rectal cancer.
Results: Mean ages were 68 years, and 7 patients in male. The average of BMI was 23.3 ± 2.8 kg/m^2. The average tumor distance from anal verge was 4.0 ± 2.0 cm. The median operative time was 226 minutes (156–263). There were no intraoperative complications including organ injury and conversion to open surgery. The median number of harvested lymph nodes was 9 (8–22). Overall positive CRM ($\leqq$0.5 mm) and DRM ($\leqq$1 mm) were 10% (n = 1) and 0%. Although postoperative complication was occurred in 8 patients (80%), there were no severe complications (Clavien-Dindo classification$\geqq$Grade3). The median length of hospital stay was 14 days.
Conclusion: Our results suggest that 2-team taTME for lower rectal cancer appears to be an oncologically safe and feasible with acceptable short-term outcomes. Further studies with more patients and longer follow-up are needed.
Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 09:00–14:00
IBD III – Hall X1

P1517 WNT2B INDUCES EPITHELIAL MESENCHYMAL TRANSITION: RELEVANCE IN FISTULA DEVELOPMENT IN CROHN'S DISEASE

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Introduction: Fibrosis and fistula development constitute the main complications associated to Crohn's disease. The Wnt signalling pathway induces fibroblast activation and epithelial mesenchymal transition (EMT) which are involved in these complications. Recent results in our laboratory have showed that Crohn's disease patients presenting a stricturing (B2) or a penetrating (B3) behavior undergoing surgical resection differ in the pattern of Wnt signaling (Ortiz-Masià, D *et al.,* ECCO Congress, 2018).
Aims and Methods: We aim to analyse the potential role of the Wnt pathway in favouring fistula development over fibrosis. CD patients were categorized according to Montreal classification (B2 orB3) and unaffected mucosa of patients with colorectal cancer was used as a control. mRNA was isolated from epithelial cells, fibroblasts or intestinal tissue and the expression of EMT markers, Wnt ligands, Wnt targets and Fzd receptors was analyzed by RT-PCR (Relative (Gene/b-actin) mRNA expression; fold induction vs control group). Isolated epithelial crypts or fibroblasts from controls were treated with WNT2b for 10 hours and the mRNA expression of EMT markers was analyzed. Fzd4 was Immunoprecipitated from surgical resections from B2 and B3 CD patients and the binding of WNT2B and FZD4 was analyzed by Western blot. Statistical analysis was performed by ANOVA + Kewman-Keuls test. Correlations between data were analysed using Pearson's correlation coefficient (* $p < 0.05$).
Results: CD patients presented an increased expression of Wnt target genes and Wnt inhibitor, DKK1 as well as a generalized overexpression of Wnt ligands (WNT2, WNT3, WNT6, WNT10A and WNT10B), with the exception of WNT2B which was up-regulated in the fistulizing group and down-regulated in the stenotic group compared with control. The expression of WNT2b significantly correlated with, VIMENTIN ($r = 0.6315$, $P = 0.0087$*), and STAT3 ($r = 0.4919$, $P < 0.0001$*), only[L1] in intestinal tissue from the fistulizing CD group. WNT2b exogenous administration increased mRNA expression of vimentin, snail1 and snail2 while decreased E-cadherin expression in isolated crypts, but no in fibroblasts. Epithelial cells and fibroblasts showed a different pattern expression of FZD receptors and higher levels of Fzd4 mRNA expression were observed in epithelial cells from B3 than B2 CD patients. Immunoprecipitation of FZD4 and Wnt2b was detected in human intestine and the signal was higher in samples from B3 than B2 CD patients.
Conclusion: Wnt2b may induce EMT and play a role in fistula development in CD patients through Fzd4 interaction.
References: P008-Differences in macrophage infiltration and Wnt ligands expression between stricturing and penetrating behavior in Crohn's disease. P. Salvador, D.C. Macías-Ceja, J. Cosín-Roger, R. Alos J. Hinojosa Del Val; F. Navarro-Vicente, J. Manyé, S. Calatayud, M.D. Barrachina, D. Ortiz-Masiá. ECCO Congres 2018.
Disclosure: Nothing to disclose

P1518 THE BENEFICIAL USE OF STW 5 IN DSS-INDUCED COLITIS IS PARTLY DUE TO AMELIORATING THE CHANGES IN GUT MICROBIOTA INDUCED BY DSS

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Introduction: DSS-induced colitis has been shown to affect rodent gut microbiota[1]. STW5 (Iberogast®), a standardized multicomponent hydro-alcoholic herbal preparation, was shown to be effective in functional dyspepsia and irritable bowel syndrome and was shown experimentally to be effective against DSS-induced colitis[2] through anti-inflammatory and antioxidant properties. Present study was designed to show whether the beneficial treatment of DSS-induced colitis with STW5 also involves its effect on gut microbiota.
Aims and Methods: The experimental model of colitis was induced in Wistar rats by administering 5% DSS in drinking water for 7 days. Treatment with STW5 was started at the same time as DSS administration by giving it orally in doses of 2 and 5 ml/kg. Rats were sacrificed 24 hours later and fecal samples from cecum were collected to study the taxonomic diversity of gut microbiota. Selected main microbial phyla and genera were quantified using quantitative Real Time-PCR.
Results: The abundance of Proteobacteria in the DSS-induced colitis group was increased more than 25 fold but this rise was largely prevented after co-administration of STW5. In addition, DSS colitis induced an increase in the relative abundance of the Bacteroidetes, Prevotella and Bacteroides. Within the Firmicutes phylum, DSS increased the abundance of Enterococcus, an effect that was almost completely prevented by co-administration of STW5. Furthermore, Blautia within the Firmicutes phylum was decreased in the DSS-induced colitis group, and the abundance was almost restored by STW5. The relative abundance of Euryarchaeota represented by Methanobrevibacter was markedly decreased in the DSS colitis group but slightly increased by STW5.
Conclusion: Many changes in gut microbiota induced by DSS have been prevented or reduced by STW5. This adds to our understanding of the mechanisms underlying the beneficial use of the herbal preparation in colitis induced by DSS.
Disclosure: Olaf Kelber and Heba Abdel-Aziz are employed by Steigerwald Arzneimittelwerk GmbH. Other authors have nothing to disclose

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P1519 RELATION OF CIRCULATING PROTEIN S (PROS1) WITH INFLAMMATORY BOWEL DISEASE (IBD) ACTIVITY, PATTERNS, AND C4-BINDING PROTEIN (C4BP)

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Introduction: Inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD) show an increased risk of thrombosis, complication where decreased levels of circulating PROS1 may play a role. PROS1 is a well-established anticoagulant, that works as cofactor for activated protein C. Additionally, PROS1 (expressed in T lymphocytes), due to an agonist function of anti-inflammatory tyrosine kinase TAM receptors TYRO3, AXL and MERTK, exhibiting an inhibitory role in the innate immunity, has been reported regulating inflammation or susceptibility in experimental colitis models (Rothlin et al. 2015, Carrera Silva et al, 2013). We hypothesized that PROS1 in IBD may result in decreased plasma levels, increasing not only the thrombosis risk, but also the inflammatory process of IBD. Of the total plasma PROS1, 40% circulate as an active free form, and the rest is linked to complement C4b-binding protein (C4BP) as an inactive complex. Thus, if so, a decrease of circulating "free" protein S, could be secondary to increased C4BP, which for excessive binding, reduce its availability.
Aims and Methods: 1) to compare PROS1 levels between CD, UC, activity status (Indexes: CDAI, Mayo), patterns (Montreal) and healthy controls, 2) to determinate C4BP levels due to its possible influence on PROS1 levels. Free PROS1 and C4BP were determined by immunoturbidimetry, Liatest, Stago, France, in 103 IBD patients (45 M, 58 F, UC: n 66, CD n 37) and 30 healthy controls (18 M, 12 F), mean ages: 37.5 ± 15.6, 41.4 ± 14.6, 38.2 ± 12.2, respectively.
Results: Mean PROS1 levels in CD ($89.9. \pm 28.0$) were significantly lower compared with controls (109.6 ± 23.9, $p = 0.0019$) and UC (104.4 ± 27.0, $p = 0.0076$). Within the CD group, a statistical difference versus controls was observed in patients with active disease (n 25, levels 84.9 ± 24.1, $p = 0.0004$), but not in patients in remission (n12: 100.2 ± 33.5). Moreover, the moderate-severe subset (n21), presented the lowest levels (84.0 ± 25.9) versus controls $p = 0.0006$. In UC, PROS1 levels did not show differences between subsets (42 active, 24 remission: 101.1 ± 26.3 and 110.0 ± 27 respectively) or with controls. CD patterns (behavior, location) and UC extent (12 proctitis, 54 more extensive) exhaustively analyzed did not show significant differences. Mean levels of C4BP in the controls were 109.9 ± 8.8. Values of C4BP in CD, unlike augmented (which could be associated with potential free PROS1 decline for excesive binding in the inactive complex), were massively decreased in all subsets (in the global sample 98.7 ± 14.4, in active patients 98.8 ± 12.0, in moderate-severe subset 98.4 ± 12.6, in remission 98.3 ± 19.1) versus controls ($p = 0.0004$, $p = 0.0008$, $p = 0.0014$, $p = 0.0222$ respectively). C4BP showed to be diminished versus controls in the overall results of the UC sample ($p = 0.0010$), especially in the severe-moderate subgroup (100.1 ± 9.8, $p = 0.0001$) which also reached significance compared with remission (105.2 ± 10.1, $p = 0.0322$).
Conclusion: 1) Free PROS1 levels were significantly lower in active CD versus controls (especially in the severe-moderate activity subsets), but in the case of UC the levels were indistinguishable from controls, 2) On contrary, C4BP levels were reduced in both diseases, 3) Decrease of Free PROS1 in CD, was not secondary to a potential increased binding of free PROS1 due to C4BP increase. These results stimulates to follow this research, in order to investigate the potential role of reduced levels of PROS1 in circulation, not only in the traditionally considered aspect related with the risk of thrombosis, but also as a possibly factor that enhances the inflammatory process in CD
Disclosure: Nothing to disclose

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P1520 ILEAL CHANGES IN PATIENTS WITH MICROSCOPIC COLITIS

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Introduction: Microscopic colitis (MC) is an important cause of chronic diarrhoea in adults. Histopathology is the gold standard for diagnosis and but colonic biopsy has a variable yield. Endoscopically the mucosa appears normal, often leading to delayed diagnosis. It is not clear whether the described changes are strictly restricted to colon or extends to other parts of GIT also. This may have a bearing on treatment decisions.
Aims and Methods: The aim of the current study was to evaluate the terminal ileum using the narrow band imaging (NBI) and high-definition white-light endoscopy (HDWLE) in patients with MC. We also aimed to document and describe the histopathological findings in the ileum of patients with MC.
Materials and methods: We prospectively recruited patients aged more than 18 years with suspected MC (July 2016 to December 2017). Patients with malignancy, coeliac disease, small intestinal bacterial overgrowth, inflammatory bowel disease, gastrointestinal tuberculosis and severe comorbidities were excluded. Patients underwent blood investigations, imaging including CECT abdomen (if indicated), stool analysis, hydrogen breath tests using glucose, lactose and lactulose. All patients underwent colonoscopy with ileal intubation if possible. Patients underwent both HDWLE and NBI during the same setting by same observer. NBI finding were recorded in a predefined format. Four pieces of biopsies were taken from caecum/ascending colon and four from pieces from descending colon/sigmoid colon. Additional four pieces of biopsies were taken from terminal ileum. Each set of biopsies was collected in separate containers and labelled for further histopathological processing and examination by an expert gastrointestinal histopathologist. The diagnosis of MC was made using statements of the European Microscopic Colitis Group 2012.
Results: Of 53 patients enrolled in the study, and a final diagnosis of MC was established in 43 [mean age – 45.83($\pm$15.92), males – 27]. 25(58.1%) patients had collagenous colitis (CC), 14 (32.5%) had Lymphocytic colitis (LC) and 4(9.4%) had mixed picture fulfilling criteria for both. The HDWLE findings of ileum revealed normal mucosa in all patients. On NBI, intravillous capillary network was regular unbranched with semi-circular pattern in 41(95.4%) in cases and in all controls. Sparse and irregular pattern was seen in 2(4.7%) cases. Dilated and meandering vessels were seen in none ($p = 1.00$). Peyer's patches domes were indistinct in 5(9.4%) cases, normal in 38(88.4%) cases and all of the controls ($p = 0.570$). Peyer's patch vessels were regular and unbranched in 38(88.4%) cases and all of the controls. They were sparse and irregular in 5 cases (11.6%) ($p = 0.570$). Histopathological findings of terminal ileum revealed normal villi in 39 (90.6%) cases of MC, with 4 patients having partial villous atrophy. The crypt villous ratio was grouped as 1:1.5, 1:3, 1:4 and 1:5 in 2 (4.6), 26 (60.4),11 (25.5%) and 4 (9.3) patients respectively. Lymphoplasmacytic infiltrate was grouped as mild, moderate and severe, and was present in 10 (23.2), 2 (4.6%) and 1 (2.3%) patients respectively. The mean ($\pm$standard deviation) number of intraepithelial lymphocytes (IEL) per high power field were 16.33 ± 24.54.
Conclusion: This prospective study, for the first time, describes the NBI findings of ileum in patients with MC. Traditionally, ileum is considered to be spared in patients with MC. However, we found histological involvement of ileum in form of increased lymphoplasmacytic infiltrate and IEL in ileal mucosa along with presence of partial villous atrophy in some patients.
Disclosure: Nothing to disclose

P1521 ORO-CECAL TRANSIT TIME AND LACTOSE INTOLERANCE IN PATIENTS WITH MICROSCOPIC COLITIS

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Introduction: Microscopic colitis (MC) is an important cause of chronic diarrhoea in elderly. Histopathology forms gold standard for diagnosis and has a variable yield. Hydrogen (H2) breath tests are used frequently to analyse the pathophysiology of functional gastrointestinal disorders, small intestinal bacterial overgrowth (SIBO), carbohydrate malabsorption and oro-cecal transit time.
Aims and Methods: Data regarding prevalence of SIBO, lactose tolerance, and oro-cecal transit time (OCTT) in patients of MC is sparse. Hence, we aimed to evaluate these in patients of MC.
Materials and methods: We prospectively recruited patients diagnosed with MC aged more than 18 years during the period July 2016 to December 2017. Glucose hydrogen breath test was done to evaluate for SIBO. A rise $\geq$12 ppm over the

fasting value in h2 concentration within 2hours of ingestion of glucose were measured by gas chromatography using Model-12 Microlyzer, (Quintron, USA) in 2 consecutive readings was taken as suggestive of SIBO. Lactulose hydrogen breath test was done to calculate OCTT. Patients were instructed to avoid taking antibiotics or probiotics 4 weeks prior to the test. They were given 15 ml lactulose syrup containing 10 gm lactulose to drink and end expiratory breath samples were taken after every 15 minutes for upto 3–4 hours. Time taken for rise in breath hydrogen by ≥12ppm over the baseline value in two consecutive readings was considered to be OCTT. Lactose breath test was done for lactose intolerance. Patients were given lactose at a dose of 25g in 250ml of water and breath samples were taken every 15 minutes up to 4 hours. A rise ≥20 ppm over the fasting value in H_2 concentration in two consecutive readings was considered suggestive of lactose intolerance.

Results: 43 patients of MC [mean age – 45.83(±15.92), males – 27] and 10 controls were recruited. Out of 43 cases with MC, 25(58.1%) patients had collagenous colitis (CC), 14 (32.5%) had Lymphocytic colitis (LC) and 4(9.4%) had mixed picture fulfilling criteria for both. In the MC group, 9(28.1%) were found to be lactose intolerant while in controls 3(42.9%) were lactose intolerant ($p = 0.654$). Glucose hydrogen breath test did not find any patient with SIBO in the MC group, however, SIBO was present in 4(9.5%) controls ($p = 0.001$). The mean (+ standard deviation) OCTT measured in MC group was 130.38 ± 47.95 mins and 97.14 ± 48.55mins ($p = 0.109$) in controls. OCTT was prolonged in 73% of patients with MC and 43% of controls.

Conclusion: Lactose intolerance was common in patients with MC, which might add to the severity of diarrhoea. OCTT was found to be prolonged in msot patients with MC. No patient with MC was found to have SIBO.

Disclosure: Nothing to disclose

P1522 HIGH-FAT DIET AGGRAVATES DEXTRAN SULFATE SODIUM (DSS)-INDUCED COLITIS THROUGH REGULATING IMMUNE RESPONSES OF GUT-ASSOCIATED LYMPHOID TISSUE

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Introduction: Inflammatory bowel disease (IBD) is characterized by inflammation and immune disorders of the gut, gut-associated lymphoid tissue (GALT, including Peyer's patch, lamina propria, mesenteric lymphatic node, et al) plays as the first line of defense in intestinal mucosa. Increasing evidences suggest worse prognosis of IBD patients with obesity, while the mechanism is not yet to be elucidated. Here we try to explore the effects of obesity on IBD through GALT perspective.

Aims and Methods: Twelve weeks of 45% high-fat diet (HFD) was used to induce obesity. After 6 weeks of HFD feeding, mice were fed with three cycles of dextran sodium sulfate (DSS) to induce chronic colitis, and each cycle was composed of 7-day 2% DSS and 14-day normal water. Animals were divided into 4 groups, namely normal diet (ND), HFD, DSS and HFD+DSS groups.

Results: The body weight decreased in DSS mice than ND mice, as well as in HFD+DSS mice than HFD mice. Compared with ND group, number of inflammatory infiltration focus in colon were higher in HFD, DSS and HFD+DSS groups, and the highest number appeared in the last group. Consistent with these, the highest serous 4KD FITC-Dextran level, an intestinal permeability marker, was observed in HFD+DSS group, followed by DSS group and HFD group. These evidenced that both HFD and DSS promoted intestinal inflammation and permeability, and HFD+DSS caused the most serious gut damage. In the meantime, the immune responses of GALT in HFD, DSS and HFD+DSS mice were disordered, especially in HFD+DSS group. In Peyer's patches, compared with those of ND mice, $CD19^+$B lymphocytes decreased in HFD, DSS and HFD+DSS mice; the accumulation of $CD3^+$T lymphocytes arranged from lowest to highest in ND, HFD, DSS and HFD+DSS mice, as well as $CD4^+$ T/$CD8^+$T ration. In lamina propria of colon, $F4/80^+CD11b^+$ macrophages, $F4/80^-Ly6G^+CD11b^+$neutrophils, $F4/80^-CD11C^+MHCII^+$dendritic cells, $CD3^+$T lymphocytes, $CD4^+$T/$CD8^+$T cells ratio and $CD19^+$B lymphocytes were higher in HFD and DSS mice than ND mice, and all of these cells were further increased in HFD+DSS mice. In mesenteric lymphatic nodes, lower $CD3^+$T lymphocytes and higher $CD19^+$B lymphocytes were observed in HFD, DSS and HFD+DSS groups than ND group.

Conclusion: DSS induces more severe colitis in obesity mice than normal mice. Immune responses of GALT are activated both in HFD and DSS mice, and HFD deteriorates this immune disorder induced by DSS. These results suggest that obesity may aggravate colitis through regulating immunoreaction of GALT.

Disclosure: Nothing to disclose

P1523 FUNGAL DYSBIOSIS FACILITATES NKP46$^-$ ILC3 IN INFLAMED MUCOSA OF UC PATIENTS THROUGH MEDIATION OF IL-23 PRODUCED BY DCS

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Introduction: Fungal dysbiosis plays important role in the pathogenesis of ulcerative colitis (UC). Type 3 innate lymphoid cells (ILC3) were also reported as a pivotal player in defending fungal invasions and inducing intestinal inflammation. However, the effect of fungal dysbiosis on bio-function of ILC3 in UC pathogenesis is not very clear.

Aims and Methods: To investigate the mucosal fungal composition, 10 untreated UC patients were recruited, and both non-inflamed and inflamed mucosae were collected for an ITS 1–2 *rRNA* sequencing. Flow cytometric analysis were performed to detect circulatory and mucosal ILCs composition and cytokines expression. *In vitro* co-culture of *Candida albicans*, bone marrow-derived dendritic cells (BMDC) and sorted Nkp46$^-$ ILC3 cells were performed to investigate the mechanism of fungal dysbiosis involved in UC pathogenesis.

Results: Compared to non-inflamed mucosa, Ascomycota decreased ($p < 0.05$) and Zygomycota increased ($p < 0.01$) at phylum level in inflamed mucosa of UC patients. *Wickerhamomyces* decreased ($p < 0.05$) and *Candida, Aspergillus, Cladosporium, Lentinula,* and *Paecilomyces* increased at genus level. Flow cytometric analysis showed an increase of pro-inflammatory Nkp46$^-$ ILC3 ($p < 0.05$) in both circulation and inflamed mucosa of UC patients. Furthermore, IFN-γ^+ Nkp46$^-$ ILC3 ($p < 0.01$) and IL-17A$^+$ Nkp46$^-$ ILC3 subset ($p < 0.05$) were increased in mucosal Nkp46$^-$ ILC3 cells in inflamed mucosa. In addition, BMDC, co-cultured with heat-killed *Candida albicans*, expressed more IL-23 ($p < 0.05$), and promoted Nkp46$^-$ ILC3 to produce IL-17A ($p < 0.05$).

Conclusion: We have demonstrated the increase of invasive fungi and pro-inflammatory Nkp46$^-$ ILC3 in inflamed mucosa of UC patients. *In vitro* analysis has shown that BMDC have been stimulated by *C. albicans* to express IL-23 and subsequently facilitates Nkp46$^-$ ILC3 to express IL-17A. These data prove that fungal dysbiosis facilitates Nkp46$^-$ ILC3 in inflamed mucosa of UC patients, which is mediated by DCs produced IL-23.

Disclosure: Nothing to disclose

P1525 CD16 MACROPHAGES ACT AS A SOURCE OF PROFIBROTIC FACTORS PROMOTING INTESTINAL FIBROSIS

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Introduction: Fibrosis is a common complication of Crohn's disease and it is related to dysregulated tissular repair following inflammation. Macrophages play a central role in both mucosal repair and fibrosis and these cells constitute an important source of pro-fibrotic factors [1]. $CD16^+$ macrophages are increased in fibrotic tissue of Crohn's disease patients [2] and we aim to analyse the relevance of CD16 positive macrophages as a source of fibrotic mediators in murine intestinal fibrosis.

Aims and Methods: Colon resections from donor mice were transplanted subcutaneously into the neck of recipient mice. After 7 days, intestinal grafts were obtained. An adjacent segment of the colon from each donor mouse was kept to be used as autologous control tissue. [3] The expression of macrophage markers, pro-fibrotic markers and Wnt ligands and receptors was analyzed by qPCR.

Results: Fibrotic tissue compared with control tissue revealed: a) increased profibrotic markers Vim (4.6 ± 1.1 vs 1.0 ± 0.1), α-Sma (13.0 ± 1.7 vs 1.1 ± 0.2) and Col1a1 (69.4 ± 17.3 vs 1.7 ± 0.7); b) increased macrophage markers F4/80 (7.9 ± 2.2 vs 1.1 ± 0.1), CD16 (23.8 ± 3.5 vs 1.3 ± 0.3), CD206 (10.2 ± 4.6 vs 1.3 ± 0.4) and CD86 (15.8 ± 2.9 vs 1.1 ± 0.2); c) increased expression of Tgf-β (2.1 ± 0.2 vs 1.0 ± 0.0). Moreover, fibrotic tissue showed: a) a positive and significant correlation between CD16 and Wnt6 and between CD16 and Tgf-β and b) a positive correlation between Wnt6 and Fzd10.

Conclusion: CD16 positive macrophages are increased in murine intestinal fibrosis and these cells may act as a source of fibrotic factors such as Tgf-β and Wnt6.

Disclosure: Nothing to disclose

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P1526 PRESENCE OF ADHERENT-INVASIVE *ESCHERICHIA COLI* IN INFLAMMATORY BOWEL DISEASE IMPACTS THE EFFICACY OF FECAL MICROBIOTA TRANSPLANTATION

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Introduction: Adherent invasive *Escherichia Coli* (AIEC) can invade the gut epithelium and colonise the mucosa of patients with inflammatory bowel disease (IBD). Despite the increasing use of fecal microbiota transplantation (FMT) to treat IBD, the mechanisms and factors affecting treatment outcome is unclear.

Aims and Methods: This study aimed to determine the prevalence and define the genetic and functional characteristic of AIEC in patients with Crohn's Disease (CD). Secondly, we assessed if the presence of AIEC compromise the efficacy of FMT in a murine model of colitis. We isolated *E Coli* from ileum tissues of Chinese Crohn's disease patients (n = 56) and healthy subjects (N = 16) and classified them as AIEC pathotype using gentamicin protection assay with Int-407 intestinal cells. Bacterial whole genome sequencing was performed on all AIEC strains isolated. We compared the virulence properties and antibiotic resistance of these isolates with AIEC strains isolated from western countries and other publicly available *E. coli* pathotypes deposited in NCBI database. Amongst 21 AIEC strains isolated, we selected AIEC62d strain which has the strongest invasion property and *E. coli* K12 (a non-pathogenic strain) to infect C57BL/6 wild type mice (n = 26). After 7 days of 2% DSS treatment, we gavaged these mice with fecal solution from healthy human subject and assessed the Disease Activity Index (DAI), colon length and histology score of the colon 7 days after fecal transplant.
Results: AIEC was present in 37.5 and 12.5 percent of mucosa of CD and healthy subjects, respectively. Most AIEC strains belonged to B2 phylogroup. Over 65 percent isolates from CD were multi-antibiotic resistant and they harboured stronger pathogenicity than the non-resistant strains ($p < 0.05$). The genome of AIEC62d resembled that of LF82 (the AIEC reference strain) and possessed nearly all virulence genes (pduC, ibeA, lpfA, etc.). Its invasion ability was greater than that of LF82 (4.25% versus 3.5% in Intestine-407 cells). Mice treated with FMT showed a significant reduction in the number of AIEC in the colon. After FMT, mice colonised with AIEC62d strain showed significant shortening of colon and had more severe histology activity than mice colonised with *E. coli* K12 non-pathogenic strain.
Conclusion: AIEC that possess antibiotic resistant properties is common in CD subjects. The presence of AIEC compromised the efficacy of FMT in mice, leading to incomplete recovery of inflammation. Future FMT practice should consider patient stratification based on AIEC presence and virulence factors and their effects on FMT outcomes. This study was supported by ANR/RGC Joint Research Scheme (RGC Project No. A-CUHK402/17).
Disclosure: Nothing to disclose

P1527 THE ASSOCIATION BETWEEN PERIANAL ABSCESS AND INFLAMMATORY BOWEL DISEASE WITH AN ANALYSIS OF PREDICTIVE VARIABLES: FINDINGS FROM THE THIN DATABASE

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Introduction: Perianal abscesses are caused by an infection of obstructed anal crypt glands resulting in a collection of pus. Previous cohort studies[1] suggested that a third of patients with Crohn's Disease who had surgery for perianal abscess underwent these procedures prior to their diagnosis of Crohn's disease. The incidence of inflammatory bowel disease after a diagnosis of perianal abscess and potential predictors of a future diagnosis of inflammatory bowel disease in this cohort is unknown.
Aims and Methods: The Health Improvement Network (THIN) represents a group of General Practices (primary care) covering 6.2% of the UK population, which is representative of the UK population structure. Incident cases of perianal abscess were identified between 1995 and 2017. Subjects with perianal abscess were matched to controls of the same age (+/− 1 year), gender, smoking and weight (within 120 days of the diagnosis of perianal abscess) within the same general practice. Primary outcome was designated as a diagnosis of Crohn's Disease or ulcerative colitis. Subjects who developed a diagnosis of inflammatory bowel disease within 6 months following the index date were excluded. A cox regression model was also used to assess potential predictors of a diagnosis of Crohn's disease or ulcerative colitis following a diagnosis of perianal abscess.
Results: The risk of Crohn's disease was higher in the perianal abscess cohort compared to the control population; adjusted HR 7.54 (95% CI 4.88–11.66), $p < 0.0001$. The risk of ulcerative colitis was higher in the perianal abscess cohort compared to the control population; adjusted HR 2.02 (95% CI 1.36–2.97), $p < 0.0001$. Anaemia in men (HR 4.11 (95% CI 2.02–8.34), $p < 0.0001$), and use of antidiarrheal medications (HR 2.49 (95% CI 1.55–3.99), $p < 0.0001$) within 180 days of index date were found to indicate an increased likelihood of a diagnosis of Crohn's disease in the future. Anaemia in men (HR 2.55 (95% CI 1.02–6.37), $p = 0.046$), diarrhoea (HR 2.24 (95% CI 1.26–3.99), $p = 0.006$) and use of anti-diarrhoeal medication (HR 2.17 (95% CI 1.13–4.18), $p = 0.030$) within 180 days of index date, were found to indicate an increased risk of future diagnosis of ulcerative colitis.
Conclusion: The results suggest that patients with a diagnosis of perianal abscess are at an increased risk of having a subsequent diagnosis of Crohn's disease and ulcerative colitis. Physicians should have a low threshold for focussed history, examination and investigation to screen for inflammatory bowel disease in the perianal abscess cohort, particularly males with anaemia and those with a co-prescription for antidiarrheals.
Disclosure: Nothing to disclose

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P1528 EXPLORING THE DIVERSITY OF MUTATIONAL LANDSCAPES IN IBD BY TISSUE PROFILING USING A TARGETED NEXT-GENERATION SEQUENCING (NGS) TUMOR PANEL

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Introduction: Inflammatory bowel disease (IBD) is accompanied by a complex interplay of intestinal microbiota, host immune genetics and environmental factors (1). During the process, chemicals released upon the immune response from neutrophils such as reactive oxygen and nitrogen species, are known to induce mutagenesis within the affected tissue. The evolving tissue morphology is underlined by focal molecular changes within the affected gastrointestinal mucosa (2). It is expected that the resulting somatic DNA mutations of specific oncogenes and tumor suppressor genes are the main drivers of malignant conversion towards IBD-associated colorectal cancer. The molecular mechanisms of this transition exhibit distinguishing features that are not observed in other pathways of colorectal carcinoma development (3).
Aims and Methods: The aim of the project was to map the occurrence of somatic DNA mutations in inflammatory tissue of IBD patients to determine their frequency and relationship to the course of neoplastic transformation, the severity of inflammation and other clinical and laboratory parameters. The mutational spectra were then compared to profiles obtained from advanced colorectal adenomas and carcinomas resulting from traditional and serrated pathways.
Tissue samples were processed from a cohort of 20 patients with various types of ulcerative colitis and Crohn's disease. In addition tissues were processed from 2 patients with sporadic adenomas (advanced tubular and advances serrated). DNA was extracted using standard protocols from tissue resections (native or FFPE). Targeted NGS sequencing of 60 genes was performed on Illumina MiSeq sequencer using SureSeq^{TM} Solid tumor hybridization-based enrichment panel (Oxford Gene Technology, Oxfordshire, UK). NGS data was processed by NextGENe sequence analysis suite (Softgenetics, State College, PA).
Results: The diverse mutation spectra obtained were remotely reflecting the "reverse" Vogelstein model of molecular progression of IBD. Unlike in advanced adenomas, the frequency of prominent genes from traditional and serrated pathways was significantly lower in IBD samples.
Conclusion: Mutations in cancer driver genes indicate initiation of malignant conversion and are useful in assessment of the risk of IBD-related colorectal cancer. At the same time, presence of specific mutations in inflammatory tissue may be relevant for prediction of IBD therapy response, however, such assumption would need further confirmation. This work was funded by project no. MO1012
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P1529 TOFACITINIB AND CYTOKINES OF THE JAK SIGNALING PATHWAY PROTECT AGAINST EXTRACELLULAR MATRIX (ECM) DESTRUCTION IN AN INTESTINAL EX VIVO MODEL

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Introduction: Chronic inflammation in inflammatory bowel disease (IBD) causes tissue damage including extracellular matrix degradation. The inflammatory cascade holds both catabolic and repair signals. Tofacitinib, a small-molecule Janus kinase (JAK) 1/3 inhibitor, is studied in the treatment of IBD. Interleukin (IL)-6, -11 and -22 are IBD relevant cytokines that signals through JAK-pathway. IL-6 is a pleiotropic cytokine that acts as both a pro-inflammatory signalling molecule and as a repair molecule of the intestinal epithelium in response to injury. IL-11,

a family member of IL-6, is suggested to have same effects as IL-6, and IL-22 is important for intestinal homeostasis and repair. Type III collagen is a main constituent of the extracellular matrix (ECM) of the intestinal interstitial matrix. Consequently matrix metalloproteinase (MMP) degraded type III collagen measured by the biomarker C3M, may serve as a surrogate of intestinal ECM remodelling *ex vivo*.

Aims and Methods: We investigated the impact of Tofacitinib, IL-6, IL-11 and IL-22 on ECM remodelling in an intestinal *ex vivo* model as a potential drug-screening tool. Biopsy punches from porcine colonic tissue were incubated in William E culture media for 72 hours. The explants were stimulated at baseline, 24 and 48 hours with Tofacitinib (1uM, 0.1uM, 0.01uM), IL-6 (50 ng/mL, 5 ng/mL, 0.5 ng/mL) and IL-11 and IL-22 (100 ng/mL) or without stimuli (w/o). A competitive ELISA setup was used to estimate MMP degraded type III collagen (C3M) at 48 and 72 hours in explant supernatant. Viability was assessed by Alamar blue.

Results: The Jak 1/3 inhibitor, Tofacitinib, significantly decreased C3M release at 48 and 72 hours in a dose dependent manner, with the lowest concentration (0.01uM) being most potent. IL-6 significantly decreased the release of C3M at 72 hours in a dose-dependent manner, with the highest concentration being most potent. IL-11 and IL-22 stimulation significantly decreased C3M release at 48 and 72 hours. Stimuli did not affect viability.

Conclusion: IL-6, IL-11 and IL-22 attenuated degradation of type III collagen, thus supporting a protective role of these cytokines. There was a bell-shaped dose response curve of Tofacitinib on C3M release and ECM remodelling, in which low concentrations was protective. The dose effect of IL-6 and Tofacitinib on C3M and ECM remodelling suggests applications of this model to profiling treatments candidates, and provide an easier to use system to investigate the effect of drugs in the complicated intestinal biology.

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P1530 ACTIVITY OF TRANSFORMING GROWTH FACTOR (TGF) β1 AND BONE MORPHOGENIC PROTEIN (BMP) IN COLONIC EPITHELIUM ESCAPES THE INHIBITION OF *SMALL MOTHERS AGAINST DECAPENTAPLEGIC* (SMAD) 7 IN COLITIS-ASSOCIATED CANCER

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Introduction: Ulcerative colitis (UC) is associated with an increased risk of developing colitis-associated cancer (CAC). An inhibitor for SMAD7 (GED-0301), a molecule involved in the TGFβ1 and BMP pathways and highly expressed in UC affected colonic mucosa, is being investigated to determine its efficacy in reducing inflammation in UC patients. While inhibiting SMAD7 may ameliorate intestinal inflammation, no evidence is currently available to determine the effect on CAC risk, as both TGFβ1 and BMP are known to enhance late stages of colorectal carcinogenesis, and may possible have a role in CAC as well. As the inhibition of TGFβ1 and BMP pathways are exerted through the SMAD7-induced inhibition of phosphorylation of both SMAD3 and SMAD 1/5/8, respectively, we aimed to evaluate the expression of SMAD proteins in non-neoplastic, dysplastic and malignant colonic epithelium. This could give us an insight into the potential effect of SMAD7 inhibition during neoplastic progression in UC patients.

Aims and Methods: To evaluate the activity of the TGFβ1 and BMP pathways, cytoplasmic expression of SMAD7 and nuclear expression of p-SMAD3 and p-SMAD 1/5/8 was assessed by immunohistochemistry in a cohort of 25 archival colon tissue samples (8 CACs, 8 dysplastic lesions and 9 non-neoplastic mucosal samples) from patients who have undergone colectomy for UC. Protein expression was evaluated by both digital quantification and validated by blinded semi-quantitative scoring by a pathologist. In the same samples, expression of *SMAD7* mRNA in the colonic epithelium was evaluated with *in situ* hybridisation with specific target probes for the mRNA and evaluated by digital quantification. Significant differences were tested with one-way ANOVA.

Results: Cytoplasmic SMAD7 shows a significant increase of expression with the progression of the neoplastic process from inflamed to malignant epithelium ($p < 0.0001$). This is linked with an increase of BMP activity, evaluated by P-SMAD1/5/8 nuclear expression ($p < 0.0001$), but not of TGFβ1 activity evaluated by p-SMAD3 expression ($p = 0.53$). The differential SMAD7 expression amongst the stages of neoplastic progression is not correlated with changes in the mRNA level, a discrepancy that could be due to still unknown post-transcriptional or post-translational regulation of the protein. Interestingly, within the cancers, higher SMAD7 expression was detected in approximately 88% of CAC samples (7/8 samples), with the exception of one cancer treated with neo-adjuvant radiotherapy before collection due to the radiation damage.

Conclusion: Within our CAC sample cohort, TGFβ1 and BMP pathways do not show suppression in the presence of increased SMAD7. The increase in SMAD7 expression during neoplastic transformation may be a protective response to negate the carcinogenic effect of TGFβ1 and BMP on cancer. Although inhibiting SMAD7 as a therapy for UC may remit inflammation, it could potentially drive neoplastic generation and progression due to further enhancement in TGFβ1 and BMP pathways. We envisage further mechanistic studies *in vitro* and *in vivo*, in particular in organoids and mice model of CAC, could help in understanding the TGFβ superfamily pathway in colitis-associated cancer.

Disclosure: Nothing to disclose

P1531 AT BIOLOGIC ONSET THE GUT MICROBIAL PROFILE IN CROHN'S DISEASE PATIENTS IS SIMILAR TO THAT OF HEALTHY CONTROLS

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Introduction: Compared to healthy controls Crohn's Disease [CD] patients show a decrease in diversity and abundance of various microbial species. To this day it remains unclear whether these findings represent etiologic factors or simple consequences of protracted inflammation. In a colonoscopy-based screening study we have shown that ≥40% of asymptomatic first degree relatives [FDR] of CD patients have subclinical intestinal inflammation (IBD 2014;20:1049) – a finding consistent with previous fecal calprotectin-based studies (*Gastroenterology* 2003;124:1728). Of those with inflammation 10% had CD at biologic onset (very early disease with typical histological features) while the remaining had minimal inflammation – a nonevolving phenotype in between that of healthy FDR and FDR with CD. Hence – because of the very initial stage of the inflammatory process – FDR represent the ideal population to test the hypothesis that dysbiosis predates *clinical* CD and might be one of its causative factors.

Aims and Methods: For microbiome analysis we used next-generation sequencing 16S (bacterial) using DNA extracted from ileo-cecal biopsies of normal healthy controls ($n = 10$), CD patients ($n = 23$) and asymptomatic FDR ($n = 25$). Endoscopy and histology had categorised FDR into healthy ([FDR_1] $n = 9$), intermediate ([FDR_2] $n = 12$) and CD phenotypes ([FDR_3] $n = 4$). Data were analysed using Illumina CASAVA pipeline version 1.8.2 (Australian Genome Research Facility). Fifteen taxa were clustered into a phylogenetic tree using hierarchical clustering. Principal coordinates analysis (PCoA) was run on weighted UniFrac distances between Operational Taxonomic Units (OTUs) counts. Univariate negative binomial regressions with log-link functions were applied to assess the association between grouping and OTUs counts for each taxon (5 of the 15 taxa were excluded due to excess of zero OTUs counts), with controls as reference group. Statistical significance was set at 10%.

Results: As previously reported *Faecalibacterium prausnitzii, Ruminococcus, Akkermansia muciniphila* were decreased while *Bacteroides fragilis and* Enterobacteriaceae were significantly increased in CD patients compared to controls with an overall decrease of microbial diversity in CD patients. In the PcoA ellipse centroids of FDR were positioned in opposite quadrants as compared to CD patients, but close to the centroid for controls. In contrast, no clear separation between the 3 FDR groups was observed. Hence the microbial profile of FDR as a whole was very similar to that of controls and dissimilar to that of CD patients. Estimates of coefficients contrasting FDR_3 and controls showed larger p-values than those for estimates of coefficients contrasting CD patients and controls in 9 out of 10 taxa. Taxa for which CD and controls had significantly ($p < 0.10$) different OTUs, but FDR_3 and controls did not ($P > 0.1$), were: unknown, Actinobacteria, Firmicutes, Synergistetes, and TM7.

Conclusion: Intestinal microbial profiling reveals significant differences between healthy controls and CD patients. However, FDR bear a microbial profile remarkably similar to healthy controls in terms of species abundance and presence of specific bacterial species. In particular the microbiome of FDR_3 – that is, patients with CD at its biologic onset – is to a large extent superimposable to that of healthy controls. This observation raises the possibility that the dysbiosis associated with *clinical* CD might only be a consequence over time of the changed intestinal micro-environment due to the disease process.

Disclosure: Nothing to disclose

P1532 SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO) IS INCREASED IN BOTH CROHN'S DISEASE AND ULCERATIVE COLITIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Gut microbial dysbiosis and decreased diversity of the gut microbial ecosystem are now considered an essential factor in driving mucosal inflammation in inflammatory bowel disease (IBD). Small intestinal bacterial overgrowth (SIBO), defined as the presence of excessive and/or abnormal type of bacteria in the small bowel, plays an uncertain role in the pathogenesis of IBD.

Aims and Methods: We aimed to establish the prevalence of small intestinal bacterial overgrowth (SIBO) in patients with IBD, both ulcerative colitis (UC) and Crohn's disease (CD) compared with controls. Using the search terms 'small intestinal bacterial overgrowth (SIBO)' and 'Inflammatory Bowel Disease (IBD)' or 'small intestinal bacterial overgrowth (SIBO)' and 'Ulcerative Colitis (UC) or Crohn's Disease (CD)', 8 case-control studies that met inclusion criteria were identified when searching relevant databases. Prevalence rates for SIBO and relevant demographic and geographic data as well as information on the diagnostic modalities were extracted and prevalence rates and 95% confidence intervals (CI) of SIBO in IBD, UC and CD and controls calculated. In addition, the influence of the diagnostic modality (breath tests, aspirate or biopsy and culture or both) was determined.

Results: The final dataset combined 8 independent studies that recruited 553 adult patients with IBD and 1930 controls. Eight studies employed breath tests (five utilized glucose breath test (GBT), one each utilized lactulose and xylose breath test) and only one study used small bowel aspirate and culture for diagnosis of SIBO. Across all testing methods, the prevalence of SIBO in patients with IBD compared with controls was increased with an OR = 6.4 (95% CI 2.73–14.76), $p < 0.000$. In patients with IBD prevalence of SIBO was 28.9% (95% CI 25.10–32.65) as compared to 9.7% (95% CI 8.33–11.03) in controls. When the method of detection was limited to breath tests, the prevalence of SIBO in IBD was 30.8% (95% CI 27.72–35.85) compared to 10.0% (95% CI 8.43–11.69) in controls. In contrast, based upon culture techniques, the prevalence of SIBO in IBD was 15.5% (95% CI 6.2–28.84) vs 7.3% (95% CI 5.24–9.34). Only studies utilizing breath tests reported separately the prevalence of SIBO in UC and CD. In patients with CD the prevalence of SIBO is 32.8% (95% CI 25.04–40.48) as compared to 15.7% (95% CI 11.39–19.91) in patients with UC. There was no evidence that the association between SIBO and IBD was influenced by publication bias.

Conclusion: Regardless of the diagnostic modalities, prevalence of SIBO is significantly increased in patients with IBD when compared to controls. The prevalence of SIBO in patients with CD is double compared to those with UC. Compared to culture-based methods, the accepted gold-standard for the diagnosis of SIBO, breath tests overestimate the prevalence of SIBO and may have insufficient diagnostic specificity. While better diagnostic tests are required, it is critical to determine if SIBO in IBD is the cause for symptoms or a consequence of other abnormalities of gut function.

Disclosure: Nothing to disclose

P1533 THE EFFECTS OF ENTERIC GLIAL CELLS ON DENDRITIC CELL AND ITS POTENTIAL IMMUNOMODULATORY ROLES IN DEXTRAN SULPHATE SODIUM-INDUCED COLITIS

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Introduction: It is demonstrated in our previous study that the Enteric glial cells (EGC) closely connect with immune cells and play a vital role in maintaining gut immune homeostasis. Here, we reported that EGCs has direct effect on DCs, and could induce tolerogenic DCs by releasing nerve growth factor (NGF), which also could restore immune tolerance in vivo, and ameliorate DSS-induced mouse colitis.

Aims and Methods: DCs were generated from mouse bone marrow (BMDC), and co-cultured with EGC (ratio 1:1) which stimulated by Lipopolysaccharides (LPS) previously ($DC_{EDC\text{-}LPS}$) or not. Then the co-culture system was treated with anti-NGF. The expression of CD40, CD80, CD86 and major histocompatibility complex II (MHC-II) on the surface of DCs was determined by flow cytometry. The NGF and IL-10 secretion in culture supernatants was measured by ELISA. C57BL/6 mice were fed with 2.5% Dextran Sulphate Sodium (DSS) for 7 days to induce experimental colitis, the therapeutic action of $DC_{EGC\text{-}LPS}$ such as: disease activity index (DAI), histopathology score and Myeloperoxidase (MPO) were evaluated, the inflammatory cytokines and chemokines (IL-10,TNF-α,IL-1β) in colon tissue were measured by ELISA. The propotion T cell subsets of Th1,Th2,Th17 and the generation of IL-10-secreting Treg (Treg1) cell in mesenteric lymph nodes (MLN) was measured by intracellular staining and flow cytometry analysis

Results: DCs co-cultured with EGC (ratio 1:1) which stimulated by LPS previously did not up-regulate MHC-II, CD40, CD80, CD86, and secreted significant levels of the anti-inflammatory cytokine IL-10 and TGF-β, compared with $DC_{Control}$ and DCs co-cultured with EGC which did not stimulated by LPS, but the anti-NGF treatment partly abrogated these effect.

$DC_{EDC\text{-}LPS}$ injection significantly ameliorated DSS colitis in mice, as DAI, histopathology score and MPO score were decreased. $DC_{EDC\text{-}LPS}$ injection strikingly reduced the production of over-expressed pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-17, in colon tissue, increased the proportion of IL-10-positive Treg cell in mice MLN, and restored the decreased IL-10 level and the imbalance of Th cell subsets.

Conclusions: EGCs could induce tolerogenic DCs by releasing NGF, and $DC_{EDC\text{-}LPS}$ could alleviate the severity of DSS induced colitis in mice. This beneficial effect might be linked that $DC_{EDC\text{-}LPS}$ could restore the imbalance of Th cell subsets, prompt the differentiation of Treg, and ultimately reduced the over-expressed pro-inflammatory cytokines and increase IL-10 level.

Disclosure: Nothing to disclose

P1534 TARGETED ANALYSIS OF SERUM PROTEINS ENCODED AT KNOWN INFLAMMATORY BOWEL DISEASE RISK LOCI

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Introduction: Few studies have investigated the blood proteome of inflammatory bowel disease (IBD). We characterized the serum abundance of proteins encoded at 163 known IBD risk loci, and tested these proteins for their biomarker discovery potential.

Aims and Methods: Based on the Human Protein Atlas (HPA) antibody availability, 218 proteins from genes mapping at 163 IBD risk loci were selected. Targeted serum protein profiles from 49 Crohn's disease patients (CD), 51 ulcerative colitis patients (UC) and 50 sex and age-matched healthy individuals were obtained using multiplexed antibody suspension bead array assays. Differences in relative serum abundance levels between disease groups and controls were examined. Replication was attempted for CD-UC comparisons (including disease subtypes), by including 64 additional patients (33 CD and 31 UC). Antibodies targeting a potentially novel risk protein were validated by paired antibodies, Western blot, immuno-capture mass spectrometry and epitope mapping.

Results: By univariate analysis, thirteen proteins mostly related to neutrophil, T- and B-cell activation and function were differentially expressed in IBD *vs.* healthy controls, three in CD *vs.* healthy controls and two in UC *vs.* healthy controls (Table; $q < 0.01$). Multivariate analyses further differentiated disease groups from healthy and CD subtypes from UC ($p < 0.05$). Extended characterization of an antibody targeting a novel, most discriminative serum marker, the laccase (multi-copper oxidoreductase) domain containing 1 (LACC1) protein, provided evidence for antibody on-target specificity.

Conclusion: Using affinity proteomics, we identified a set of IBD-associated serum proteins encoded at IBD risk loci. These candidate proteins hold potential to be exploited as diagnostic biomarkers of IBD.

Comparison	Gene	Antibody	p-value	q-value
IBD-CTRL	LACC1	HPA040150	1.3E-05	3.0E-03
IBD-CTRL	IL2RA	HPA054622	4.7E-05	4.0E-03
IBD-CTRL	LACC1	HPA061537	6.1E-05	4.0E-03
IBD-CTRL	LNPEP	HPA043642	6.8E-05	4.0E-03
IBD-CTRL	CNTF	HPA046534	9.1E-05	4.1E-03
IBD-CTRL	LPXN	HPA061441	1.0E-04	4.1E-03
IBD-CTRL	BTNL2	HPA039844	1.9E-04	6.1E-03
IBD-CTRL	IFNAR2	HPA029229	2.2E-04	6.1E-03
IBD-CTRL	CARD11	HPA052984	2.3E-04	6.1E-03
IBD-CTRL	JAK2	HPA058253	3.8E-04	8.6E-03
IBD-CTRL	PEX13	HPA061468	4.0E-04	8.6E-03
IBD-CTRL	SLC22A5	HPA063062	5.4E-04	9.8E-03
IBD-CTRL	IFNG	HPA063125	5.4E-04	9.8E-03
CD-CTRL	LACC1	HPA040150	1.8E-05	2.1E-03
CD-CTRL	SAA	HPA059733	2.0E-05	2.1E-03
CD-CTRL	LNPEP	HPA043642	1.2E-04	8.4E-03
UC-CTRL	CNTF	HPA046534	8.3E-05	7.8E-03
UC-CTRL	LPXN	HPA061441	8.9E-05	7.8E-03

[Antibodies and corresponding proteins with differential abundance in patients with IBD and subtypes of the disease compared to controls]

Disclosure: This study was supported by unrestricted research grants from AstraZeneca Translational Research Program (Post-genomic applications in IBD: exploitation of genetic information toward improved diagnosis and therapy).

P1535 INFLUENCE OF SMOKING ON THE MRNA EXPRESSION OF CYTOKINES IN MUCOSA OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: It is well known that smoking is a risk factor for developing and clinical course of Crohn's disease (CD), but at the other side smoking is protective factor of ulcerative colitis (UC). Molecular pathways that are influenced by smoking in CD and UC are poorly understood.

Aims and Methods: The aim of our study was analyze influence of smoking on the mRNA expression of cytokines in mucosa of patients with CD as well as UC. We performed cross-sectional study. The cohort consists of 87 IBD patients (47CD patients and 40 UC patients) followed at IBD center of University Hospital Bratislava- Ružinov. We recorded demographic and clinical data of each patient including smoking. We performed colonoscopy in each patient and took biopsy from inflamed and non-inflamed sigma (CD,UC) and terminal ileum (CD). mRNA was extracted from mucosal biopsy samples for each cytokines (IL-6, IL-8, IL-12, IL-17, IL-23, TNFα, CCR1, CCR2, CCR5, CCR9, CCL5, TLR2, TLR4, TLR5, CD207, CD206) and transcription factor FoxP3 and was normalised to house-keeping gene (GAPDH). Finaly, we compared mRNA expression of target cytokines in mucosa of smokers and non-smokers of IBD patients.

Results: Smokers with Crohn′s disease had significant higher mRNA expression of proinflammatory cytokine TNF α ($p = 0.003$) in inflamed mucosa in sigma in compared with non-smokers. In smokers with ulcerative colitis we observed significant higher mRNA expression of anti-inflammatory cytokine IL 10 ($p = 0.022$) in non-inflamed mucosa of sigma. Similarly, smokers with UC have significant higher mRNA expression of cytokines TLR 2 ($p = 0.024$) and CCR1 ($p = 0.049$) in non-inflamed mucosa of sigma.

Conclusion: According to our, smoking stimulates mRNA expression of anti-inflammatory cytokine IL-10 in smokers with UC, but on the other side smokers with CD had significant higher mRNA expression of pro-inflammatory cytokine TNF in mucosa of sigma.

Disclosure: Nothing to disclose

P1536 SHALLOW WHOLE-GENOME SEQUENCING PREDICTS THE FUTURE CANCER RISK OF LOW-GRADE DYSPLASTIC LESIONS ARISING IN ULCERATIVE COLITIS

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Introduction: The management of low-grade dysplasia (LGD) in ulcerative colitis (UC) is uncertain due to the variable risk of progression to colorectal cancer (CRC). Chromosomal copy number alterations (CNAs) are known to occur in colonic epithelial cells of UC patients who have developed CRC. The burden of CNAs in precursor LGD relative to high-grade dysplasia (HGD) and CRC has not been defined, and the correlation between LGD CNA burden and future CRC risk is unknown.

Shallow whole genome sequencing[1] is a novel, high-throughput, cost-effective technique for high-resolution CNA assessment in formalin-fixed, paraffin-embedded tissue. We have successfully utilised this technique using as little as 500 picograms of relatively degraded DNA that has been extracted from archival tissue as much as 20 years old, at a cost of approximately €75 per tissue sample.

Aims and Methods: To define the genomic changes that differentiate LGD from both HGD and CRC, we identified 19 UC proctocolectomy specimens with HGD and/or CRC, and analysed 77 neoplastic regions of interest (36 LGD, 34 HGD and 7 CRC).

To determine the utility of shallow whole genome sequencing in predicting future CRC, we then analysed dysplastic tissue from 35 patients: 13 'progressor' patients with 27 LGD lesions who subsequently developed HGD and/or CRC a median 427 days later (IQR 213–777 days), and 22 'non-progressor' patients with 26 LGD lesions who remained free of HGD and CRC at least 5 years later. The two patient groups are matched for age, gender, disease duration and LGD location.

Histological diagnosis was confirmed by two blinded pathologists. Shallow whole-genome sequencing (0.1x) was performed using a standardised pipeline for epithelial cell enrichment, DNA extraction, library preparation, next generation sequencing and bioinformatic analysis.

Results: A median 12% of the genome of LGD tissue from proctocolectomy specimens showed CNAs (IQR 4–32%), compared to 23% in HGD/CRC (IQR 19–42%, $p = 0.003$). Similarly, the number of CNA events was greater in HGD and CRC compared to LGD ($p < 0.001$). Multiple CNAs involving key driver genes were more frequent in HGD/CRC compared to LGD (adjusted p values < 0.05), including 8q gain (*MYC* loss, OR 17.2), 4q loss (OR 4.59) and 18q loss (*DCC*/*SMAD4* loss, OR 4.15).

Both the maximal total CNA burden and number of CNA events are greater in the LGD lesions of progressor patients compared to the LGD lesions of non-progressor patients ($p < 0.01$).

A Kaplan-Meier survival analysis of the 35 grouped 'progressor' and 'non-progressor' patients demonstrates that patients in this cohort bearing LGD with the 25% greatest number of copy number alteration events are significantly more likely to develop future CRC/HGD than the remaining 75% of patients (HR 7.1, $p < 0.001$).

Conclusion: LGD lesions demonstrate a surprising genomic diversity in copy number alteration burden, with some LGD lesions bearing CNA profiles indistinguishable from HGD and CRC. Shallow whole genome sequencing has potential translational utility, by stratifying patients with LGD according to their future risk of progression to HGD and/or CRC.

Disclosure: Nothing to disclose

Reference

1. Scheinin I, Sie D, Bengtsson H et al. DNA copy number analysis of fresh and formalin-fixed specimens by shallow whole-genome sequencing with identification and exclusion of problematic regions in the genome assembly. *Genome Res*. 2014 Dec; 24(12): 2022–32. doi: 10.1101/gr.175141.114. (PMID: 25236618).

P1537 ROLE OF FACTORS RELEASED FROM ADIPOSE TISSUE, CYTOKINES AND MYOKINES IN FORCED TREADMILL EXERCISE-INDUCED EXACERBATION OF EXPERIMENTAL COLITIS IN MICE FED STANDARD DIET AND DIET-INDUCED OBESITY. RELEVANCE OF PHYSICAL ACTIVITY TO THE COURSE OF IBD IN HUMANS

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Introduction: Inflammatory bowel diseases (IBDs) are a heterogeneous group of disorders exhibited by two major phenotypic forms: Crohn's disease and ulcerative colitis. Although the etiology of IBD is unknown, several factors released from the white adipose tissue (WAT) and skeletal muscles including adipokines and myokines, as well as changes in intestinal microbiome were proposed. Recently, we have reported that the voluntary wheel running reduced colonic inflammation in rodent models of colitis but the effect of forced treadmill exercise has not been extensively studied.

Aims and Methods: The role of protective myokines such as irisin and adipokines including adiponectin affecting the course of IBD in experimental animals forced to exercise has not been fully elucidated. We determined the effect of moderate forced treadmill running for 6 weeks with the speed 12 cm/sec in mice fed a high-fat diet (HFD) compared to those on a standard chow diet (SD) with intrarectal administration of 2,4,6-trinitrobenzenesulfonic acid (TNBS) colitis. To minimize distress, mice did not run during or after TNBS colitis. The disease activity index (DAI), colonic blood flow (CBF), the colonic tissue content of IL-17, IFNγ, TNF-α, IL-1β, IL-6 and IL-10 using Luminex Multiplex Assays, the stress oxidative markers MDA, reduced glutathione, SOD and plasma myokine irisin, adipokines leptin and adiponectin levels and real-time PCR and protein expression of proinflammatory factors in colonic mucosa and mesenteric fat were assessed.

Results: Macroscopic and microscopic colitis in sedentary SD mice was accompanied by a significant fall in CBF and moderate increase in colonic tissue weight and a significant increase in the plasma levels of TNF-α, IL-6 and IL-1β ($p < 0.05$). In sedentary HFD mice, colonic lesions were aggravated, colonic tissue weight increased and the IL-1β, TNF-α, IL-6, IL-17, and IFNγ and leptin levels significantly increased. Simultaneously, a significant decrease in the plasma irisin and adiponectin levels was observed in HDF fed mice compared with SD mice ($p < 0.05$). Treadmill exercise significantly increased the macroscopic and microscopic colitis, substantially decreased CBF and raised the plasma TNF-α, IL-6, IL-1β, and leptin levels while decreasing both, the plasma irisin and the plasma and WAT concentrations of adiponectin in HFD mice ($p < 0.05$). The protein expression of heme oxygenase (HO-1) and hypoxia inducible factor1α (HIF-1α) were significantly increased in colonic mucosa of treadmill exercising HFD mice with colitis.

Conclusion: We conclude that: 1. experimental colitis is exacerbated in HFD mice, possibly due to a fall in colonic microcirculation and an increase in the plasma and mesenteric fat content of proinflammatory biomarkers, and 2. forced treadmill running exacerbates the severity of colonic damage in mice fed a HFD through the rise in oxidative stress, the increase in expression and activity of proinflammatory factors including leptin released from WAT and the attenuation of protective mediators irisin and adiponectin.

Disclosure: Nothing to disclose

P1538 DIFFERENT METABONOMIC PROFILES BETWEEN CROHN'S PERIANAL FISTULA AND IDIOPATHIC (CRYPTOGLANDULAR) PERIANAL FISTULAS MAY OFFER CLUES TO UNDERLYING PATHOGENESIS

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Introduction: The pathogenesis of perianal fistulas is poorly understood. The reasons why fistulas originate have been explained in idiopathic cases, with the cryptoglandular theory being widely accepted. However, in Crohn's disease, it is thought to involve interplay between microbiological, immunological and genetic factors. It remains unclear why the fistula persists.

Aims and Methods: We undertook a pilot study with the aim of defining how metabolic profile varies in idiopathic (cryptoglandular) cases of perianal fistula and Crohn's perianal fistula. Fistula tissue biopsy was obtained from the fistula tract of 31 patients with idiopathic perianal fistula and 20 patients with Crohn's anal fistula. Ultraperformance liquid chromatography-mass spectrometry (UPLC-MS) profiling in positive mode was implemented to detect metabolites present in fistula samples. Samples were analysed using hydrophilic liquid chromatography (HILIC). The validated hydrophilic liquid (HILIC) chromatographic method developed at the MRC-NIHR National Phenome Centre, IRDB Building, London, UK(1).

Multivariate data analysis was performed using the SIMCA software (v.14.0.2, Umetrics, Umeå, Sweden). Principle component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA) models were built to find metabolites that can predict IBD fistula.

Metabolite putative identification was conducted by matching accurate *m/z*measurements of detected chromatographic features to theoretical value from in-house databases and on-line databases such as the human metabolite database (HMDB, http://www.hmdb.ca/) KEGG (http://www.genome.jp/kegg/ligand.html), METLIN (http://metlin.scripps.edu/) and previous publications.

Results: Significant OPLS-DA model (p.value CV-ANOVA 0.0117) separated well between idiopathic and IBD fistula patients. Robust statistical parameters were obtained with R2X 0.212 R2Y 0.658, Q2Y 0.260).

Eighty features were selected from the OPLS-DA model as potential predictors of the group separation. From these, 26 putatively assigned including validation of the arginine with standard. 18 of these 26 features were increased and 8 decreased in CD perianal fistula.

Conclusion: This study highlights the potential for metabolite profiling to differentiate Crohn's and idiopathic perianal fistula groups. Further work is required to understand the pathways to which the significant amino acids described may be related to, as these may offer clues as to the underlying pathogenesis.

Disclosure: Nothing to disclose

Reference

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P1539 ASSOCIATION BETWEEN POLYMORPHISMS -318 C/T, 49 A/G OF CTLA-4 GENE AND POLYMORPHISM IVS 3 +17 T/C OF CD28 GENE AND CROHN'S DISEASE : A CONTROLLED STUDY

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Introduction: Crohn's CD disease is a pathology characterized by a chronic inflammation of the intestinal tract engendered by an excessive activation of lymphocytes T, which would be responsible for a change of the immune answer. The gene CTLA-4 (Cytotoxic-T-Lymphocyte Antigen 4) and the gene CD28 (Cluster of differentiation), represent two good candidates genes to explain the physiopathology of CD. While the molecule CTLA-4 plays a leading role in the negative control of Lymphocytes T activated, the protein CD28 assures an opposing role, by guaranteeing their activation, their survival and their expansion. Besides, several studies analyzed the possible association of these two genes with certain autoimmune diseases as type 1 diabetes, celiac disease and rheumatoid arthritis.

Aims and Methods: Searching a correlation between polymorphisms of -318 C/T, 49 A/G CTL-4 gene and SNP IVS 3 17 T/C CD28 gene studied by PCR-SSP and CD and compare the results to control group.

Results: The study concerned 50 CD's patients and 108 controls. The frequency of the allele C of the SNP-318 C/T was more important in CD patients (94%) than in controls (91.2%). The frequency of the allele A of the SNP 49 was more frequent in patients (75%) than in controls (70.8%), The frequency of the allele T of the SNP IVS 3 17 T/C was also superior in patients (83%) than in healthy (80.1%) and a frequency of the more considerable haplotype TCA was more frequent in CD patients (61.8%) than in controls (52.3%). However, these differences were not significant (p = 0.3917; p = 0.4422; p = 0.54; p = 0.1133).

Conclusion: We concluded to the absence of an association between allelic and haplotypic polymorphisms Crohn's disease studied population. Our results are in agreement with most of the studies. To our knowledge, for the gene CD28, our study is the first one that searched an association between the disease of Crohn's disease and the polymorphism. Other studies with more large scales with various ethnic groups and stratification according to the risk factors are necessary to explore the exact role of the polymorphisms of the gene CTLA-4 and CD28 in the physiopathology of Crohn's disease.

Disclosure: Nothing to disclose

P1540 CROHN'S DISEASE PHENOTYPE DIFFERS BY BODY MASS INDEX AT PRESENTATION

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Introduction: There is increasing appreciation that patients with Crohn's disease (CD) are likely to have either a low or high body mass index (BMI) at presentation, compared to subjects with ulcerative colitis (UC) and healthy controls. It is possible that the pathogenesis of CD may be different between patients with low and high BMI at presentation. The relationship between BMI at presentation and CD phenotype has not been previously evaluated.

Aims and Methods: 182 subjects diagnosed with CD between 1976 and 2017 had their BMI recorded at the time of diagnosis (n = 97) or by validated recall (n = 85), together with their disease location and disease behaviour at the time of diagnosis. Association between BMI at diagnosis, phenotype and risk factors were analysed by logistic regression, adjusting for year of diagnosis, age at diagnosis and sex.

Results: The table shows the distribution of CD location, CD behaviour, risk factors and patient characteristics, across the different BMI categories.

Variables	Low BMI (n = 13)	Normal BMI (n = 85) (reference)	Overweight BMI (n = 49)	Obese (n = 35)
Age at Dx: Mean (SD)	32.4 (15)	33.3 (16)	35.1 (14)	38.1 (14) (p = 0.02)
Sex (Male)	6 (46%)	45(53%)	19(44%)	21(60%)
Year of Dx: Mean (SD)	2005 (16%)	2008 (11%)	2007 (13%)	2010 (11%)
Location L1	4 (31%)	12 (12%)	9 (22%)	13 (37%) (p < 0.04)
Location L2	3 (23%)	14 (15%)	15 (35%)	7 (20%)
Location L3	6 (46%)	57 (67%)	19(44%)	14 (40%) (p < 0.01)
Behaviour B1	3 (23%)	16 (19%)	14(32%)	11(31%)
Behaviour B2	6 (46%)	38 (45%)	10(23%)	16 (46%)
Behaviour B3	4 (31%)	25 (29%)	14 (32%)	7 (20%)
Behaviour Perianal	3(23%)	13(16%)	6(14%)	5(14%)
Surgery	6 (46%)	39 (46%)	15 (35%)	7 (20%) (p < 0.05)
Extraintestinal manifestations	3 (23%)	2 (2%)	3 (6%)	6 (17%)

[Results Table]

Dx: diagnosis, SD: standard deviation, Disease location L1: ileal, L2: colonic, L3: ileocolonic, Disease behaviour B1: non stricturing non penetrating, B2: stricturing, B3: penetrating.

There was evidence that CD phenotype differed according to BMI. Extremes of BMI were associated with an ileal location. Obesity at the time of diagnosis was associated with an older age at diagnosis, and a reduced need for surgery. Ileocolonic disease was associated with a normal BMI at diagnosis. There was a trend for smoking to be associated with low BMI at diagnosis.

Conclusion: Evidence is presented for an association between BMI at presentation and differences in CD phenotype. Further study is recommended to evaluate these relationships further.

Disclosure: Nothing to disclose

P1541 FEMALE GENDER INCREASES THE RISK OF ANXIETY AND DEPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDER ANTI-TNFα THERAPY

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Introduction: Depression and anxiety are significant predictors of worse health-related qualify of life in inflammatory bowel disease (IBD) patients. Nevertheless, the role of anxiety and depression in IBD patients under anti-TNFα treatment has been poorly investigated.
Aims and Methods: The aim of the study was to evaluate both the frequency of anxiety and depression symptoms in IBD patients under anti-TNFα therapy, and the potential factors influencing the development of these symptoms.
A prospective observational cohort study was designed. All IBD patients older than or with 18 years under treatment with anti-TNFα were consecutively included. Prevalence of anxiety and depression was assessed in IBD outpatients using the Hospital Anxiety and Depression scale (HAD). When using this scale we considered scores of 8 or higher to be abnormal. Relapse was defined in Crohn's disease (CD) as a Harvey and Bradshaw index higher than 4, and in ulcerative colitis (UC) as a Partial Mayo index higher than 2. Patient demographics and disease characteristics were also collected: age, sex, marital status, smoking habit, type of IBD, phenotype included in Montreal classification, extra-intestinal manifestations, clinical activity, prior surgery, perianal disease and steroid or immunosuppresant use. Results are shown as OR and 95% CI, and analysed by logistic regression.
Results: Eighty patients were consecutively included (37 male, mean age 40 years, range from 20–67). Sixty patients (75%) had CD and twenty ulcerative colitis (25%); sixty-one (76%) of them were under maintenance treatment with infliximab and nineteen (24%) with adalimumab. Anxiety and depression symptoms were presented in 49.4% and 25.3%, respectively. Females were more likely to have anxiety (OR = 4.73; 95% CI: 1.82–12.26; p = 0.001) and depression (OR = 3.56; 95% CI: 1.14–11.06; p = 0.028). Patients with active disease were no more likely to have anxiety (OR = 1.001; 95% CI: 0.973–1.029; p = 0.972) or depression (OR = 1.013; 95% CI: 0.984–1.042; p = 0.389). None of the other socio-demographic and clinical parameters were significantly associated with the development of anxiety or depression.
Conclusion: An important number of IBD patients under anti-TNFα present anxiety or depressive symptoms. Female gender is associated with more anxiety and depression in this group of patients. However disease activity was not associated with an increase in either anxiety or depression.
Disclosure: Nothing to disclose

P1542 PREVALENCE OF ANAEMIA IN INFLAMMATORY BOWEL DISEASE: PRELIMINARY RESULTS OF THE OBSERVATIONAL ITALIAN MULTICENTRE IG-IBD STUDY RIDART 1

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Introduction: Anaemia is the most common extra-intestinal manifestation in inflammatory bowel disease (IBD).
Aims and Methods: The RIDART 1 is an independent, observational, multicentre study, promoted by the Italian Group for the study of Inflammatory Bowel Disease (IG-IBD) with the primary aim to define the prevalence of anaemia in an unselected population of Italian patients with IBD. 3220 unselected Italian patients with IBD were included. The follow-up of anaemic patients was extended up to six months after recruitment in order to evaluate how anaemic patients were treated and if the ECCO guidelines for the treatment of iron deficiency anaemia in IBD were correctly applied. Here we showed preliminary results describing the main features of IBD patients with anaemia in terms of demography, disease activity, anaemia pathogenesis and severity 20 months after starting the study.
Results: Of the 3220 IBD patients included, 392 (12.2%) had anaemia. No difference between anaemic and non-anaemic subjects were observed as far as patient age, gender and disease duration. Body mass index was significantly (p = 0.0051) lower in the anaemic group (22 ± 2.5 kg/m^2) compared with the non-anaemic one (24 ± 2 kg/m^2). In most cases (86%) anaemia was mild (Hb≥9.5 g/dL), and only 2% of patients had severe anaemia (Hb < 8.0 g/dL). Hb was lower in patients with active disease and correlated significantly with CDAI in Crohn's disease (p = 0.0182) and CAI in ulcerative colitis (p = 0.0021). An isolated iron deficiency was responsible for 61.7% of anaemic cases, while the remaining cases had anaemia of chronic disease (12.8%), vitamin deficiencies (2.8%), and various combinations of iron and/or vitamin deficiencies and inflammation (22.7%).
Conclusion: The lower prevalence of anaemia in RIDART1 (12.2%) in comparison to that reported in previous European studies may be due to the fact that, in recent years, more attention is paid to the impact of anaemia in IBD patients, and both anaemia and IBD are more efficiently treated than in the past. Caution, however, must be used in the interpretation of the present data since the RIDART 1 study is still under way.
Disclosure: Nothing to disclose

P1543 THE IMPACT OF CROHN'S DISEASE ON PERIODONTAL STATUS – PRELIMINARY RESULTS FROM POLIBD STUDY

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Introduction: Periodontitis is a disease manifested by the loss of clinical attachment, deepening of the gingiva pockets, loss of bone supporting the teeth roots and their mobility leading consequently to the need for teeth extraction. Periodontal disease is the second cause (just after the dental caries) of premature loss of natural teeth. The course and severity of periodontitis are significantly influenced by the virulence of the plaque bacteria, as well as the immune defenses of the organism.
Aims and Methods: The aim of the study was to determine the state of periodontium based on CPITN index in correlation to smoking habits and type of treatment in patients suffering from Crohn's disease (CD).
The 110 subjects (80 with Crohn's disease and 30 healthy control) aged 18–65 (mean 34.9) were included to the study. Disease phenotype at diagnosis was classified according to the Montreal classification. Studies included only these patients who had conducted a complete diagnostic workup of the entire gastrointestinal tract. The complete assessment of the periodontium was based on the CPITN index which is a simple and quick screening tool.
Results: In the studied population, a statistically significant difference was found between the groups in the range of CPITN (p = 0.018). In the CD group, symptoms of inflammation (codes 1–4) were noted in 87.5% of subjects, while in the healthy group they concerned 76.9%. In CD patients group codes 3 and 4 (evidence of occurrence shallow or deep periodontal pockets) in total were found in 18.8% while in the control group it was 6.7% and only related to code 3. Code 4 has not been recorded in anyone in the control group.
A statistically significant relationship was found between CPITN and the age of patients in the entire studied population (p = 0.0004). There was no significant correlation between periodontium and gender or type of treatment in CD.
Statistical analysis showed no significant differences between the groups in the field of cigarette smoking despite the fact that in the group with CD current and past smokers were up to 47.5%, while in the control group they constituted 26.7%, respectively. In the studied population there was no significant correlation between cigarette smoking and the value of CPITN.
Conclusion: The results of the study indicate higher CPITN values in people with CD compared to the control group regardless of gender, type of treatment and smoking. This may indicate the association of the Crohn's disease with periodontal health.
Disclosure: Nothing to disclose

P1544 PREDICTING FACTORS OF PROXIMAL DISEASE EXTENT IN ULCERATIVE COLITIS IN THE BIOLOGIC ERA

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Introduction: Ulcerative colitis (UC) is a chronic inflammatory bowel disease of unknown aetiology. UC typically affects the rectum and may extend towards the proximal colon over time. This disease behaviour is clinically relevant and impacts on long-term outcomes. It is known that proximal disease extent is associated to higher burden of systemic inflammation and greater severity. Extensive colitis is also related to a higher colorectal cancer risk. The natural course of UC is unpredictable and the risk factors associated to proximal progression have not been clarified. It is important to identify patients at high risk of proximal disease extent in order to optimize treatment and follow-up.
Aims and Methods: The aim of this study was to investigate the rate of proximal disease progression and to identify risk factors associated with extent of disease in rectal and left-side UC in the biologic era. This is an observational, retrospective study, that included all cases diagnosed with rectal and left-side UC confirmed from January 2005 to December 2016. Proximal disease extent was assessed according to Montreal Classification criteria: proctitis (E1) when the involvement is limited to rectum, left-side colitis (E2) if extent is distal to splenic flexure, and extensive colitis (E3) if colonic involvement extends proximal to splenic flexure. Proximal disease extent was defined as progression from E1 or E2 to E3, confirmed by endoscopy. Demographic, clinical, endoscopic, laboratory and drugs received data were collected on all patients. Mann-Whitney test were performed for continuous variables and chi-square test for categorical variables to compare the baseline characteristics between the non-extent group and the extent group. The Cox logistic regression model was used to identify risk factors associated with proximal disease extent.
Results: We included 71 patients with distal UC: 36 E1 and 35 E2; 46.5% were male. Median follow-up of 7 (IQR 4–9) years. A total of 14 (19.7%) progressed to extensive colitis; median time to progression was 5 (IQR 1–8) years. 3 patients underwent colectomy during follow-up (2 in non-extent group). At diagnosis, 3 patients received anti-TNF therapy and only 2 patients had extent and 1 no progressed. Baseline patient characteristics including age, gender, smoking habit, hypertension, obesity, diabetes mellitus, history of appendectomy, family history of inflammatory bowel disease and initial laboratory data were not significantly different in the extent group compared with patients whose ulcerative colitis did not extend. However, extent group were more likely to suffer from primary sclerosing cholangitis (14.3% versus 0%, $p = 0.016$). Furthermore, there was no significant difference in Mayo score at diagnosis between the two groups. In the multivariate analysis, risk factors associated with proximal disease extent were female sex (HR 6.7, 95% CI 1.4–32.5) and arthropathy at diagnosis (HR:3.7, 95% CI 1.1–12.8), whereas the use of oral 5-aminosalicylic acid since the diagnosis was a protective factor of proximal disease extent (HR: 0.19, 95% CI 0.04–0.82).
Conclusion: The disease proximal progression was observed in 19.7% of patients with limited UC over time. This study suggests that female sex and arthropathy represent risk factors to proximal disease extent, whereas the use of 5-aminosalicylic acid oral at diagnosis is associated as a protective factor of disease extent in patients with limited UC. No conclusion can be drawn from the possible influence of biologic treatment on the proximal disease extent.
Disclosure: Nothing to disclose

P1545 THE ROLE OF SLEEP DISORDERS IN INFLAMMATORY BOWEL DISEASES (IBD) CLINICAL COURSE

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Introduction: Etiology of Crohn's disease (CD) and ulcerative colitis (UC) has not been clearly defined and is multifactorial. Sleep may modulate the activity of the immunologic system. Mouse colitis model showed that sleep continuity disturbances exacerbated clinical and histopathological signs of the disease. The role of the sleep disturbances in inflammatory bowel diseases (IBD) clinical course is poorly understood.
Aims and Methods: The aim of the study was to evaluate compare the sleep patterns in patients with of IBD depending on the disease activity.
25 individuals with IBD in exacerbation (age: 45 ± 13.5; 45% of men) and 25 in remission (age: 43 ± 14.5; 68% of men) were included in the study and completed questionnaires assessing sleep quality: Pittsburgh Sleep Quality Index (PSQI), Athens insomnia scale (AIS). The mood level (using Beck Depression Inventory (BDI)) and the level of pain (using Visual Analogue Scale (VAS) and Laitinen Pain Scale (LPS)) were measured. The active disease will be defined as the Harvey-Bradshaw index score >6 on the CD and the partial Mayo scale >3 in the UC. Information about the progress of the disease, methods of treatment and socio-demographic variables were also collected.
Results: Differences between quality of sleep and the type of IBD were not significant (CD: $n = 24$ 5 ± 1.5 and UC: $n = 26$ 5 ± 2 $p = 0.977$ for PSQI; CD: 6 ± 2.25 and UC: 4 ± 4 $p = 0.691$ for AIS). Patients in exacerbation presented decreased quality of sleep in both PSQI (6 ± 2 $p = 0.035$) and AIS (8 ± 3.5 $p = 0.001$) compared to remission group (4 ± 1.5 for PSQI and 4 ± 2 for AIS). Additionally, exacerbation group score was higher in VAS (5 ± 2.5 $p = 0.006$), LPS (5 ± 3 $p = 0.004$) and BDI (9 ± 5 $p = 0.003$) scale than in remission group (2 ± 1.5 for VAS, 2 ± 1.5 for LPS; 5 ± 3.5 for BDI). Subsequent ANCOVA analysis has shown that sleep disorders in exacerbation were more severe than in remission and were independent of covariates such as VAS, LPS and BDI regarding both sleep questionnaires PSQI ($p = 0.010$) and AIS ($p < 0.001$).
Conclusion: Patients with UC have similar sleep problems compared to those with CD. Decreased sleep quality may not depend on pain and depression, which are generally recognized as factors influencing sleep quality. The problem of sleep disturbances in IBD exacerbation should be considered in the disease treatment.
Disclosure: Nothing to disclose

P1546 SELECTED CYTOKINES IN PERIODONTITIS IN PATIENTS WITH CROHN'S DISEASE – PRELIMINARY RESULTS FROM POLIBD STUDY

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Introduction: Il-1β is a universal factor that stimulates the inflammatory reaction and can induce the secretion of other cytokines. Interleukin-6 (Il-6) is secreted to stimulate immune response in the inflammatory and auto-immune processes. Pro inflamatory cytokines mediate inflammation in both Crohn's disease (CD) and periodontitis conditions. However, the influence of periodontitis ovelaping CD on cytokine levels has not been elucidated up to the date. From clinical point of view, characteristic patern of inflammatory cytokines may be usefull durning the differentiation between common periodontitis and early stage of oral manifestation of CD.
Aims and Methods: The aim was to determine the serum levels of selected cytokines for CD patients depending on the condition of the periodontium as well as the habit of smoking, the type of treatment, the time elapsed from the diagnosis and disease phenotype according to the Montreal classification.
40 patients aged 18–65 years (mean 33.8) with Crohn's disease were involved to the studies. Patients completed survey and dental examination with CPITN index calculating according to WHO recommendations was performed. Following, the data on the Il-1β and Il-6 levels were assessed by MagPix 13-plex bone panel.
Results: Overall cytokine levels were low. Il-1β levels were 0.20–1.68 pg/mL (mean 0,59 pg/mL) and Il-6 levels were 2.03–100.50 pg/mL (mean 11,73 pg/mL). Levels of both interleukins were significantly statistycally positively correlated ($R = 0.32$, $p = 0.039$).
Suprisingly, Il-1β was negatively correlated with state of periodontium related to CPITN ($R = -0.31$, $p = 0.047$).
We didn't find any relationship between interlekin levels and smoking. The disease phenotype, type of tretment and time elapsed from diagnosis weren't significantly correlated with Il-1β nor Il-6 levels.
Conclusion: Since cytokine levels, including Il-1β and Il-6, are expected to be increased in the course of Crohn's disease, our results differ from results obtained by other authors. We noticed differences in Il-1β serum level of CD patients related to the state of periodontium. Some other findings reported changes (an increase) in periodontitis only in salivary or gingival fluid levels of Il-1β and Il-6 but not in serum.
Disclosure: Nothing to disclose

P1547 PREDICTIVE FACTORS OF BONE LOSS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Patients with inflammatory bowel disease (IBD) have an increasing risk of developing bone and mineral metabolism disorders. Osteopenia and osteoporosis are a frequent but often underestimated complications in these patients. Several factors could contribute to osteopenia, while pathogenetic mechanisms are still ambiguous.
Aims and Methods: The aim of this study is to assess the prevalence and the risk factors associated with bone loss in IBD patients.
We conducted a prospective and descriptive study including 104 patients with IBD supervised within our department. Only patients who had bone densitometry and a phosphocalcic biology analysis were included. Bone mineral density (BMD) was measured with diphotonic x-ray absorptiometry of the lumbar spine and the neck of the left femur. Results were expressed with T score (osteopenia: -2.5 standard deviation (SD) $< T <$ -1 SD, osteoporosis: $T < -2.5$ SD) according to the World Health Organization (WHO) specifications.
Results: 104 patients with IBD were included (55 women, 49 men), 55 had Crohn's disease (CD) (52.88%), 40 had ulcerative colitis (UC) (38.46%), and 9 had indeterminate colitis (8.65%). The average age at diagnosis was 37.86 years [15–73]. BMD was normal in 47 patients (45.2%) and reduced in 57 patients (54.8%). In 22 cases osteopenia was diagnosed (21.15%) and 35 patients had osteoporosis (33.65%). In patients with Crohn's disease, 56% of cases (31/55) had a reduced BMD (osteopenia in 13 cases and osteoporosis in 18 cases). 60% of patients with UC (24/40) had reduced BMD (osteopenia in 8 cases and osteoporosis in 16 patients) and 22% of patients with indeterminate colitis (2/9) had a reduced BMD (osteopenia in 1 case and osteoporosis in 1 patient), rheumatologic manifestations were found in 19 patients with a reduced BMD, 27% of which had ankylosing spondyloarthritis. 29 patients received a full

corticosteroid therapy dose for at least 4 weeks. The univariate analysis showed a statistically significant relationship between osteoporosis and age over 38 years (0.04), active tobacco consumption (0.049), diabetes ($p = 0.04$), and low body mass index, particularly below 20 kg/m^2 ($p = 0.022$).
Conclusion: Bone Loss and osteoporosis are commonly reported in patients with IBD. Bone Mineral Density screening must be conducted systematically for patients with IBD. The predictive factors of osteoporosis found in our series are age over 38, smoking, diabetes and low body mass index, particularly below 20 kg/m^2.
Disclosure: Nothing to disclose

P1548 THE EPIDEMIOLOGICAL PROFILE OF INFLAMMATORY BOWEL DISEASE IN EASTERN REGION OF MOROCCO

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Introduction: Initially described in Northern Europe and the USA, inflammatory bowel disease (IBD) is now present worldwide. Africa is considered a continent of low incidence. However, the frequency of infectious colitis and the inadequacy of health systems in these countries explain the difficulty of assessing the actual incidence of these diseases.
Aims and Methods: The objective of our study was to describe the epidemiological and sociodemographic profile of IBD in the eastern region of Morocco.
Descriptive and analytical retro-prospective study including 240 patients who were diagnosed with IBD at the Hepato-gastroenterology department of Mohamed VI University Hospital of Oujda over a course of 6 years and 3 months from January 2011 to April. 2017. The data was collected using an exploitation sheet and the statistical analysis was done using Excel version 2010 and SPSS version 21.0.
Results: Among all eastern oriental inhabitants, the overall IBD prevalence was estimated at 10.3 / 100,000. The incidence of IBD progressively increased, especially for Crohn's disease (CD), during the studied period. The average age was 38.2 ± 13 (14–80 years) with a slight female predominance (sex ratio to 1.1). The majority of our patients came from an urban setting (93.3%). In this study 240 patients with established IBD diagnosis were included. among them, 132 patients were diagnosed with CD (55% of the total), 79 patients with ulcerative colitis (32.9% of the total), and 29 cases (12.1%) of indeterminate colitis (IC). In the CD group, patients were younger than those in ulcerative colitis, with average ages of 35.84 ± 12.8 and 41.56 ± 14.6 years, respectively. In our study, active smoking was noted in 3.8% of ulcerative colitis (UC) patients, and 7.5% of CD patients ($p = 0.2$). There was a personal history of appendectomy in 2 patients with UC (2.5%) compared with 19 patients (14.4%) in the CD group ($p = 0.003$). The presence of anoperineal lesions was significantly associated with the male sex ($p = 0.03$). Ten (10) patients with CD (7.6%) and 12 patients with UC (15.2%) had a family history of IBD ($p = 0.06$).
Conclusion: Our study allows a better knowledge of the epidemiological profile of IBD in the eastern region of Morocco. These patients appear to be young with a female predominance and predominantly of urban origin. The creation of a national registry of IBD is necessary and will not only allow the knowledge of the epidemiological and socio-demographic data but also an improvement of the subsequent care presented to these patients.
Disclosure: Nothing to disclose

P1549 PRESENCE OF GRANULOMAS IN INTESTINAL BIOPSIES FROM PATIENTS WITH CROHN'S DISEASE CORRELATES WITH DISTINCT DISEASE CHARACTERISTICS

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Introduction: Detection of granulomas in intestinal biopsies is highly suggestive of a diagnosis of Crohn's Disease (CD). The clinical significance of granulomas for the phenotype and natural history of CD has not been established yet, as previous studies produced conflicting results.
Aims and Methods: We aimed to evaluate if granuloma detection correlated with specific characteristics and/or a particular disease course in a defined cohort of patients with CD.
We retrieved all histological reports from an 8-yr period (2010–2017) that corresponded to the cohort of patients with CD with a regular and complete follow-up at our tertiary, reference IBD centers. Patients were classified according to the presence (or absence) of granulomas. The two groups were compared for various epidemiological, laboratory and clinical characteristics, as well as the clinical course and response to treatment.
Results: We identified biopsies from 220 patients with CD [male = 95, age 40.5 ± 14.8 yrs, 17–76 (mean ± SD, range)] during the study period. Seventy-one patients (32.3%) were found to have epithelioid granulomas in at least one biopsy. The presence of granulomas was significantly associated with younger age at symptom initiation (37.2 ± 13.1 vs. 42.2 ± 15.3 years, $P = 0.015$), active smoking status ($P = 0.032$), weight loss and bloody stools at presentation ($P = 0.001$ and $P = 0.012$ respectively). Patients with granulomatous disease showed a trend towards colonic localization of the disease (non-L1 Montreal phenotype) ($P = 0.097$), and increased number of flares during follow-up (3.4 ± 2.4 vs. 2.6 ± 1.8 flares, $P = 0.079$). The latter trend persisted even when duration of follow was taken into account (0.6 ± 0.5 vs 0.5 ± 0.4 flares per year of follow-up, $P = 0.071$).
Conclusion: The presence of granulomas in biopsies from patients with CD was associated with specific disease characteristics and more frequent disease flares. Thus, granulomas may serve as a surrogate marker for a distinct subgroup of CD patients who may demonstrate more aggressive disease behavior.
Disclosure: Nothing to disclose

P1550 EPIDEMIOLOGY, INCIDENCE OF COLORECTAL CANCER, MORTALITY AND THE USE OF BIOLOGICAL THERAPY IN ULCERATIVE COLITIS PATIENTS BETWEEN 2007–2016 IN HUNGARY

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Introduction: Risk of colorectal cancer is increased among patients with ulcerative colitis.
Aims and Methods: Study design: Retrospective data analysis using the National Health Insurance Fund social security databases including inpatient-, outpatient care, medications as well as the special drug reimbursement database of patients with the diagnosis of ulcerative colitis (UC) from 2007 to 2016. This is an observational / non-interventional, retrospective, epidemiological study.
Study population: All of the adult – over 18 years of age – UC patients between the examined period.
Eligibility criteria: Patients who have at least two events in all of relevant health care services or at least 1 inpatient event only with UC diagnosis (ICD codes: K51) K50 (Crohn's disease-CD) and K51 (UC) occurrence together: 80:20 distribution ratio. A patient having colorectal cancer (CRC) is defined using ICD codes (C1500 – C2690) with the requirement of having at least two appearances in the in- or outpatient care (with the corresponding codes).
Primary endpoint: Analyze patient characteristics, epidemiology, CRC incidence and treatment patterns of UC patients in Hungary.
Results: The number of all UC patients between 2007–2016 was 27,850; 0.24% of total Hungarian population suffered from UC in 2016. The annual incidence of UC varies from 15.1 to 29.5 with a declining tendency. The female/male ratio is 55/45%. The median age of the patients with UC is 51 (male 49, female 53) in the examined period. Two thousand four hundred and fifty-two patients were diagnosed with CRC (8.8% of the total UC population). Ratio of mortality was 14.2% in the total group, 3941 of 27850 patients died. 24.8% of the total death was observed among patients with UC and CRC. Median survival of CRC was 64.7 months (95% CI 58.4–77.7). No significant difference can be observed between the different age groups, the confidence intervals are very wide due to the small sample size in the younger age groups. One thousand and ninety-five patients (2.89%) were treated with biological therapy between 2007–2016, while 2.1% of total UC population was treated with anti-TNF alpha therapy in 2016 that is more than 490 patients. The prevalence was 1.2% for ADA and 1.1% for IFX in the total UC population. The onset of biological therapy is between 20 and 39 years in the majority of the patients, average age is 37 years. This is 16 years less compared to the average age of total UC population.
Conclusion: Both the prevalence and incidence of UC are high in Hungary. While the ratio of co-existing CRC was 8.8%, 24.8% of these patients died during the examined decade. 2.89% of the UC population was treated with biological therapy in the examined period. Patients receiving biological therapy are typically from the younger part of the total UC population
Disclosure: Nothing to disclose

P1551 NEXT-GENERATION SEQUENCING DERIVED MIRNA SIGNATURES FOR ACTIVE ULCERATIVE COLITIS

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Introduction: MicroRNAs (miRNAs) are short non-coding RNAs that regulate gene expression. Growing number of studies have shown that miRNAs are highly involved in different inflammatory diseases including ulcerative colitis (UC). To date, miRNA deregulation profiles in active UC have not been fully explored.
Aims and Methods: The aim of this study was to evaluate and compare miRNA profiles in tissues of active UC, UC in remission (inactive UC) and healthy controls. In the initial stage, miRNAs were sequenced in tissue samples of 32 healthy controls, 23 active UC and 21 sample of UC in remission using next generation sequencing platform. Most deregulated miRNAs were further validated in a second cohort of individuals with 38 healthy controls, 38 aactive UC and 36 inactive UC patients using RT-PCR based arrays. A multidimensional scaling analysis using Spearman's correlation distance was performed to identify the similarities in miRNA expression profiles.
Results: Next-generation sequencing results of tissue samples from patients with active UC and healthy controls revealed 108 differentially expressed miRNAs, while 74 miRNAs were deregulated comparing active UC and UC in remission. Interestingly, only 31 deregulated miRNAs were found comparing healthy control and inactive UC tissues. In the validation phase, eight miRNAs (hsa-miR-223-3p, hsa-miR-155-5p, hsa-miR-146a-5p, hsa-miR-431-5p, hsa-miR-146b-3p, hsa-miR-493-3p, hsa-miR-1180-3p and hsa-miR-424-3p) have been confirmed as consistently deregulated when comparing active UC and healthy controls. In parallel, only three miRNAs (hsa-miR-223-3p, hsa-miR-431-5p and hsa-miR-1180-3p) were confirmed as deregulated between healthy controls and inactive UC tissues.
Conclusion: Ulcerative colitis has unique miRNA signatures in colon tissues comparing active disease stage and disease in remission, which also differ from healthy controls. Furthermore, individuals with UC in remission have a more comparable miRNA expression profile with healthy controls than with active UC.
Disclosure: Nothing to disclose

P1552 A COMBINATION OF CLINICAL, SEROLOGICAL AND GENETIC FACTORS PREDICTS COMPLICATED DISEASE COURSE IN PAEDIATRIC-ONSET CROHN'S DISEASE: RESULTS FROM A POPULATION-BASED STUDY

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Introduction: Identification of patients at high risk of disabling disease course would be invaluable to guide initial therapy in Crohn's disease (CD). Clinical parameters at diagnosis are insufficient to predict a disabling course of CD (1). The objective of this study was to evaluate a combination of clinical, serological and genetic factors to predict complicated disease course in paediatric-onset CD.
Aims and Methods: Paediatric-onset CD patients, diagnosed before 17 years between 1988 and 2004 and followed more than 5 years were extracted from the French population-based Epimad registry. Complicated disease course was defined by the progression from an inflammatory (B1) to a complicated behavior (stricturing B2, or penetrating B3) or an intestinal resection within five years after diagnosis. Available data included clinical data at diagnosis, serological markers at inclusion (ASCA, ANCA, anti-OmpC, anti-Cbir1, anti-Fla2, anti-Flax) and 370 candidate Single Nucleotide Polymorphisms (SNP) associated with CD or other immune-mediated diseases or having a role in inflammation pathways, interaction with micro-organisms, or modulation of innate immunity. A lasso logistic regression model with stability selection was used to select variants associated with severe disease. After this selection step, a final lasso logistic model was performed including clinical, serological and selected variants.
Results: Two-hundred and nineteen patients were included, with a median age at CD diagnosis of 14.3 years (IQR [11.9–16.0]). Among the 156 patients with inflammatory disease (B1) at diagnosis, 35% (n = 54) progressed to a severe disease defined by a complicated behaviour or an intestinal resection during the five years following diagnosis. Final model included location at diagnosis (L1 or L3 at higher risk), ANCA (protective) and ASCA-IgG (higher risk) and 15 SNPs. Half of SNPs were known as susceptibility loci of IBD or CD including NOD2. This model showed good predictive measures with an AUC of 0.85, a sensitivity of 77%, a specificity of 80%, a positive predictive value of 68% and a negative predictive value of 87%.
Conclusion: In this population-based paediatric-onset CD cohort, a combination of clinical, serotypic and genotypic variables is able to predict disease progression with a high accuracy. After validation in an independent cohort, this prediction score will be helpful to identify patients needing early biological therapy.
Disclosure: Nothing to disclose

Reference

1. Savoye et al. *Inflamm Bowel Dis* 2012.

P1553 THE ROLE AND EXPRESSION OF MICRORNAS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are the two major diseases that make up the inflammatory bowel disease (IBD). The major clinical manifestations occur in the gastrointestinal tract, especially in the small intestine and colon. The etiology is multifactorial, with an interaction between individual genetic characteristics, predisposition and environment. These factors must be involved in the modification of the immune response with consequent formation of altered inflammatory response. Studies indicate that several genes, in addition to those involved in the modulation of the immune response, are differentially expressed in patients with CD. vs UC. The discovery of microRNAs (miRNAs) as important regulators of gene expression and their role in human diseases, including inflammatory and chronic degenerative diseases, have indicated miRNAs as ideal candidates for diagnostic biomarkers, prognostics and potential therapeutic targets. An important feature of miRNAs is their stability and easy detection in body fluids.
We aimed to identify deregulated miRNAs in DII and to apply bioinformatic analysis strategies to identify target mRNAs and molecular pathways modulated by miRNAs through meta-analysis of literature data.
Aims and Methods: A meta-analysis was performed for the identification of miRNA expression data in IBD. Inclusion and exclusion criteria were applied and 10 studies were selected, from which relevant miRNAs with increased or decreased and statistically significant expression were collected compared to controls, type and number of analyzed samples (serum, plasma or tissue) with CD and / Or UC, platforms used for analysis of global miRNAs expression and validation of data, author name and date of publication. Significantly deregulated miRNAs in DIIvs. Controls were used in bioinformatic analysis to predict the target mRNAs regulated by these miRNAs. Prediction analyzes of miRNA target transcripts and enrichment of biological functions of the target genes were performed.
Results: The results showed 6 CD miRNAs with increased expression and 51 UC. On the other hand, miRNAs with decreased expression were found 51 CD and 26 UC.
The miRNAs that showed the greatest number of interactions with DII deregulated genes were let-7a-5p, let-7b-5p and miR-199a-5p, miR-150-5p, miR-362-3p and miR-224- 5p. In the RCU were -155-5p and miR-24-5p, miR-335-5p and miR-16-5p. Suggesting that they may play an important role in the molecular mechanisms of disease. In addition, the results were used to identify gene interactions and biologic processes with: inflammatory process and response to the immune system. We show that miRNAs and target genes may be useful biomarkers for the development of new therapeutic strategies for patients with IBD.
Conclusion: Several interrelated genes and miRNAs were identified as potential regulators of gene expression. Such miRNAs and genes may play important roles in the development and progression of inflammatory bowel disease. The miRNAs regulate several target genes and important molecular pathways, knowledge of these altered molecular pathways may be useful for the future development of more accurate treatment strategies for patients with DII.
Disclosure: Nothing to disclose

P1554 BOWEL PREPARATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Patients with inflammatory bowel disease (IBD) should undergo multiple colonoscopies during their clinical history. Adequate bowel preparation is essential to high-quality colonoscopy but in our tertiary referral center for IBD it is not uncommon to find suboptimal bowel cleansing in these patients. In literature only few studies on bowel preparation in IBD patients can be found.
Aims and Methods: To assess bowel preparation in IBD patient, identify possible causes for suboptimal bowel cleansing and identify strategies for its optimization. Consecutive outpatients with IBD (ulcerative colitis [CU] and Crohn's disease [CD] were prospectively enrolled before (ileo) colonoscopy at Gastroenterology and Endoscopy Unit of ASST Fatebenefratelli Sacco in Milan. Patients answered to a questionnaire with different items (type of bowel preparation, completeness of preparation, adherence to instructions given for preparation, palatability, side effects, Bristol Scale of stools in the previous weeks). Informations about IBD type, duration of disease and treatment were also collected. Bowel preparation was evaluated by Boston Bowel Preparation Scale (BBPS); BBPS $\geq$ 6, at least 2 in every segment was considered adequate preparation. In a second part of the study, bowel preparation instructions were modified according to the last guidelines and patients received a telephone call to stress the importance of adherence to the suggested bowel preparation; the same questionnaire of the first part was administered to patients.
Results: In the first part we enrolled 120 patients (58 UC, 60 CD, 2 undetermined colitis) who had taken low volume PEG (lvP) in 57%, high-volume PEG (hvP) in 20%, stimulant laxatives (SL) in 16%, other (i.e. mix between PEG and stimulant laxatives) in 7% of cases. 53% of patients assumed correctly (i.e. respect of the timetable, completeness, correct diet) the preparation. 6% of patients assumed the preparation with a split modality. Median time between preparation and colonoscopy was 15 (5–25) hours. 28% of patients fasted on the lunch before preparation. Adequate bowel preparation was observed in 67% of patients, without differences with the type of IBD. In the second part of the study we enrolled 161 patients (80 UC, 80 CD, 1 undetermined colitis). LvP was assumed in 60%, hvP in 8%, SL in 24%, other in 8%. 70% of patients assumed correctly (i.e. respect of the timetable, completeness, correct diet) the preparation. 14% of patients assumed the preparation with a split modality. 6% of patients fasted on the lunch before preparation. Median time between preparation and colonoscopy was 14 (3–22) hours. Adequate bowel preparation was observed in 75% of patients, without differences with the type of IBD. In this second group of patients, independent predictors of adequate bowel preparation were age (OR 0.97, 95%CI 0.95–1), constipation (OR 0.08,95%CI 0.02–0.46) and time between preparation and colonoscopy (= R 0.82, 95%CI 0.72–0.94).
Conclusion: Few studies are available on bowel preparation in IBD patients. The results of our study suggest that motivation of the patient to follow instructions for the preparation (including split preparation) may be beneficial. Special attention to older patients and bowel habits when prescribing colonoscopy are needed to assure adequate preparation. The role of the referring gastroenterologist may be of pivotal importance in stressing the importance of accurate execution of bowel preparation.
Disclosure: Nothing to disclose

P1555 UTILITY OF THIOPURINE METABOLITE TESTING IN INFLAMMATORY BOWEL DISEASE

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Introduction: Thiopurine use in inflammatory bowel disease is limited by drug toxicity and lack of therapeutic efficacy. 6-Thioguanine (TGN) levels between 235 and 450 pmol/8 $\times$ 10^8 erythrocytes (RBC) have been found to correlate with therapeutic response while 6-methyl mercaptopurine (6-MMP) levels greater than 5700 pmol/8 $\times$ 10^8 RBC correlate with hepatotoxicity. Traditionally, thiopurine dosing has been weight based, but recent studies suggest basing doses on thiopurine metabolite testing might improve outcomes.
Aims and Methods: Single-center observational study including all consecutive patients undergoing thiopurine metabolite testing between July 2016 and September 2017. Demographics, dose, test indication, clinical status, action taken, and outcome were obtained. We assessed the utility of thiopurine metabolite testing and the relationship between disease activity, dose, and metabolite levels in a real-world setting.
Results: A total of 122 patients (65.6% Crohn's disease, 32% ulcerative colitis and 2.5% IBD-unclassified) were included. Median age was 44.5 years (IQR: 34–53) and 59.8% were male.
A total of 114 (93.4%) patients were on azathioprine (median dose 2.1 (IQR 1.7–2.4) mg/kg/day) and 8 (6.6%) on mercaptopurine (median dose 1.0 (IQR 0.8–1.3) mg/kg/day).
Test indication was: active disease (8.2%), adverse effects (12.3%), to check compliance (9.8%), to adjust dose in patients with combined treatment with biologics (therapy de-escalation) (25.4%), to check thiopurine levels after dose adjustment for toxicity (18.1%) and others (26.2%). Twelve (9.8%) patients presented a shunt toward 6-MMP in their thiopurines metabolism.
TGN levels were sub-therapeutic in 30 (25%), therapeutic in 43 (36%), and supratherapeutic in 46 (39%). The results for patients receiving either azathioprine or mercaptopurine were combined and analyzed by weight-based dosing. An association between dosing and categorized distribution of TGN levels could not be found (p = 0.09)
Therapy was changed as a result of testing in 72 (59%) patients. Table 1 outlines rates of change in therapy by test indication.
Conclusion: Metabolite testing resulted in a change in management in most patients not responding to thiopurines or experiencing adverse events. Weight-based dosing did not associate a higher proportion of subjects presenting therapeutic levels.
Disclosure: Nothing to disclose

P1556 THE EVALUATION OF IL-33/ST2 LEVELS CAN PREDICT MUCOSAL RESPONSE TO ANTI-TNF THERAPY IN ULCERATIVE COLITIS

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Introduction: Tumor necrosis factor (TNF) inhibitors (anti-TNF) are considered to be effective in inducing mucosal healing in patients with moderate-to-severe Ulcerative Colitis (UC). The role of IL-33 and its receptor, ST2, in intestinal inflammation is incompletely understood, with both pro-inflammatory and regulatory properties described. Recent evidence has shown that anti-TNF is able to modulate the IL-33/ST2 axis in inflammatory conditions.
Aims and Methods: The aim of our study was to explore the potential role of the IL-33/ST2 axis in the mucosal healing process mediated by anti-TNF therapy in UC.
Endoscopic MAYO score was calculated before the first anti-TNF infusion (T0) and after 6 weeks (T2). 26 UC patients (MAYO score at T0 $\geq$ 2), grouped into 14 responders with mucosal healing (MAYO score $\leq$ 1) and 12 non-responders to anti-TNF at T2 (MAYO score $\geq$ 2) were enrolled. 10 healthy controls undergoing routine colonoscopy for tumor screening were also enrolled. At each time point, serum samples were collected. ELISA and western blot were performed to assess IL-33/ST2 protein levels and to evaluate protein isoforms, respectively. Intestinal biopsies were also taken from the rectum and IHC was done to evaluate mucosal IL-33/ST2 expression and localization.
Results: IL-33 protein levels were significantly increased in responders *vs.* non-responders, both at T0 and T2. Among responders, IL-33 protein was slightly reduced at T2 vs. T0, while unchanged in non-responders. Interestingly, significantly higher levels of ST2 were found in responders *vs.* non-responders at T0, while no differences between groups were found at T2. Among responders, ST2 levels were dramatically reduced at T2 *vs.* T0. No significant differences were

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Table 1: Change in therapy by test indication

	Active disease n = 10	Adverse effect n = 14	Check compliance n = 12	De escalation n = 31	After adjustment n = 22	Other n = 32	Shunters n = 12
Change in management, n (%)	9 (90)	14 (92.9)	10 (83.3)	19 (61.2)	8 (36.4)	12 (38.7)	11 (91.7)
Change drug, n (%)	5 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cease drug, n (%)	0 (0)	1 (7.1)	4 (33)	9 (29)	2 (9.1)	0 (0)	1 (8.3)
Change dose, n (%)	2 (20)	10 (71.4)	3 (25)	10 (32.2)	5 (22.7)	11 (35.5)	4 (33.3)
Encourage compliance, n (%)	0 (0)	0 (0)	3 (25)	0 (0)	0 (0)	0 (0)	0 (0)
Dose reduction + Allopurinol, n (%)	2 (20)	2 (14.3)	0 (0)	0 (0)	1 (4.5)	1 (3.2)	6 (50%)

found in non-responders at both time points. Healthy controls showed significantly lower levels of both IL-33 and ST2 compared with other groups. Full-length, bioactive IL33 (31 kDa), ST2L (76 kDa) and sST2 (52 kDa) were expressed in all experimental groups; the cleaved, less active form of IL33 (24 kDa) was increased in only non-responders vs. responders and healthy controls. IHC confirmed these observations. In particular, IL-33 and ST2 staining was more intense within the inflamed and ulcerated mucosa of responders compared to non-responders at T0. After 6 weeks, ST2 staining was even more evident in responders, notably localized to the healed mucosa and in close proximity to areas of re-epithelialization. Little to no staining for both IL-33 and ST2 was present in healthy controls.
Conclusion: Our results suggest a possible role for IL-33/ST2 in predicting gut mucosal wound healing in patients with moderate-to-severe UC treated with anti-TNF. IL-33/ST2 axis could thus represent a useful diagnostic tool to evaluate therapeutical options in IBD patients. Further studies are underway to determine mechanisms of action that support these findings.
Disclosure: Nothing to disclose

P1557 CLINICAL AND COST EFFECTIVENESS OF THERAPEUTIC DRUG MONITORING (TDM) OF INFLIXIMAB IN ADULT INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS

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Introduction: Infliximab (IFX) is very effective in active IBD but up to 60% of patients will lose response or experience attenuated response to IFX due to fluctuating drug levels or formation of antibodies to IFX (ATI). There is growing evidence of efficacy of TDM. The National Institute of Health and Care Excellence (NICE) do not recommend routine TDM in the NHS.
Aims and Methods: Our primary objective was to assess clinical and cost effectiveness of IFX TDM in IBD. We retrospectively analysed 122 IFX drug levels and 89 ATI levels from 85 patients [54 male (64%), 32 females (36%); mean age: 39.13 years (±14.25); Crohn's Disease (CD) n = 62, Ulcerative Colitis (UC) n = 23; 46 patients (54%) were on combination immunosuppressive therapy]. Patients were allocated to 3 groups based on the intent of TDM: Maintenance group (MG)- proactive TDM on patients with quiescent IBD, secondary loss of response group (SG)- reactive TDM on active patients with established primary response to IFX and post-induction group (PG)-TDM at week 14 post induction. In each sub-group, patient baseline characteristics (CRP, haemoglobin, calprotectin, colonoscopy, MRI, CT) were assessed to construct a global assessment of patient state (active, remission or responding to drug) prior and after TDM led patient management for efficacy of IFX. Cost of IFX (INFLECTRA) was £123.50 (+VAT) per 100mg while cost of TDM (IDKMONITOR ELISA KIT) was £45 per drug level assay and £45 per ATI assay. Calculations were done comparing TDM to empirical IFX dose escalation and switching of drug. Patients were compared to empirical dose escalation; once, before class drug change in PG and twice in SG. Patients on MG were assumed to be left on stable dose for one year with levels being monitored twice a year.
Results: In MG (n = 51), 10 (20%) patients were de-escalated or stopped IFX and maintained in remission and 41 (80%) IFX was continued. The mean IFX level was 1.89mg/l vs 4.34, (p = 0.06) and mean ATI 85.10 vs 9.22, (p = 0.0007) respectively in the two subgroups. The 20% (n = 10) of patients were maintained in remission till date for a mean of 12.2 months (Range 3–30 months) and were previously on IFX for a mean of 61.7 months (Range 20–132months). In the 80% of patients (n = 41), 2 became active after de-escalation, 2 became active despite having therapeutic IFX, 36 remained in remission and 1 patient's status was unknown after stopping IFX (not included in cost savings calculation). Potential cost savings in MG was £669 per person per year (17% savings). In SG(n = 63), 21 (33%) patients switched drug or had surgery post TDM and in 42 (67%) IFX dose was escalated or maintained. The mean IFX levels was 2.24mg/L vs 3.48mg/L (p = 0.19), mean ATI 74.90IU vs 10.29IU (p = 0.0005) respectively in the two subgroups. 16 of 21 patients improved with change of drug, (remission = 8, 2 active, 3 unknowns) showing a 76–90% efficacy post TDM. 28 of 42 from IFX dose escalated SG subgroup improved (12 in remission), 12 patients were still active and 2 unknowns. Cost savings for SG group was £318.61 per person (13% savings). In PG, 2 of 8 achieved remission and 6 of 8 remained active and their mean IFX level were 2.2 vs 0.8 mg/L (p = 0.09) and mean ATI 0 IU vs 16.7 IU (p = 0.22) respectively. Cost saving of £607 per person in the PG group.
Conclusion: IFX TDM in IBD is clinically useful and has saved cost in all three patient groups with proactive TDM in post-induction and maintenance group benefitting the most
Disclosure: Nothing to disclose

P1558 CLINICAL OUTCOMES OF CONCOMITANT PRIMARY SCLEROSING CHOLANGITIS AND INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic immune-mediated liver disease commonly associated with inflammatory bowel disease (IBD) with the majority being diagnosed with ulcerative colitis (UC). The impact of PSC on clinical outcomes of IBD is unclear. Appropriate management for this patient group is also not well adapted.
Aims and Methods: Our aim was to perform a systematic review of all studies to further characterise the distinct risk of CRN in patients with concomitant PSC-IBD, risk of colectomy as well as response to biologic therapy. A systematic review of studies assessing risk of primary outcomes was conducted. Searches for relevant English language studies from 2000-March 2018, assessing primary outcomes comparing patient cohorts of PSC-IBD and IBD alone, were performed in MEDLINE, EMBASE and Cochrane Library according to PRISMA guidelines. All studies were appraised using the Newcastle-Ottawa Scale.
Results: Twelve studies were identified exploring risk of CRN in PSC-IBD, with 5 studies also reporting colectomy risk. Increased risk of CRN was shown in 11 out of 12 studies which included all 5 PSC-UC studies (RR: 2.58–10.0), 1 study with associated Crohn's disease (CD) (OR = 6.78; 95%CI: 1.65–27.9; P = .016) and 5 studies with unspecified IBD (HR: 2.01 [95%CI: 1.09–3.71] – 21.4 [95%CI: 9.6–47.6]) as shown in table. PSC-CD patients were isolated in 2 other studies; 1 study finding that the risk of CRN in patients with concomitant PSC-CD appeared to be similar to the risk in patients with CD alone (2.9% vs 2.6%) and the other study also concluding that PSC did not increase the risk of CRN in patients with CD (HR = 0.45; 95% CI 0.18–1.13; P = 0.09). Overall, a decreased risk of colectomy was found in 3 of the 5 studies (RR: 0.46–0.67).
The data for response to biologic therapy in PSC-IBD patients is limited by cohort studies with significant heterogeneity. Regarding anti-TNF therapy, a cohort study demonstrated safety and efficacy in all 5 treated patients with PSC-IBD. Conversely, a remission rate of 26% was found in a larger cohort of 19 PSC-IBD patients on anti-TNF therapy. The evidence is similarly limited for the use of vedolizumab in PSC-UC patients; 2 studies were included with clinical remission rates of 21% and 57% at 30 and 29 weeks respectively. The evidence for biologic therapy outcomes are largely found in case reports and series.
Conclusion: The risk of developing CRN in PSC-UC patients is higher while possibly being lower in PSC-CD patients. The risk of colectomy is not paralleled, perhaps due to vigilant colonic surveillance and endoscopic intervention. Further characterisation is needed to better understand and manage these patients. This review also demonstrates the paucity of data regarding the utility of biologic

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Table 1: Study characteristics and results

Author	Year	PSC-IBD (n)	IBD (n)	IBD Type	Risk/Incidence of CRN in PSC-IBD	Risk/Incidence of CRN in IBD	Risk/Incidence of colectomy in PSC-IBD	Risk/Incidence of colectomy in IBD	NOS score
Loftus et al.	2005	71	142	IBD	CI = 5 yr: 33%	CI = 5 yr: 13%	CI = 5 yr: 26%	CI = 5 yr: 56%	4/1/3 (8/9)
Sokol et al.	2008	75	150	IBD	OR = 6.9	N/A	CI = 25 yr: 25.1%	CI = 25 yr: 37.3%	4/2/3 (9/9)
Terg et al.	2008	39	78	UC	CI = 10 yr: 11%	CI = 10 yr: 2%			4/2/3 (9/9)
Lindstrom et al.	2011	28	46	CD	OR = 6.78	N/A			4/2/3 (9/9)
Ye et al.	2011	21	63	UC	CI = 20 yr: 50%	CI = 20 yr: 5%			4/2/3 (9/9)
Braden et al.	2012	166	216	UC/CD	CI = 7.5%/CI = 2.9%	CI = 2.9%/CI = 2.6%			3/2/3 (8/9)
Boonstra et al.	2013	402	722	UC	SIR = 8.6	SIR = 1.2			4/2/3 (9/9)
Ananthakrishnan et al.	2014	224	10777	IBD	OR = 5.00	N/A			4/2/3 (9/9)
Navaneethan et al.	2016	43	159	CD	HR = 0.45	N/A	CI = 34.9%	CI = 70.5%	3/1/3 (7/9)
Fraga et al.	2017	57	2687	UC	CI = 4.2%	CI = 0.8%	CI = 39.6%	CI = 8.3%	4/1/3 (8/9)
Sorensen et al.	2018	257	8231	IBD	HR = 21.4	N/A	HR = 2.15	N/A	4/2/3 (9/9)
Shah et al.	2018	293	1618	IBD	HR = 2.01	N/A			4/1/3 (8/9)

PSC, primary sclerosing cholangitis; IBD, inflammatory bowel disease; NOS, Newcastle-Ottawa Scale; CRN, colorectal neoplasia; CRC, colorectal carcinoma; aCRN, advanced colorectal neoplasia; UC, ulcerative colitis; CD, Crohn's disease; CI, cumulative incidence; OR, odds ratio; SIR, standardized incidence ratio.

therapy in PSC-IBD patients and represents a need for future studies regarding its role.
Disclosure: Nothing to disclose

P1559 PLATELET ACTIVATION BY ACTIVATED VON WILLEBRAND FACTOR IS A MARKER OF INTESTINAL WOUND HEALING IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is a chronic inflammatory condition of the intestinal tract resulting in ongoing tissue damage and impaired wound healing. The reduced ability of CD patients to heal damaged tissue is reflected by the tendency of CD patients to develop fistula and fibrosis. ADATMS13-processing of von Willebrand factor (VWF) reflects activated VWF, which is essential for initiation of primary hemostasis. Activated VWF is one of the rate-limiting factors in platelet activation and tethering to the damaged endothelium, and consequently is considered a surrogate biomarker for platelet activation. Any dysregulation in VWF processing could contribute to the development and progression of CD due to impaired and dysregulated wound healing, leading to a failure in the secondary hemostasis response.
Aims and Methods: The aim of the study was to investigate the processing of VWF, a marker of endothelial dysfunction, in patients with CD to assess primary hemostasis and platelet activation.
We developed two biomarkers specifically targeting the ADAMTS13-processed form of VWF (VWF-A), and formation/endothelial release of VWF by quantification of the pro-peptide (VWF-N). Serum samples from 13 irritable bowel syndrome (IBS) patients with high-grade inflammation and 51 CD patients and were included in the study together with 10 age-matched healthy subjects.
Results: Levels of VWF-N ($p < 0.05$; $p < 0.0001$) and VWF-A ($p < 0.05$; $p < 0.01$) and were significantly increased in CD and IBS patients compared to healthy subjects, respectively. VWF-N level ($p < 0.001$) discriminated CD and IBS patients from healthy subjects with an area under the curve (AUC) of 0.94. No significant differences were observed in the ratio of VWF-N/VWF-A between CD, IBS and healthy subjects.
Conclusion: CD and IBS patients showed an increased formation, but notably also an increase in activated VWF, indicating a sustained elevated primary wound healing response as compared to healthy subjects. Biomarkers of the dynamics of wound healing activation could serve as supplementary markers of intestinal healing in patients with inflammatory bowel diseases.
Disclosure: Manon-Jensen T, Sun S, Bay-Jensen AC and Karsdal MA are full time employees of Nordic Bioscience, Herlev, DK. Manon-Jensen T, Bay-Jensen AC and Karsdal MA are stock owners of Nordic Bioscience. Remaining authors has nothing to disclose.

P1560 SERUM SIALIC-ACID-BINDING IMMUNOGLOBULIN-LIKE LECTIN (SIGLEC)-7 AS A FIBROGENIC BIOMARKER IN CROHN'S DISEASE

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Introduction: Currently, there are no serologic biomarkers useful in clinical practice for predicting the risk of developing strictures in Crohn's disease (CD) and for identifying early stages of intestinal fibrosis with the aim of optimising the therapeutic management. Current biomarkers in CD are only predictors of a disabling disease course. Serum sialic-acid-binding immunoglobulin-like lectin (Siglec)-7 is an inhibitory natural killer receptor, whose serum levels are associated with advanced liver fibrosis in hepatitis C virus infection. This study aimed at assessing serum Siglec-7 in CD patients with fibrostenosing phenotype.
Aims and Methods: Blood samples were collected from 30 CD patients (nine with fibrostenosing phenotype, eight with penetrating phenotype and 13 with inflammatory phenotype), 15 patients with ulcerative colitis (UC) and 26 control subjects. Serum concentrations of soluble Siglec-7 were measured by a commercially available quantitative ELISA kit.
Results: Among CD subgroups, serum Siglec-7 was significantly ($p < 0.05$) increased in CD patients with fibrostenosing phenotype (median 2071 pg/ml, range 1367–3292) in comparison to those with penetrating (median 1331 pg/ml, range 995–2132) or inflammatory (median 1356 pg/ml, range 846–1909) behaviour. No difference was found between penetrating and inflammatory phenotypes. In addition, serum Siglec-7 was significantly ($p < 0.05$) up-regulated in patients with stricturing CD in comparison to both UC patients (median 1519 pg/ml, range 846–2909) and control subjects (median 1114 pg/ml, range 750–1506). Serum Siglec-7 was significantly ($p < 0.001$) higher in all the 30 CD patients (median 1411 pg/ml, range 846–3292) in comparison to control subjects.
Conclusion: Our study showed an increase of serum levels of Siglec-7 in CD patients with fibrostenosing behaviour in comparison to those with penetrating or inflammatory CD. These preliminary results support a role for serum Siglec-7 as a fibrogenic biomarker in CD.
Disclosure: Nothing to disclose

P1561 BASEMENT MEMBRANE REMODELLING AS A BIOMARKER FOR MONITORING DISEASE ACTIVITY IN CROHN'S DISEASE PATIENTS – THE ROLE OF LAMININ

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Introduction: Patients with inflammatory bowel disease (IBD) have varying disease courses with phases of inactive disease and flares of active disease with impairment of the intestinal epithelial barrier leading to tissue damage. Due to the large surface area, basement membrane is abundant in the intestinal tissue and its constituents, such as laminins, play an important role in the intestinal epithelial homeostasis. The laminin gamma 1 chain is highly abundant along the entire crypt-villus axis in the basement membrane.
Aims and Methods: We investigated if a serum biomarker of the basement membrane (LG1M) could serve as surrogate biomarkers for disease activity in a rat *in vivo* colitis model and in IBD patients. Serum from male Sprague Dawley rats that received 5–6% dextran sulfate sodium (DSS) ($n = 21$) or regular drinking water ($n = 9$) for 5 days was included and scored for disease activity index (DAI). In addition, serum from 44 Crohn's disease (CD) patients with inactive ($n = 20$) or active ($n = 24$) disease and healthy subjects ($n = 20$) was included in this study. A competitive ELISA for matrix metalloproteinase (MMP) 9 mediated degradation of the laminin gamma 1 chain (LG1M) was used to estimate the level of laminin degradation in serum. Sections of the distal colon from the rats were assessed histologically for structural changes.
Results: LG1M were significantly elevated in CD patients serum compared to healthy subjects ($P < 0.001$; $P < 0.001$), but with lower levels in active CD compared inactive CD. The findings of LG1M were confirmed in the *in vivo* colitis model, in which the levels of LG1M in DSS rat serum with high DAI were significantly lower ($P = 0.004$) compared to controls. LG1M correlated negatively to DAI ($r^2 = 0.2153$; $P < 0.01$). The structure of the distal colonic tissue in DSS rats was disrupted compared to controls with loss of crypt architecture and total surface area.
Conclusion: Our data indicate that the basement membrane biomarker, LG1M, may be applied as non-invasive surrogate biomarker of disease activity in CD patients and thus aid in monitoring patients. We report lower serum levels of LG1M in active disease compared to inactive disease in both the *in vivo* model and patient samples. The decreased amount of LG1M during active disease corresponds to the apparent loss of surface area in the intestine, which results in a reduction of the total amount of laminins for MMP mediated degradation.
Disclosure: M. Lindholm and J.H. Mortensen are full time employees at Nordic Bioscience. T. Manon-Jensen and M.A Karsdal are full time employees and stock owners at Nordic Bioscience. A. Krag, J. Kjeldsen, A. Di Sabatino, G. Mazza, P. Giuffrida and M. Pinzani have nothing to disclose.

P1562 ASSOCIATION OF BODY COMPOSITION AND MUSCLE STRENGTH WITH DISEASE ACTIVITY IN PATIENTS WITH IBD

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Introduction: Inflammatory bowel disease (IBD) is commonly associated with alteration in fat and lean mass. The conventional indices for assessment of nutritional status such as body mass index (BMI) have been suboptimal and therefore require better modalities which can be assessed by bioimpedance analysis. In addition, correlation of body composition with disease activity has not been well studied. The aim of this study was to evaluate the association of body composition and muscle strength with disease activity in adult patients with Crohn's disease (CD) and ulcerative colitis (UC).
Aims and Methods: All patients underwent the analysis of body composition measured by bioelectrical impedance analysis (TANITA body composition analyser, BC-420MA). Lean mass (LM), fat-free mass index (FFMI) and skeletal muscle index (SMI) were calculated using standard formulae. Muscle strength was obtained from handgrip strength values (HS) measured with Jamar Hydraulic Hand Dynamometer. Medical history data were obtained from clinical and electronic medical records. In order to evaluate disease activity, we used

clinical indices: Crohn's Disease Activity Index (CDAI) for CD patients and Partial Mayo Score for UC patients.
Results: In this study we have enrolled 75 patients (CD = 58, UC = 17; 50.7% male, 49.3% female). Clinically active disease (defined as CDAI > 150 or Partial Mayo Score≥3) was present in 25 patients (16.9% CD and 42.9% UC). There were no statistically significant differences among patients with active and inactive disease in FFMI [kg/m^2] 17.7 (14.9–20.1) vs. 18.2 (15.3–26.2), SMI [kg/m^2] 8.9 (7.1–10.7) vs. 9.3 (7.8–10.8), LM [kg] 50.4 (43–72.4) vs. 55 (43.3–90.5), and fat mass [%] 19.7 (14.9–45) vs. 23 (17.5–45), $p > 0.05$. Muscle strength was significantly lower in patients with active disease (26.6 ± 10.9 kg) comparing to inactive group (32 ± 11.5 kg), $p = 0.048$. Underweight patients, defined as BMI < 18.5 kg/m^2, were significantly more prevalent in active group comparing to inactive (27.8% vs 8.8%, $p = 0.04$, $\chi^2 = 4.219$).
Conclusion: Results of our study haven't shown consistent association between body composition and disease activity. However, muscle strength was lower in group of patients with clinically active disease**.** Body composition analysis by BIA could be useful tool in evaluation of patients with inflammatory bowel diseases; however, there is a need to define age, gender and disease specific, percentile-based thresholds which can simplify the screening procedures in clinical practice.
Disclosure: Nothing to disclose

P1563 ASSOCIATION BETWEEN PROPOSED DEFINITIONS OF CLINICAL REMISSION/RESPONSE AND WELL-BEING IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Recently, definitions of remission/response based on stool frequency (SF) and abdominal pain (AP) have evolved; however, data to support the validity of this approach are lacking. This analysis examined the association between the Inflammatory Bowel Disease Questionnaire (IBDQ) item 10 (**Table**), which can be considered a measurement of wellbeing, and clinical remission/response defined by SF and AP scores derived from the Crohn's Disease Activity Index (CDAI).
Aims and Methods: Analyses included patients (pts) from 2 adalimumab (ADA) phase 3 and 1 upadacitinib (UPA) phase 2 Crohn's disease trials with SF ≥4 and/or AP score ≥2 at baseline. IBDQ item 10 responses (scores ranging from 1–7) were categorized into 1/2 (feeling unwell all/most of the time), 3/4/5 (feeling unwell a bit/some/little of the time) and 6/7 (feeling unwell hardly any/none of the time) and analysed vs change from baseline to week 12/16 in SF and AP scores and clinical remission at week 12/16 defined as SF ≤2.8, AP score ≤1.0 and neither worse than baseline. Item 10 response change categories were also grouped (≤−2 to ≥+2-point-change from baseline) and analysed vs percentage change from baseline to week 12/16 in SF and AP with clinical response defined as ≥30% decrease in average daily SF and/or AP score; both not worse than baseline. Statistical differences were based on Mood's two sample median test or chi-square test (2-sided alpha = 0.05).
Results: Overall, 695 pts (40% with prior anti-tumour necrosis factor [TNF] exposure) from the ADA and 163 from the UPA (96% with prior anti-TNF exposure) trials were included. In the ADA trials, the median percentage changes from baseline to week 12 in SF (−62%; n = 194) and AP scores (−83%; n = 193) were greater (both $P < 0.001$) in pts with IBDQ item 10 response scores 6/7 vs 1/2 (−13% [n = 127] and −3% [n = 128], respectively). In the UPA trial, changes in SF and AP (−76% and −73%, respectively [both n = 38]) were greater (both $P < 0.001$) in pts who responded 6/7 vs 1/2 (−14% and 0% [both n = 38]) at week 16. A significantly greater number of pts who responded 6/7 to item 10 in the ADA (62%) and the UPA (61%) trials met the definition of clinical remission compared with pts who responded 1–5 (both $P < 0.001$; **Table**). Pts in the ADA trials with ≥+2-point change in the IBDQ item 10 had greater median percentage reduction in SF (−50% [n = 339]) and AP scores (−64% [n = 338]) vs pts with +1-point (−32% and −31%, respectively [both n = 137]), 0-point (−17% [n = 139] and −14% [n = 138]), or −1-point change (−19% [n = 58] and 0% [n = 57]) from baseline. In the UPA trial, pts with ≥+2-point change (n = 71) had greater change in SF (−68%) and AP scores (−55%) vs pts with +1-point (−35% and −25% [n = 33]), 0-point (−8% and −3% [n = 46]), or −1-point change (−22% and 0% [n = 13]).
Conclusion: The strong association demonstrated between SF and AP defined remission/response and overall wellbeing support the validity of these measures in clinical trials.

Studies	IBDQ Item 10 "How often during the last 2 weeks have you felt generally unwell?" Response Category	n	Clinical Remission* Individual Category (%)	Clinical Remission* Grouped Categories (%)
Adalimumab	1. All of the time; 2. Most of the time	37; 91	0; 4	3
	3. A good bit of the time; 4. Some of the time; 5. A little of the time	110; 119; 144	11; 13; 31	20
	6. Hardly any of the time; 7. None of the time	134; 60	58; 70	62
Upadacitinib	1. All of the time; 2. Most of the time	11; 27	9; 11	11
	3. A good bit of the time; 4. Some of the time; 5. A little of the time	32; 28; 27	6; 14; 48	22
	6. Hardly any of the time; 7. None of the time	27; 11	48; 91	61

IBDQ, Inflammatory Bowel Disease Questionnaire. *Defined as very soft/liquid SF ≤2.8, AP score ≤1.0, and neither worse than baseline.
[Table: Proportion of Patients Who Met the Clinical Remission Definition At Week 12 (Adalimumab) or Week 16 (Upadacitinib) by IBDQ Item Category]
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P1564 AGREEMENT BETWEEN ULTRASOUND ELASTICITY AND MAGNETIC RESONANCE IMAGING IN IDENTIFYING BOWEL WAL FIBROSIS IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Bowel wall fibrosis is a relevant complication of Crohn's disease (CD), as its emergence is associated with stenosing and penetrating complications, reduced response to medical therapy and increased need for surgical interventions. To evaluate the relative proportion of fibrotic vs. inflammatory tissue in CD affected segments may be helpful to guide therapeutic decisions. In the last few years, ultrasound elastography (UE) and magnetic resonance imaging (MRI) have demonstrated good accuracy in quantifying CD-related ileal fibrosis as compared with histological examination.
Aims and Methods: The present study was aimed to compare the diagnostic performances of MRI and UE in the quantification of CD-related ileal fibrosis. Consecutive patients with ileal or ileocolonic CD underwent UE and MRI 5 days apart. Bowel wall stiffness at UE was quantified by calculating the strain ratio (SR) between the mesenteric tissue and the bowel wall. Strain ratio ≥2 was used to identify severe ileal fibrosis. Parameters evaluated at MRI included wall thickening, edema, pattern andprogression of contrast enhancement 70 seconds (70s) and 7 minutes (7m) following gadolinium injection.
Results: 28 CD patients (20M, mean age 28 yrs.) were prospectively included in the study. 21 patients (75%) had ileal and 7 ileocolonic (25%) localization. A significantly higher percentage of lesions with stratified contrast pattern at 70s was found in patients with severe fibrosis at UE with respect to patients with mild/moderate fibrosis (50% vs. 8%, $p < 0.05$). A highly significant correlation was observed between SR at UE and progression of contrast enhancement at 7m at MRI ($r = 0.65$, $p = 0.002$). Additionally, patients with severe fibrosis at UE (SR≥2) were characterized by significantly higher values of contrast

enhancement progression at 7m with respect to patients with low/moderate fibrosis (14.5% vs -0.7%, p = 0.001). By using UE as a gold standard, ROC curve analysis identified a cut-off value of 8.85% for MRI contrast enhancement progression at 7 min which was able to identify severe ileal fibrosis with a sensitivity of 87.5 and a specificity of 100%.
Conclusion: Results of this study demonstrate a good agreement between UE and MRI in identifying ileal fibrosis in patients with CD.
Disclosure: Nothing to disclose

P1565 PREDICTORS AT ADMISSION OF COLECTOMY WITHIN ONE YEAR IN PATIENTS WITH ACUTE SEVERE ULCERATIVE COLITIS

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Introduction: Definition criteria of acute severe ulcerative colitis (ASUC) are well established, as well as the treatment strategy after hospital admission. In contrast, there are few data regarding predictors of colectomy at hospital admission. The aim of this study was to build a predictive score of colectomy based on clinical, biological and endoscopical parameters in patients with ASUC.
Aims and Methods: All consecutive patients with ASUC treated with intravenous corticosteroids, ciclosporin or tumor necrosis factor antagonists (anti-TNFs), and hospitalized in two French academic hospitals between January 2002 and January 2017 were included. Clinical, biological and endoscopical parameters at hospital admission were retrospectively collected. Treatment exposure was recorded and patients were followed until occurrence of colectomy or loss of follow-up. Predictors of colectomy within one year after admission were assessed by Cox survival analysis. The risk factors identified by multivariate analysis were used to build a predictive score of colectomy within one year after admission for ASUC.
Results: A total of 270 patients with ASUC were included with a median follow-up of 2.0 years (interquartile range [IQR] 0.5–4.8). Median age at occurrence of ASUC was 32 years (IQR 24–47), 30% (81) and 12.6% (34) had a past or current exposure to thiopurines and anti-TNFs at admission, respectively. Median C-reactive protein (CRP) and albumin level at hospital admission were 53mg/L (IQR 18.6–110) and 30.7g/L (IQR 26.3–35.2), respectively. *Clostridium difficile* infection was diagnosed at hospital admission in 4.3% of patients (10) and 93.7% (253) were treated with intravenous corticosteroids as first line treatment. One year after occurrence of ASUC, 54.8% (148) were exposed to thiopurines, anti-TNFs or vedolizumab. The cumulative risk of colectomy was 12.7% (95%CI, 8.8–17.3) and 21.5% (95%CI, 15.7–27.9) at one and five years after the episode of ASUC, respectively. By multivariate analysis, previous treatment by anti-TNFs or thiopurines (Hazard ratio (HR), 3.93; CI 95% 1.85–8.34), presence of *Clostridium difficile* infection (HR, 3.65; CI95% 1.09–12.28), CRP level above 30mg/l (HR, 3.08; CI95% 1.12–8.52), and albumin level below 30 g/l (HR, 2.66; CI95% 1.20–5.90) were associated with an increased risk of colectomy within one year after admission. We developed a score based on these four predictors (1 point for each item, from 0 to 4). The cumulative risk of colectomy within one year extended from 0 to 100% in patients with a score of 0 and 4, respectively (Table 1).

Score	N patients	Cumulative risk of colectomy at 3 months (%)	Cumulative risk of colectomy at 1 year (%)
0	41	0,0	0,0
1	91	7,1	9,6
2	113	6,5	10,7
3	24	24,1	53,0
4	1	100	100

[Table 1]
Conclusion: In this exploratory cohort of consecutive patients with ASUC, we identified previous treatment by anti-TNFs or thiopurines, presence of *Clostridium difficile* infection, CRP level above 30mg/L, and albumin level below 30 g/L as independent predictors of colectomy within one year. A score combining these predictors is highly predictive of the occurrence and risk magnitude of colectomy within one year after admission. These results need to be validated in a replicative cohort.
Disclosure: Nothing to disclose

P1566 ROLE OF SERUM TREFOIL FACTOR 3 AS A BIOMARKER OF INTESTINAL INFLAMMATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Several studies have shown the protective function of trefoil factors in the gastrointestinal tract and their up-regulated expression at the site of mucosal damage. However, the role of serum trefoil factor 3 (TFF3) in inflammatory bowel disease (IBD) still needs to be clarified.
Aims and Methods: The aim of the current study was to evaluate the role of TFF3 as a biomarker of intestinal inflammation in patients with IBD and to compare TFF3 values with those of fecal calprotectin (FCP) in IBD patients. This prospective study enrolled 128 patients with IBD and 16 healthy controls. The patients were divided into four groups: with active ulcerative colitis (UC) (n = 32), with UC in remission (n = 32), with active Crohn's disease (CD) (n = 32), and with CD in remission (n = 32). Serum levels of TFF3 were measured by ELISA, FCP levels were evaluated with quantitative immunochromatographic point-of-care test (Quantum Blue).
Results: The patients with active UC had the highest TFF3 levels. They were significantly higher than those of the controls ($p < 0.001$), active CD patients ($p < 0.001$), UC patients in remission ($p < 0.001$) and CD patients in remission ($p < 0.001$). UC patients in remission had really close mean values of TFF3 to those of the control group, with no significant difference ($p = 0.720$). There was a moderate correlation between TFF3 and FCP values in patients with active UC ($r = 0.516$, $p = 0.041$) and in UC patents in remission ($r = 0.593$, $p = 0.015$). In healthy controls and in CD patients correlation was not found.
Conclusion: Serum human TFF3 correlated well with FCP levels and was able to identify patients with active UC. It has potential for being used as a marker for mucosal healing in UC patients. Further validation is needed to better establish the utility of TFF3 in IBD patients
Disclosure: Nothing to disclose

P1567 DETERMINATION OF ANORECTAL FUNCTION WITH HIGH RESOLUTION ANORECTAL MANOMETRY IN ULCERATIVE COLITIS DURING DISEASE ACTIVITY AND AFTER REMISSION

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Introduction: Ulcerative colitis (UC) can impair anorectal function, resulting in distressing and disabling symptoms such as incontinence and increases in the stool frequency, urgency and tenesmus. Previous studies have linked rectal disorders during UC to an overactive rectum with an increased anorectal sensitivity and decreased rectal compliance. However, these results were based on conventional anorectal manometry, with the well-known limit provided by the use of less sensors, usually water perfused. Actually, there are no data reported on the rectal function in UC investigated with High-resolution anorectal manometry (HRAM).
Aims and Methods: The aim of this prospective study was to assess the anorectal function with HRAM in patients with mild-to-moderate UC at the first presentation. Secondary aims were to verify modifications after remission and to compare these data with those obtained in healthy volunteers (HVs).
Patients with UC satisfying the following inclusion criteria were included: an established diagnosis of UC, mild-to-moderate left- side colitis or proctitis according to the endoscopic Baron index. The exclusion criteria for patients with UC were a first disease flare, severe UC, previous anorectal surgery, strictures, or any other anal pathology.
The subjects' gender, age at diagnosis, anorectal symptoms (pain, number of liquid stools per day, urgency, sensation of incomplete evacuation, tenesmus, leakage, fecal incontinence), endoscopic disease activity and treatments (including steroids, 5-ASA, immunosuppressants) were recorded.

Abstract No: P1567

Table 1: HRAM features before and after remission in UC vs HV (* $p < 0.05$)

	Anal resting pressure (mmHg)	Maximum anal squeeze pressure (mmHg)	Anal length (cm)	First sensation threshold (air ml)	desire to defecate threshold (air ml)	urgency to defecate threshold (air ml)	maximum discomfort threshold (air ml)	Rectal compliance (ml/mmHg)
UC before treatment	70.8 ± 18.1	170.7 ± 49.2	3.4 ± 0.6	27.4 ± 13	55.5 ± 12.2*	101.1 ± 8.5*	115.5 ± 26.6*	8 ± 4*
UC after remission	71.8 ± 19.8	165.1 ± 42	3.4 ± 0.6	33.4 ± 13.3	70.5 ± 28.1	118.8 ± 28.5	141.5 ± 29.1	14 ± 7
HVs	74.3 ± 13.3	160.7 ± 35.8	3.6 ± 0.3	32.4 ± 10	75.4 ± 18.2	125.8 ± 22.5	175.5 ± 33.1	16 ± 5

All UC patients underwent HRAM before starting treatment and after remission. HRAM was performed with Sandhill InSight equipment, with a 7 cm long recording sites catheter. All recording sites were constituted by 4 recording pressure sensors arranged radially (28 pressure sensors). Two additional pressure sensors were located at the distal tip of the catheter in order to record intrarectal pressure and intra-balloon pressure. A disposable inflatable balloon was located at the tip of the catheter. The procedure was performed in left lateral (Sims) position after water enema irrigation. After accommodation time, the following parameters were assessed: anal resting pressure (ARP), length of anal canal, pushing endorectal pressure (PEP), recto-anal gradient pressure (RAGP, defined as the pressure difference between rectal pressure and lowest anal canal pressure during straining), rectal sensation and rectal compliance.

Results: Ten patients with UC (8 females) and 10 healthy volunteers (HV, 5 females) were prospectively enrolled. Before therapy, UC patients showed similar values for anal sphincter function to HVs, whereas rectal threshold volume for first sensation, desire to defecate, urgency to defecate and maximum discomfort were significantly lower than HVs values ($p < 0.05$). Rectal compliance was significantly impaired in UC than HVs ($p < 0.001$). After remission, rectal threshold volumes, as well as rectal compliance significantly increased (Table 1). An inverse linear correlation was found between regression of urgency and stool frequency and rectal compliance ($r = 0.811$).

Conclusion: HRAM can provide useful information about anorectal function in UC patients complaining urgency symptoms, in particular assessing the compliance of rectal wall that seems to be the responsible of the genesis of these symptoms.

Disclosure: Nothing to disclose

P1568 DREAM ANXIETY IN INFLAMMATORY BOWEL DISEASE

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Introduction: Sleep quality decreases in inflammatory bowel disease (IBD) but there is no study analyzing their dream characteristics. In this study we aimed to measure depression, anxiety, sleep quality, sleepiness level and dream anxiety level quantitatively.

Aims and Methods: Patients who were following up in our IBD-specific outpatient clinic were enrolled prospectively into the study. Control group enrolled from the healthy relatives of other diagnosed patients from other outpatient clinics. Socio-demographic data collected from all participants. The Van Dream Anxiety Scale (VDAS), The Pittsburg Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS) Beck Depression Index (BDI) and State Trait Anxiety Inventories (STAI) were used to assess the depression, anxiety levels, sleep quality and dream anxiety of all participants. Crohn's Disease Activity Index (CDAI) and Mayo Score were calculated to measure the disease activity.

Results: Demographic data were summarized in Table 1. Depression, state anxiety, trait anxiety and dream anxiety were higher in healthy controls (HCs) when compared to IBD patients and it was statistically significant ($p = 0.004$, $p = 0.0001$, $p = 0.004$, $p = 0.0001$ respectively). There was no statistically significant difference in sleep quality but sleepiness in daytime seen more common in HCs when compared to IBD patients ($p = 0.99$ and $p = 0.0001$ respectively). There was not any statistically significant difference seen in depression, state anxiety, trait anxiety, dream anxiety, sleep quality and sleepiness in daytime between CD and UC patients. There was not any correlation between disease activity indices and psychological parameters.

Conclusion: In our study anxiety and depression levels were lower in IBD patients as compared to controls on the contrary to results of previous studies; moreover dream anxiety score were higher in HCs. This may be due to traditional social support to sick people in our society, which alleviates burden of all daily living costs and care. Alexithymia seen common in IBD and it may affect the awareness and expressing IBD patients' mood status. Lastly most of our patients were in remission, it may affect psychological parameters positively. Comparative studies investigating coping strategies of IBD patients who had different sociocultural background are needed.

	IBD Patients (n = 136)	Healthy Controls (n = 168)	p
Age (years)	39.28 ± 12.75	36.54 ± 14.14	0.077
Gender (n)	Female:58 (42.6%) Male:78 (57.4%)	Female:89 (52.7%) Male:80 (47.3%)	0.073
Marital Status (n)	Married:95 (69.9%) Divorced: 2 (1.5%) Partner lost: 2 (1.5%) Never married: 37 (27.2%)	Married:75 (44.6%) Married but living separate:3 (1.8%) Divorced:18 (10.7%) Partner lost:1 (0.6%) Never married: 71 (42.3%)	0.0001*

[Table 1:Sociodemographic data of patients and healthy controls.]

Disclosure: Nothing to disclose

P1569 CHARACTERIZATION OF IBD PATIENTS ADMITTED IN AN INTENSIVE CARE UNIT

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Introduction: Inflammatory bowel diseases (IBDs) are chronic inflammatory diseases characterized by a relapsing-remitting course that may result in appreciable morbidity. Little is known about the characteristics of patients with IBD admitted to intensive care units (ICU).

Aims and Methods: Retrospective cohort study including consecutive patients with IBD admitted to a gastroenterology ICU between June 2003 and February 2018. We aimed to characterize the outcomes of these patients.

Results: 55 patients were included, 27 with ulcerative colitis (UC) and 28 with Crohn's disease (CD). Mean age was 47 (15–81) years and 60% were female (n = 30). Cirrhosis was present in 7 patients (12.7%), the etiology being primary sclerosing cholangitis in 3, nonalcoholic steatohepatitis in 3, and chronic hepatitis B in one. At ICU admission, 19 patients (34.6%) were treated with corticosteroids, 16 (29.1%) with immunomodulators (14 with azathioprine; 2 with 6-mercaptopurine), and 10 (18.2%) with biological therapy (7 with infliximab, 1 with adalimumab and 2 with vedolizumab). During hospitalization, 28 patients (50.9%) started corticosteroids, 5 azathioprine (9.1%), 3 ciclosporine (5.5%), 2 6-marcaptoprine (3.6%), and 1 Infliximab (1.8%). Nine patients (16.3%) received total parenteral nutrition.

The most common causes of admission were: 36.4% IBD flares/complications, 25.5% infectious complications, and 18.2% toxic megacolon. Regarding patients admitted for IBD flares/complications, in 25% it was the inaugural manifestation of IBD.

During hospitalization, 37 patients (67.3%) developed infectious complications, being the most common infection pneumonia (24.3%), Cytomegalovirus colitis (24.3%), urinary tract infection (21.6%), secondary peritonitis (8.1%), and pelvic abscess (5.4%).

Fifteen patients (27.3%) were submitted to a surgery for IBD complications, 10 with UC (18.2%) and 4 with CD (7.2%). Surgery indications were: toxic megacolon (33.3%), refractory UC (26.7%), iatrogenic pneumopetitoneum after colonoscopy (13.3%), hemorrhagic shock (13.3%), abscess (6.7%), and intestinal occlusion (6.7%).

Eight patients (14.5%) died, of whom, 3 patients (37.5%) were under immunomodulatory (n = 2) and biological therapy (n = 1), and 4 patients (50.0%) had cirrhosis. Causes of death were: multiorgan failure in the context of septic shock in 7 cases and hemorrhagic shock in 1 case.

Conclusion: Infections are a major cause of ICU admissionin IBD patients and constitute an important complication during hospitalization, contributing to morbidity and mortality in these patients. Early identification of infectious signs, especially in patients under immunosuppression is essential for the optimal management of these patients.

Disclosure: Nothing to disclose

P1570 METASTATIC VULVAR CROHN'S DISEASE: A RARE ENTITY

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Introduction: Crohn's disease is an inflammatory bowel disorder with several well-known extraintestinal manifestations, such as erythema nodosum, uveitis, and arthritis. Less commonly observed are cutaneous, so-called metastatic lesions of the vulva, which represent a diagnostic and therapeutic dilemma and require a multidisciplinary approach.
Aims and Methods: The objective of this study was to report a case series of patients with vulvar Crohn's disease (VCD), describe its clinical features, histopathologic characteristics and therapeutic management.
In this retrospective study, we reviewed all cases of VCD seen in our department between 2008 and 2016. Data concerning age at diagnosis of VCD, vulval symptoms at presentation, histologic findings, and different treatment modalities were recorded. Only patients with both clinical features of VCD [knife-cut fissures, edema, ulceration] and histologic confirmation were included. A total of 3 cases were identified among 106 female patients with CD.
Results: Case 1: A 58-year-old patient, presented with a 4-year history of vulvar pain and itching. She had no bowel complaints. Clinical examination revealed hypertrophic exophytic lesions associated with linear ulcearations involving the vulva. A biopsy from the lesional skin showed non caseating gigantocellular granuloma. In view of the clinical and histopathological features, a diagnosis of Crohn's disease of the vulva was made. Anti TNF treatment with adalimumab was started, resulting in a significant regression of the lesions.
Case 2: A 47-year-old patient presented to our department with complaints of painful, persisting vulvar ulcers, and resulting dysperunia for 2 years. On clinical examination she had unilateral vulvar oedema with multiple ''knife-cut'' linear ulcers. A skin biopsy was done which revealed dense inflammatory lymphocytic infiltrate with non caseating granulomas. Treatment with adalimumab was initiated. An improvement of symptoms was noted.
Case 3: A 16-year-old patient with no remarkable medical history, presented with a 2-year- history of persistent cheilitis and vulvar pain. Clinical examination of the external genitalia revealed 'knife-cut' vulvar fissures with important bilateral labial swelling and multiple papules on the surrounding skin. Histological analysis showed chronic inflammatory infiltrate with noncaseating tuberculoid granulomas. Anti-TNF treatment with infliximab was started with partial regression of lesions.
Conclusion: Our findings highlight the importance of keeping VCD on the differential diagnosis when faced with a range of vulvar symptoms. Anti-TNF agents seem to be an efficient treatment strategy for this particular localization.
Disclosure: Nothing to disclose

P1571 HIGH PREVALENCE OF UNTREATED AND UNDERTREATED VITAMIN D DEFICIENCY IN PATIENTS WITH IBD

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Introduction: Vitamin D is a hormone with immunomodulatory properties that could potentially influence inflammatory bowel disease (IBD) pathogenesis and activity. Epidemiological data have shown an increased risk of IBD, hospital admission, surgery, and loss of response to biologic therapy in patients with vitamin D deficiency. On the other hand, Crohn's disease (CD) and ulcerative colitis (UC) can also lead to vitamin D deficiency. This two-way relationship between vitamin D and IBD suggests the need for monitoring and regular supplementation of vitamin D. Our goal was to investigate prevalence of untreated and undertreated vitamin D deficiency among IBD patients.
Aims and Methods: In this cross-sectional study levels of vitamin D were measured in a random sample of Caucasian patients with IBD during winter in Croatia. Levels of vitamin D lower than 50 nmol/L were considered deficiency, and between 50 and 75 nmol/L as insufficiency. Patients receiving treatment were defined as those taking vitamin D supplementation of 800–1600 IU daily. Untreated patients were defined as those with vitamin D deficiency and not receiving vitamin D supplementation, while undertreated group was defined as those receiving vitamin D supplementation and with vitamin D deficiency. Medical history data were recorded from clinical and electronic medical records. Disease activity was defined as Crohn's Disease Activity Index (CDAI) <150 or Partial Mayo Score ≥ 3 for CD and UC, respectively.
Results: Levels of vitamin D were measured among 83 patients with IBD (64 CD, 19 UC). There was statistically significant difference in distribution of patients on vitamin D supplementation therapy and those with vitamin D deficiency ($p=0.01$, $\chi^2=6.45$). Prevalence of vitamin D deficiency was 71.1% (N = 59), while prevalence of patients receiving vitamin D supplementation therapy was 16,9% (N = 14). Among analysed patients we noticed relatively high proportion of untreated (63.9%, N = 53) and undertreated (7.2%, N = 6) patients. Median concentrations of vitamin D levels in patients receiving supplementation were 53.5 (36–111) nmol/L which belonged into the group of vitamin D insufficiency, and were significantly different comparing to 36 (26–49) nmol/L in untreated group (p = 0,015). Prevalence of vitamin D insufficiency was 20.4% (N = 17). Multivariate analysis showed that vitamin D deficiency was associated with resection of terminal ileum (OR = 4,04, 95% CI (1,1–14,6), p = 0,03), and was not associated with, gender, phenotype, disease activity, disease duration, small bowel involvement, or smoking status ($p > 0.05$).
Conclusion: Not only vitamin D deficiency is common among IBD patients, but the proportion of untreated and undertreated patients is considerably high. Lower concentrations of vitamin D could be partially explained with lower sun exposure during winter. Resection of terminal ileum is the largest risk factor for vitamin D deficiency. We suggest regular monitoring of vitamin D levels in IBD patients regardless of vitamin D supplementation therapy.
Disclosure: Nothing to disclose

P1572 PREVALENCE AND FACTORS ASSOCIATED WITH SEXUAL DYSFUNCTION AND QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory Bowel Disease (IBD) has a negative impact on quality of life (QOL) and sexuality is one of its major determinants. The impact of disease characteristics on sexuality and intimacy is one of the main concerns of IBD patients. Despite the obvious relevance of this problem, knowledge of the extent and the determinants of sexual dysfunction in persons with IBD is limited. The main goal of the study was to determine the prevalence of sexual dysfunction (SD), erectile dysfunction (ED) and association with quality of life (QOL) in patients with IBD, and to search for factors associated with SD and ED.
Aims and Methods: In this cross-sectional study a random sample of patients treated in outpatient clinic fulfilled anonymous validated questionnaire on their sexual function and QOL. In International Index of Erectile Function (IIEF) for males, five domains were evaluated through questions on erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. In women were six domains assessed, desire, arousal, lubrication, orgasmic function, satisfaction and pain. For both scores, higher scores indicated a better function. Patients also fulfilled IBDQ-32, a validated questionnaire for assessing quality of life in IBD patients. IBDQ-32 score is ranging from 32 to 224 with higher scores representing better quality of life. Disease activity was defined as Crohn's Disease Activity Index (CDAI) >150 or Partial Mayo Score ≥ 3 for CD and UC, respectively.
Results: We have enrolled in the study 95 patients who fulfilled the questionnaire (64 CD, 31 UC). Among them were 51 man and 44 women. Average age of included patients was 38 (95% CI: 36.9–44). In women, SD rates were 38.6% (N = 17), and were significantly higher than 9.8% (N = 5) in men ($p=0.001$, $\chi^2=10.19$). QOL was significantly lower in patients with SD, in which IBDQ-32 score amounted 163 (141–192) vs. 192 (163–203). An ED was reported by 22% (N = 11) of male IBD patients, and was significantly higher in patients with active comparing to inactive disease (57.1% vs. 16.7%, p = 0.03). Patients with erectile dysfunction had lower IBDQ-32 score (178 (138.5–188.75) vs. 196 (181–205), p = 0.03). Multivariate analysis showed that the significant predictors for SD were female gender (OR = 6.3, 95% CI 1.84–21.73) and perianal disease (OR = 7.2, 95% CI 1.7–29.7). Disease duration, disease activity, history of lower abdominal surgery, presence of stoma and current biological treatment were not significant predictors of sexual dysfunction.
Conclusion: The results show that SD is highly prevalent in IBD patients, with women to man ratio of almost 4 to 1. Erectile dysfunction is present in approximately every fifth male patient. Patients with both SD and ED have lower QOL. Significant and strong predictors for SD are perianal disease and female gender. Improvement of QUL is one of the main goals in treating IBD patients. Because of its strong connection with sexual function and satisfaction, it is important to identify those problems and to provide proper psychological support, medical treatment and educational information.
Disclosure: Nothing to disclose

P1573 SEROLOGICAL ASSESSMENT OF TYPE XVI COLLAGEN REFLECTS INTESTINAL STRICTURES IN CROHN'S DISEASE PATIENTS

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Introduction: Stricturing disease remains one of the biggest complications leading to intestinal resection in Crohn's disease (CD), and affecting 30–50% of patients with CD. Intestinal strictures are caused by fibrosis development, as a result of increased collagen deposition. Intestinal fibroblasts and myofibroblasts are the main effector cells for intestinal fibrosis development and intestinal subepithelial myofibroblasts have shown to produce significantly elevated levels of type XVI collagen in CD patients.
Aims and Methods: We investigated a novel serum biomarker, quantifying type XVI collagen (C16-C), as a biomarker for intestinal fibrosis in CD patients.

Serum from CD patients (n = 44) and healthy subjects (n = 50) was included. The Montreal classification for CD disease behaviour (B1, non-stricturing/non-penetrating: n = 20; B2: stricturing, n = 11; B3: penetrating n = 13) and disease location (L1, ileum: n = 14; L2, colon: n = 5; L3, ileum + colon: n = 25) was applied. The patients were classified as having inactive disease (n = 20) or active disease (n = 24) based on the Crohn's Disease Activity Index (CDAI) score. Competitive ELISA was applied for the quantification of C16-C in serum from CD patients (total serum samples: n = 94).
Results: The biomarker C16-C was significantly elevated in patients with CD compared to healthy donors ($P < 0.001$, AUC: 0.81). CD patients with strictures (B2) demonstrated significantly elevated serum levels of C16-C compared to CD patient without strictures (B1 and B3), and healthy donors. Furthermore, the diagnostic accuracy to separate CD patients with strictures (B2) from CD patient without strictures (B1 and B3) was 76% ($P < 0.01$, AUC: 0.76) and healthy donors 96% ($P < 0.001$, AUC 0.82). In addition, C16-C was also elevated in CD patients with ileum or ileum+colon disease involvement compared to only colon involvement and healthy donors ($P < 0.05$). There was no significant difference between patients with active or inactive disease.
Conclusion: Our data demonstrates that type XVI collagen can be quantified in serum from CD patients. The biomarker C16-C was significantly associated with stricturing disease phenotype, indicating that this biomarker might be a biomarker for intestinal fibrosis in CD, and may predict intestinal fibrosis development in CD.
Disclosure: Joachim H. Mortensen, Majken Lindholm, Morten Asser Karsdal and Tina Manon-Jensen are fultime employees at Nordic Bioscience.

P1574 PREVALENCE AND PREDICTORS FACTORS FOR COMPLICATIONS IN ULCERATIVE COLITIS

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Introduction: Patients with ulcerative colitis may develop short-term or long-term complications such as malabsorption, arthropathies, erythema nodosum or primary sclerosing cholangitis, but the most serious complication is severe acute colitis.
Aims and Methods: The aim of this study was to assess the prevalence of complications in UC and to determine the risk factors related to the occurrence of these complications.
Our study included 76 patients with UC supervised within our department, we studied the following parameters in all these patients: age at the time of diagnosis, sex, smoking habits, extent of the disease, delayed diagnosis or therapy instaurment, therapeutic means and the occurrence of complications. The data was collected with an exploitation sheet.
Results: There was 48 women and 28 men. The average age at diagnosis was 39, 94 (17–74) years. The average duration of disease progression was 38.7 months. No patient had a history of appendectomy. UC was classified as E3 in 50% of cases, E2 in 41% of cases and E1 in 9% of cases. The treatment was based on 5 AZA (5-aminosalicylic acid) in 45 patients (59, 21%), Thiopurines in 23 patients (30, 26%), methotrexate in 4 patients (5.2%) and anti -TNF in 4 patients. All patients in our series had the following complications: malabsorption in 71 patients (93, 4%), acute severe ulcerative colitis in 29 patients (38,15%) of which 12 (15,7%) had a subtotal colectomy, peripheral joint involvement in 24 patients (31.5%), ankylosing spondyloarthropathy in 10 patients (13.5%), thromboembolic complications in 4 patients (5.26%) and a single case of anterior uveitis (1.31%). In a univariate analysis, anemia and the use of corticosteroid therapy in the course of UC were statistically correlated to a delay of 5-AZA therapy establishment of more than 2 months of symptoms onset (p: 0.029, p: 0.05). The delayed diagnosis is statistically related to malabsorption occurrence (p: 0.016), the E3 profile increases the risk of acute severe ulcerative colitis occurrence (p: 0.02) and therefore the resort to colectomy (p: 0.016).
Conclusion: The occurrence of complications in ulcerative colitis is frequent particularly malabsorption. In our study: delayed diagnosis and 5-AZA treatment establishment of more than 2 months and the E3 profile are risk factors for occurrence of complications during UC.
Disclosure: Nothing to disclose

P1575 SERUM BIOMARKERS REFLECTING TISSUE-REMODELLING CORRELATES WITH THE SIMPLE ENDOSCOPIC SCORE FOR CROHN'S DISEASE

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Introduction: Endoscopy is a mainstay in Crohn's Disease (CD) monitoring. However, endoscopic evaluation of the intestinal mucosa is time-consuming and inconvenient for the patients. Therefore biomarkers that can substitute the need for endoscopic examinations are warranted. Currently, the best validated biomarker for endoscopic disease activity in CD is faecal calprotectin (fCalp).
Aims and Methods: We investigated, whether circulating levels of the tissue-remodeling biomarkers VICM, basement membrane turnover (P4NP, C4M) and Pro-C3, reflects endoscopic disease activity in CD.
We investigated blood samples from 9 CD patients before and after 4 weeks of adalimumab treatment (n = 18) along with serum from male Sprague Dawley rats treated with 1–3% DSS for 7 days (n = 42) and the disease activity index (DAI: faecal consistency, visible blood in faeces and weight loss) was applied. CD patients underwent colonoscopy before and after adalimumab treatment. Endoscopic disease activity was scored by the Simple Endoscopic Activity Score in CD (SES-CD). We measured levels of the biomarkers VICM, P4NP, C4M and Pro-C3 by ELISA. The serum levels of the biomarkers were combined in a backwards multivariate regression model. This model was correlated with the SES-CD score compared with fCalp and C-reactive protein (CRP) levels.
Results: In the samples from CD patients (n = 18) the only biomarkers that contributed significantly to the multivariate analysis model were VICM, P4NP/C4M and Pro-C3. fCalp and CRP did not contribute and was therefore excluded. This model (VICM; $P = 0.003$, P4NP/C4M; $P = 0.025$, and Pro-C3; $P = 0.022$) correlated significantly with the SES-CD score (overall model; $r^2 = 0.53$, $P < 0.001$). fCalp had a moderate correlation with the SES-CD score alone ($r^2 = 0.30$, $P = 0.016$), and CRP did not correlate with SES-CD ($r^2 = 0.03$, $P = 0.40$). Lastly, only the combination of the tissue remodeling biomarkers (VICM, P4NP/C4M, Pro-C3) could separate patients with mild (SES-CD < 7) from patients with moderate to severe endoscopic disease activity (SES-CD > 6) ($P < 0.01$, AUC: 0.89 [CI:0.75–1.0]), fCalp did not demonstrate significant discriminative power ($P = 0.12$, AUC:0.76 [CI:0.43–1.0]). At day 7 the DSS rats with DAI > 7 had significantly elevated serum levels of C4M and P4NP compared to controls ($P < 0.05$). C4M ($r^2$0.29, $P < 0.001$) and P4NP ($r^2$0.21, $P = 0.005$) correlated with DAI score in DSS-treated rats.
Conclusion: The combined tissue-remodeling biomarkers correlated significantly with the endoscopic disease activity in CD. The data was supported by findings from the DSS model. These biomarkers performed better than the established biomarkers fCalp and CRP, and may be used as surrogate markers for endoscopic disease activity assessment.
Disclosure: Joachim H. Mortensen, Majken Lindholm, Morten Asser Karsdal and Tina Manon-Jensen are fultime employees at Nordic Bioscience.

P1576 THE CONTROLLING NUTRITIONAL STATUS SCORE AS A METHOD OF NUTRITIONAL SCREENING AND PREDICTOR OF SEVERITY IN ULCERATIVE COLITIS

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Introduction: The consequences of malnutrition in ulcerative colitis (UC) are multiple and include significant reductions in bone mineral density, prolongation of disease activity time, and shortening of the duration of clinical remission. The Controlling Nutritional Status Score (CONUT) is based on the determination of albumin, total cholesterol and absolute lymphocytes to offer high sensitivity and specificity in the detection of malnutrition. This score has been used as a predictor of severity and mortality in various malignant and inflammatory pathologies, however, there have been no reports associated with UC.
Aims and Methods: The aim of the present study was to determine the utility of the CONUT score as a nutritional screening method and predictor of severity in UC patients.
A prospective study was conducted, which included 60 UC patients (period November 2016 to October 2017). All patients were adults, of both genders, Mexican mestizos, with diagnosis of UC confirmed by histology. Clinical records were reviewed to obtain the demographic, clinical and biochemical characteristics of the disease. The severity of the disease was measured using the Truelove and Witts score (TW). The risk of malnutrition was assessed using the CONUT score (low risk, 0–4 points, moderate, 5–8 points, and high, 9–12 points).
Results: The proportion was equal between gender. The mean age of presentation was 40.6 ± 13.3 years. The extent of the disease at the time of diagnosis was proctitis in 61.7% of patients, pancolitis (30%) and left colitis (8.3%). Patients presented an intermittent course of the disease (45%) or active and then inactive (36.7%), only 18.3% presented continuous activity. Regarding the activity of the disease by TW, 8.3% behaved as inactive, 18.3% mild activity, 60% moderate activity and 13.3% severe activity. 19 patients (31.8%) presented extraintestinal manifestations Thirty-three patients (55%) had as sole treatment 5-aminosalicylates. Fourteen patients (23.3%) required surgical treatment. When measuring the CONUT score, 93.3% of the patients presented a risk of malnutrition (mild 15 patients, moderate 26 patients and severe 15 patients). The patients with the highest CONUT score showed moderate to severe activity on the TW score, while those with a lower CONUT score had mild activity or inactivity (6.84 ± 2.86 vs 4.1 ± 3.02, $p = 0.009$). A higher score of CONUT was associated with C-reactive protein (CRP) values ≥ 45 (7.37 ± 2.45 vs. 4.97 ± 3.19, $p = 0.002$) and erythrocyte sedimentation rate (ESR) ≥ 30 (6.78 ± 2.78 vs. 4.60 ± 3.26, $p = 0.009$). A cut point of 6-points CONUT score (AUC:0.75, $p = 0.001$) was obtained by means of a ROC curve to discriminate between patients with inactive

or mild UC compared with those with moderate to severe activity, with a sensitivity of 64% and specificity of 88%; the positive predictive value (PPV) and negative predictive value (NPV) was 93 and 47% respectively. A CONUT score ≥6 points confers risk of moderate to severe activity by the TW score (OR:12.25 (2.46–60.91) p = 0.001). This same cut-off point (≥6 points) confers risk to present elevated biochemical markers: ESR > 30 (OR: 5.0 (1.51–16.56) p = 0.005), with a sensitivity of 63% and specificity of 75, PPV 83% and NPV 50%; and CRP > 45 (OR: 3.5 (1.2–10.19) p = 0.02), with a sensitivity of 67% and specificity of 64%, PPV 60% and NPV 70%.
Conclusion: CONUT score could be a predictor of clinical/biochemical severity in UC patients, as it is related to the severity measured by the TW score and with values of CRP≥45 and ESR≥30, the latter being independent predictors of colectomy and severity in UC patients.
Disclosure: Nothing to disclose

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P1577 ANALYSIS OF COSTS, USE OF HEALTH RESOURCES AND IMPACT ON WORK PRODUCTIVITY AND QUALITY OF LIFE IN ULCERATIVE COLITIS: A PROSPECTIVE SINGLE-CENTER STUDY

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Introduction: Ulcerative colitis (UC) is a chronic condition with a heavy economic burden for the health system and the society. The need of lifelong treatments, hospitalizations and surgery causes significant direct costs and indirect costs due to sick leave, reduced employment opportunities and early retirements. Previous cost of illness analyses are available, but very few data have been published in Italy, especially in the south.
Aims and Methods: Our aim was to evaluate prospectively, in a one-year period, the costs of UC in a consecutive cohort of Sicilian patients (pts), and assess their correlation with diseases activity (evaluated by Mayo Score), location, WPAI scoring and quality of life. Pts giving informed consent were asked to fill questionnaires on Quality of life (Eq5D), Work Productivity (WPAI-RCU), Cost of Illness (COI) and use of health resources (HRU). We collected data on hospitalizations, type of hospital stay, surgery, number of visits to the treating physician and in the emergency room, laboratory tests, radiological or endoscopic examinations, histology and drugs. This report concerns data at 6 months.
Results: We recruited 77 consecutive pts with UC coming to our IBD clinic between May and November 2017. 2 of the 77 patients enrolled abandoned the study. Mean age was 46.81 ± 13.64 years, 40 were males (54%). Disease location was pancolitis in 31 pts (40.3%), UC was limited to the left colon in 46 (59.7%). At baseline, 24 (31.2%) were in clinical remission, 24 (31.2%) had mild UC, and 19 (24.7%) had moderate UC. At 6 months, 3 patients underwent endoscopic evaluation because of active disease. Mean cost/patient was 5738.77 € in the 6 months observation period, being higher in pts with extensive disease (7.243.38€) than in limited disease (4.472.2€). The main component of direct costs is due to drugs. There was a statistical difference in costs among pts on biologics (11.140.56 €), as compared to thiopurines (354.47 €), and other treatments (766.86 €). (p < 0.001). Regarding HRU, 11 pts had at least one diagnostic procedure, 3 submitted to endoscopy; 70 had at least one lab test, 4 were hospitalized, 4 had a visit to the emergency room. As far as concerns work productivity, 38 pts were unemployed, and 37 had a job. There was no significant relationship between disease activity and work impairment, assessed by the WPAI score. Disease activity was significantly related to quality of life assessed by the EQ5D Index (p < 0.012). Mean work missing hours (absenteeism) were 19.6 hours.
Conclusion: Our preliminary results confirm that in Southern Italy, UC has high direct costs mainly related to biological therapy. Mean cost/patient was 5738.77 € in 6 months. Disease activity does not significantly impact on work productivity, but significantly impacts on quality of life. We expect data of this ongoing study will provide useful information to all stakeholders, from health authorities to drive resource allocation, patients' association and physicians to improve disease management.
Disclosure: Nothing to disclose

P1578 FAECAL CALPROTECTIN AS SURROGATE MARKER OF TRANSMURAL HEALING ASSESSED USING MRI IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Mucosal healing (MH) is to date the most validated target in Crohn's disease (CD). However, its use is limited by the low acceptability of repeated endoscopies. In this context, faecal calprotectin (Fcal) is a more convenient tool to monitor MH. Recently, transmural healing assessed using MRI was associated with sustained clinical remission and lower risk of surgery. We aimed to assess the performances of Fcal to assess transmural healing in CD.
Aims and Methods: We included consecutively and prospectively all CD patients requiring MRI. MRI was performed with injected and diffusion-weighted sequences with no bowel cleansing and no rectal enema. The bowel was divided into five segments to be analysed (ileum, right colon, transverse colon, left/sigmoid colon and rectum). MRI quantitative parameters such as apparent diffusion coefficient (ADC) or relative contrast enhancement (RCE) were assessed. Clermont score [2] and Magnetic Resonance Index of activity (MaRIA) [1] were also calculated. Transmural healing was defined as previously published (no segmental Clermont score > 8.4 [2,3] or MaRIA > 7 [4] with no stricture and no fistula).
Results: Overall, 118 patients were prospectively included (mean age = 25.9 ± 12.7 years, 53.4% of female, 34.6% of current smokers, 33.9% with perianal lesions and 22.9% with prior intestinal resection. Montreal classification was: L1 = 41.0%, L2 = 10.3%, L3 = 48.7%, B1 = 32.5%, B2 = 40.1%, B3 = 27.4%. The patients were treated with anti-TNF (90.0%), thiopurines (39.0%), methotrexate (8.5%) and/or steroids (17.8%). The median values of CDAI, CRP and Fcal were 170 [82–246], 5.9 mg/L [2.3–20.4] et 598 µg/g [139–1800]. The correlation was moderate between Fcal and total MaRIA or total Clermont score ($\rho = 0.40$ for both). The correlation between Fcal and MaRIA or Clermont score, respectively, were $\rho = 0.39$ (p = 0.006) and $\rho = 0.38$ (p = 0.007) for patients with isolated ileal location and $\rho = 0.42$ (p = 0.001) and $\rho = 0.45$ (p < 0.001) for patients with ileocolonic location. The correlation was almost perfect between MaRIA and Clermont score ($\rho = 0.96$; p < 0.0001). Overall, 25 patients (21.2%) achieved transmural healing. The median value of Fcal was significantly lower in patients with transmural healing (284 µg/g [100–931] vs 620 µg/g [191–1800], p = 0.023). Using a ROC curve, Fcal < 400 µg/g was the best cut-off value to detect transmural healing (AUC = 0.64; Se = 0.68; Spe = 0.63; PPV = 0.33; NPV = 0.88; accuracy = 0.64).
Conclusion: Fcal was moderately correlated with transmural healing in patients with CD. These two tools could be complementary to monitor patients with CD.
Disclosure: Nothing to disclose

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P1579 FEATURES OF SMALL INTESTINE PERMEABILITY IN AUTOIMMUNE DISEASES OF THE DIGESTIVE SYSTEM: INFLAMMATORY BOWEL DISEASES AND AUTOIMMUNE LIVER DISEASES

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Introduction: There is a close relationship between the intestine and the liver, due to the anatomical structure and its unique vascular structure. The liver receives about 75% of its blood supply from the intestine. The protective mechanism of maintaining immune homeostasis in the liver largely depends on the intestinal barrier function and detoxification ability of the liver in a healthy stage. Therefore, the evaluation of intestinal barrier function in inflammatory bowel diseases (IBD) and autoimmune liver diseases (AILD) is a great interest.
Aims and Methods: We aimed to assess the comparative condition of small intestine permeability in patients with IBD and AILD.
125 people were included in to the study. Of these, 60 patients with IBD (31 (52%) women, 29 (48%) men) and 45 patients with AILD (39 (87%) women and 6 (13%) men), 20 – a group of healthy individuals. The average age at IBD – 35.02 ± 1.1 years, AILD – 50.6 ± 7.4 years, in the control group – 30.13 ± 1.5 years.
Determination of small intestine permeability was conducted by a double "sugar test" (the ratio of lactulose/mannitol) using the method of high – performance liquid chromatography – mass spectrometry.
Results: Increased permeability of the small intestine was found in IBD and AILD. Thus, the average ratio of lactulose/mannitol at IBD was 0.024 [0.014;

0.05] ($p < 0.001$) and AILD – 0.101 [0.065; 0.257] ($p < 0.001$), which is higher than in the control group – 0.011 [0.009; 0.017]. In patients with IBD and AILD the differences in the degree of barrier dysfunction – the ratio of lactulose/mannitol was in patients with AILD was higher – 0.101 [0.065; of 0.257] than in patients with IBD – 0.024 [0.014; 0.05] ($p < 0.001$).
Conclusion: Patients with IBD and AILD has increased small intestine permeability by comparison to the control group. The degree of barrier function impairment was higher in patients with AILD than in patients with IBD.
Disclosure: Nothing to disclose

P1580 PATIENT-NEAR ADALIMUMAB TROUGH-LEVEL TESTING BY A NOVEL QUANTITATIVE RAPID TEST; THE QUANTUM BLUE ADALIMUMAB ASSAY

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Introduction: Therapeutic drug monitoring (TDM) has become standard clinical practice and overwhelming clinical evidence indicates that dose-optimization improve clinical outcome by decreasing the risk for anti-drug-antibodies and improves the efficacy of the drug itself. Watanabe et al recently demonstrated that increasing trough levels were closely associated with endoscopic response and mucosal healing (*Clin Gastroenterol Hepatol* in press) However, this has been hampered by the high cost of and the absence of a near patient testing.
Aims and Methods: This was to co correlate a CE -marked Point of Care (POC) rapid test for Adalimumab (ADA) trough level, with an established laboratory test used by Norwegian physicians. This POC facilitates the Quantum Blue reader developed by the BüHLMANN Laboratories, AG, Basel, Switzerland. We also wanted to investigate whether a nurse without ordinary lab training could successfully perform this assay.
The study comprised 49 pts with IBD receiving ADA treatment; At the day of infusion, blood for ADA-trough level was collected in addition to 3 ml serum for QB-ADA rapid test.
Part A: All the practical work was performed by the nurse (IL). After vortexing for 3 seconds, the serum was diluted 10uL in 190 uL assay buffer and vortexed for 5 sec. 80uL was applied to the rapid test cassette and read after 15 min using the QB reader.
Results: There was a good correlation between the QB-ADA rapid test and the laboratory based test, Spearmann rank $r = 0.88$, $p < 0.001$. The average within/between assay CV was 23.0/16.9 respectively. More importantly, the ADA-POC correctly identified all the 8 trough values < 5, and the 19 > therapeutic range of 12ug/ml. 22 values was between 5 and 12, the POC correctly identified 21 of these.
Conclusion: In this investigation, we document a close correlation between a 15 min. rapid test for ADA trough level with that of a standard lab-test. We have also shown the robustness of this test since a nurse can accurately perform it. This means that TDM now can be performed in a near-patient facility like an IBD nurse in an out patient clinic without any significant delay.
Disclosure: Dr Arne Røseth is a medical consultant for Bûhlmann labs, the manufactures of the ADA-trough kits.

Reference

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P1581 SERUM ALBUMIN CONCENTRATIONS ARE ASSOCIATED WITH ENDOSCOPIC DISEASE ACTIVITY IN NEWLY DIAGNOSED CROHN'S DISEASE PATIENTS

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Introduction: Serum albumin concentrations may be reduced in Crohn's disease due to malnutrition and because albumin is an acute phase protein. The aim of this study was to investigate if serum albumin concentrations are associated with disease activity.
Aims and Methods: Seventy patients aged 16 years and above with newly diagnosed, untreated Crohn's disease were consecutively included in a cross-sectional study between April 1, 2012 and December 1, 2016. Descriptive data, including age, gender and disease distribution were registered, as well as serum albumin concentrations. Disease activity was evaluated using the Simple Endoscopic Score for Crohn's Disease (SES-CD), fecal (f)-calprotectin, CRP and the Harvey Bradshaw Index (HBI). Correlations were calculated by Spearman rank order test, and associations between albumin and disease activity markers were explored by linear regression analysis and measurements of albumin quartile concentrations vs. SES-CD scores.
A receiver operating characteristics (ROC) analysis was performed to determine a cut-off for s-albumin for severe vs. non-severe disease activity. SES-CD scores were categorized in non-severe (0–15) and severe disease activity (16 or above).
Results: Study participants had a median (range) age of 32 (16–78) years, and 44% were males. Small intestinal (49.3%) and ileocecal (37.3%) disease distribution were most frequent. Median SES-CD was 7.5 (1–37), and albumin 37.4 g/L (18.3–51.0). The SES-CD correlated best with CRP ($r = 0.66$) and albumin ($r = -0.66$), $p < 0.001$ for both, followed by f-calprotectin ($r = 0.51$, $p < 0.001$) and HBI ($r = 0.34$, $p = 0.004$).
A linear regression model using log-transformed SES-CD as dependent variable showed significant association with albumin ($r^2 = 0.45$, $B = -0.67$, $p < 0.001$). SES-CD increased significantly with decreased s-albumin concentrations for the three lowest quartiles (Fig.1).
A ROC analysis using SES-CD ≥ 16 as indicator for severe disease gave an area under the curve of 0.873 (std. error 0.063, $p < 0.001$, 95% CI 0.750–0.997). The optimal cut-off of s-albumin was 35.0 g/L, with a sensitivity of 81.3% and a specificity of 90.7%
Conclusion: Serum albumin concentrations were significantly associated with SES-CD, and decreasing albumin quartile concentrations corresponded with increased SES-CD scores in patients with newly diagnosed Crohn's disease. An albumin concentration of 35.0 g/L was identified as the optimal cut-off for severe disease as defined by SES-CD. CRP, f-calprotectin and HBI scores were also significantly correlated with SES-CD. Albumin may be an indicator of disease activity in newly diagnosed Crohn's disease.
Disclosure: Nothing to disclose

P1582 THE ACCURACY OF THREE DIFFERENT METHODS ON THERAPEUTIC DRUG MONITORING OF SB2

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Introduction: Therapeutic Drug Monitoring is widely used in the adjustment of Infliximab (IFX) therapy and is expected to be used in the adjustment of biosimilars. SB2, a biosimilar of the originator IFX, has been recently approved by the European Medicines Agency (EMA) for the treatment of Inflammatory Bowel Disease (IBD).
Aims and Methods: The aim of this study was to evaluate the accuracy of three different methods for the quantification of biosimilar SB2. Moreover, the existence of IFX, CT-P13 and SB2 cross-immunogenicity was also evaluated. Three different IFX quantification assays were evaluated: an in-house built method, a commercially-available ELISA assay and a point-of-care device (POC-IFX). Spiking with known concentration of originator IFX, CT-P13 and SB2 were performed in donors' samples and the percentage of recovery of each assay was evaluated. Reactivity of SB2 to patients-extracted anti-IFX and anti-CT-P13 antibodies was quantified using the in-house built method.
Results: The results show that all tested IFX-optimized assays are equally accurate in measuring SB2 levels: the intraclass correlation coefficient (ICC) between theoretical and measured concentrations varied from 0.945 to 0.983. Quantitative comparison showed an excellent ICC between the three assays when evaluating SB2, originator IFX and CT-P13. Regarding SB2, ICC was 0.986, 0.979 and 0.974 for POC IFX/in-house ELISA/in-house and ELISA/POC IFX, respectively. Finally, the anti-IFX and anti-CT-P13 sera reacted almost to the same extent to SB2, originator IFX and CT-P13, with ICCs ranging from 0.986 to 0.993
Conclusion: Our results suggest that either ELISA commercial assay, POC IFX or the in-house method can be used to measure IFX biosimilar SB2 in an accurate fashion. Moreover, these drugs were shown to have a high cross-immunogenicity: this means that switching between them in a patient that has measurable levels of anti-drug antibodies will likely yield no clinical benefit.
Disclosure: FM served as speaker and received honoraria from Merck Sharp & Dohme, Abbvie, Vifor, Falk, Laboratorios Vitoria, Ferring, Hospira and Biogen.

P1583 QUANTIFIED TERMINAL ILEAL MOTILITY DURING MR ENTEROGRAPHY AS A BIOMARKER OF CROHN'S DISEASE ACTIVITY: A PROSPECTIVE STUDY

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Introduction: Previously, quantified MRI small bowel motility has been demonstrated as a non-invasive, objective biomarker of Crohn's Disease (CD) inflammatory activity in retrospective investigations (1,2). In this study we prospectively evaluate the accuracy of quantified small bowel motility for CD activity against endoscopic and histopathological standards of reference. We also include the MaRIA score (validated MRI index of CD severity) to provide context (3).
Aims and Methods: 82 subjects (42 male, median age 32.5 years) recruited from two centres, underwent colonoscopy and MR enterography separated by median 5 days (range 0 to 14). The Crohn's Disease Endoscopic Activity Index (CDEIS) was scored in the terminal ileum (TI), and a histopathological activity score (eAIS) derived. TI motility was quantified using a validated motility algorithm based on image registration and the magnetic resonance index of severity (MaRIA) score calculated. Sensitivity and specificity of Motility (> 0.3 AU) and MaRIA (≥ 11) for disease activity (CDEIS ≥ 4 or eAIS ≥ 1) was compared using McNemar's test, and Receiver Operating Characteristic (ROC) area under the curves constructed. Motility was correlated with reference standards using Spearman's rank.
Results: Against CDEIS, motility had sensitivity and specificity of 92.7% and 66.7%, which was significantly higher & lower respectively than MaRIA (78.1% $P = 0.03$ and 80.5% $P = 0.05$). Against eAIS, motility had sensitivity and specificity of 91.7% and 73.5% for inflammatory activity. Sensitivity, but not specificity, was significantly higher than MaRIA (75.0% $P = 0.03$ and 73.5% $P = 1.0$ respectively). Motility had moderate negative correlations with eAIS $R = -0.61$, $p < 0.001$) and CDEIS ($R = -0.59$, $p < 0.001$) and had a ROC AUC of 0.86 (CDEIS), 0.87 (eAIS) respectively.
Conclusion: In this dual-site prospective study, quantified motility appears a valid biomarker for endoscopic and histopathological activity in Crohn's disease.
Disclosure: Alex Menys is the CEO of Motilent Ltd.

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P1584 SERUM CHITINASE 3-LIKE-1 IS A RELIABLE SURROGATE MARKER OF MUCOSAL HEALING AND AN EFFECTIVE TOOL TO PREDICT CLINICAL RELAPSE IN PATIENTS WITH CROHN'S DISEASE

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Introduction: A tight control of inflammation based on symptoms and faecal biomarkers is now recommended in patients with Crohn's disease (CD) [1]. However, questionnaires from large cohort demonstrated that venipuncture is more acceptable than stools collection for CD patients [3]. While faecal chitinase 3-like 1 (CHI3L1) is highly accurate to assess endoscopic activity in CD [3], the performances of serum CHI3L1 to evaluate mucosal healing in patients with CD remains unknown.
Aims and Methods: We aimed to assess the performances of serum CHI3L1 to assess mucosal healing and to monitor the risk of clinical relapse in patients with CD.
We enrolled in this prospective multicenter study (8 centers), all the patients with CD requiring ileo-colonoscopy. Blood samples were taken just before performing the endoscopy (cross-sectional study) and every three months during one year (longitudinal study) to measure the level of serum CHI3L1 (ELISA assay). Clinical relapse was defined as CDAI > 150. Non-parametric tests (Mann-Whitney) were used to compare the level of CHI3L1 in patients with or without mucosal healing. ROC curves were performed to define the best threshold to detect mucosal healing according to clinical relevance. For the longitudinal study, ANOVA for repeated measures was used.
Results: Overall, 103 patients with CD were included (42.7% male, 35.0% active smokers, 43.7% with prior bowel resection). Among them, 29.1% had isolated ileal CD, 11.6% had isolated colonic CD and 59.3% presented with ileocolonic CD. Complicated CD was observed in 45.7% of the patients (stricturing CD (B2) = 28.2% and fistulizing CD (B3) = 17.5%). The median CDAI was 101 [51–214] and the median calprotectin was 100 µg/g [74–295].
The median level of serum CHI3L1 was significantly lower in patients with mucosal healing defined as no ulcer (52.3 vs 81.9; $p = 0.004$), CDEIS = 0 (52.5 vs 77.1; $p = 0.0228$), CDEIS ≤ 3 (60.0 vs 91.5; $p = 0.0294$), SES-CD = 0 (51.1 vs 90.8; $p = 0.0006$) and SES-CD < 2 (60.1 vs 91.6; $p = 0.0366$). Using ROC curves, we determined the most relevant thresholds to detect endoscopic activity defined as no ulcer (cut-off value = 75.0; AUC = 0.65, Se = 54.9%, Spe = 75.0%, PPV = 71.8%, NPV = 58.9%), CDEIS = 0 (cut-off value = 75.0; AUC = 0.69, Se = 55.9%, Spe = 81.5%, PPV = 88.4%, NPV = 42.3%), CDEIS > 3 (cut-off value = 77.0; AUC = 0.64, Se = 60.0%, Spe = 67.0%, PPV = 46.2%, NPV = 78.6%), SES-CD = 0 (cut-off value = 75.0; AUC = 0.68, Se = 57.7%, Spe = 79.1%, PPV = 76.9%, NPV = 60.7%) and SES-CD ≤ 2 (cut-off value = 87.0; AUC = 0.62, Se = 60.0%, Spe = 64.0%, PPV = 30.8%, NPV = 85.7%).
Overall, 25 patients were monitored with serum CHI3L1 testing every 3 months (83 measurements). Serum CHI3L1 was significantly increased in the patients with clinical relapse within 3 months ($p < 0.0001$). Using a ROC curve, we identified CHI3L1 > 64.0 as the best threshold to predict clinical relapse in patients with CD (AUC = 0.70, Se = 82.4%, Spe = 56.1%, PPV = 32.6%, and NPV = 92.5%.
Conclusion: Serum CHI3L1 is a promising surrogate marker of mucosal healing and may be a highly acceptable tool to predict the risk of relapse (high NPV).
Disclosure: This study was granted by Lesaffre company.

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P1585 CAPSULE ENDOSCOPY IN A TREAT TO TARGET APPROACH TO CROHN'S DISEASE PATIENTS

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Introduction: In recent years a proactive attitude is getting more common in treating inflammatory bowel disease (IBD) patients. We now look beyond symptoms and imaging, biomarkers and drug monitoring help guide the treatment changes.
This strategy that is based on regular assessment of disease activity by using objective clinical, imagistic and biological outcome markers and the subsequent adjustment of treatment is called ''treat to target approach''.
Aims and Methods: Capsule endoscopy has a well-defined role in Crohn's disease patients' diagnosis and monitoring. We present our experience of capsule endoscopy use in Crohn's disease patients monitored in a treat to target manner.
We prospectively evaluated 17 Crohn's disease patients followed in proactive manner using fecal calprotectin in a single center.
Rapid reader 8 software and Pillcam colon 2 capsule were used in the study. A panendoscopy examination was realized setting the capsule to record before swallowing it.
Results: Seventeen patients with known Crohn's disease had a pan-enteric endoscopy. All patients had high levels of fecal calprotectin, but only 13 of them had symptoms. We had an incomplete examination due to capsule retention in the ileum for 9 hours. Active lesions were found in 15 patients: two of them had ileocolic ulcerations, one had gastro-duodenal and ileal lesions, one had a peri-anastomotic fistula and 11 patients had ileal disease. Two patients had no lesions. Pan-enteric endoscopy examination identified lesions in 88% of patients with raised fecal calprotectin (even in asymptomatic patients).
Conclusion: In selected Crohn's disease patients (inflammatory pattern) without known/suspected stenosis the pan-enteric endoscopy using colon capsule might

be used in conjunction with biomarkers to actively monitor the patients in a treat to target approach. This helps to stratify disease activity (due to well known limitations of clinical assessment) and can be paramount to guide therapeutic modifications.
The addition of FICE 1 and blue mode can detect even subtle lesions and therefore the risk of recurrence in this patients.
Disclosure: Nothing to disclose

P1586 PERSONALISED CARE WITH THE TELEMEDICINE TOOL MYIBDCOACH IS COST-EFFECTIVE. A COST-UTILITY ANALYSIS OF THE MYIBDCOACH TRIAL

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Introduction: Value-based care is a promising strategy to improve quality of care and control costs, but warrants systematic measurement of patient-reported outcomes. Telemedicine is a powerful tool to enable continuous monitoring of outcomes in chronic diseases. For inflammatory bowel diseases (IBD), implementation of telemedicine previously showed to reduce outpatient visits and hospital admissions (1). However, cost-utility analyses are lacking. We therefore evaluated the incremental cost-utility of telemedicine versus standard care for IBD patients.
Aims and Methods: We used data from the 12-month myIBDcoach trial in which 909 IBD patients were randomized to telemedicine (n = 465) or standard care (n = 444). Direct healthcare costs were estimated based on resource use multiplied by the appropriate unit prices, indirect or productivity costs were calculated using the friction-cost method, a license fee of €40 was calculated for patients using telemedicine, and utilities were assessed using EQ5D (Dutch tariff). Cost-utility and uncertainty were estimated using the non-parametric bootstrapping method.
Results: Telemedicine resulted in a mean yearly cost saving of -€554 per patient (95%CI, [€-987, €2,094]; mean costs of €9495 for standard care and €8941 for telemedicine) and was associated with a small mean gain in quality adjusted life years (QALY) of 0.002 (95%CI, [-0.022, 0.018]). As myIBDcoach results on average in lower costs and somewhat better health, overall this innovative intervention dominates usual care. Telemedicine was cost-reducing in 76% of the replications. However, there is still uncertainty, as dominance occurs only in 57% of the replications (figure 1).
Conclusion: Telemedicine with myIBDcoach is on average cost-reducing compared to standard care with maintained quality of life. However, there is large uncertainty and it might be of interest to detect whether a subgroup can be identified in which use of myIBDcoach results in higher QALY without higher costs. Trials with longer follow-up are required to determine whether telemedicine can improve quality of life and disease outcomes on the long term.
Disclosure: Nothing to disclose.

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P1587 WHAT DO IBD PATIENTS KNOW ABOUT DIET AND PREVENTIVE PRACTICES IN IBD?

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Introduction: The IBD patients' understanding of their disease is of extreme importance for its long-term management.
Aims and Methods: We aim to evaluate the knowledge of IBD patients have about the role of diet, sun exposure, vaccination and smoking habits on their disease.
A cross-sectional observational study was performed through the application of a questionnaire (by e-mail using *google forms* platform) to patients of our IBD outpatient clinic and members of the national association of IBD patients.
Results: We received 412 valid questionnaires (66.3% females, mean age ± SD of 37 ± 13years, 63.6% patients with Crohn's Disease and 57.8% patients under immunosuppression/biologic therapy).
The majority of participants acknowledged diet as an exacerbation factor for IBD (76.7%) and have modified their diet after the diagnosis of their disease (83%). The majority have never received advice on sun exposure (68%), thus being unaware of the risk of skin cancer associated with IBD and/or IBD therapy (66.5%). Most patients have never done skin cancer screening (88.9%), nor have they adjusted their lifestyles with reference to sun exposure (65.3%). The majority of patients (54.6%) discussed the vaccination plan with their gastroenterologist, presenting an updated vaccination plan (92.7%). Only 46.8% of the participants take influenza vaccine yearly. The anti-pneumococcal vaccine had been prescribed in 43.4% of patients. The majority never smoked (56.8%), nor did they discuss the topic of smoking with their gastroenterologist (62.9%). Only 15% of patients have changed their smoking habits after diagnosis: 54 out of 60 quit smoking and 8 out of 234 began smoking.
Conclusion: The participants in this study revealed limited knowledge about the role of diet, sun exposure, vaccination and smoking in IBD. It is absolutely necessary to invest in IBD patients' education about these issues in order to provide them with an active role in the treatment of their disease and prevention of its complications.
Disclosure: Nothing to disclose

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P1588 DOES FECAL CALPROTECTIN BASED MONITORING HAVE AN IMPACT ON LONG-TERM OUTCOMES IN FINNISH ADULT PATIENTS WITH CROHN'S DISEASE: RETROSPECTIVE MULTI-CENTRE CHART REVIEW STUDY

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Introduction: To assess descriptively, whether Crohn's disease (CD) patients with fCal testing one year after biological treatment initiation have different characteristics and outcomes compared to patients without such testing in real-life treatment setting.
Aims and Methods: A non-interventional, retrospective patient chart review study was carried out in 4 Finnish gastro clinics (EUPAS17190 registration). The study included patients with confirmed CD diagnosis, who had initiated a biological therapy for CD at any time between January 2010 – June 2016 (N = 186). The collected data included patient characteristics, CD characteristics, drug treatments, laboratory test results, health care resource use and outcomes. fCal had been assessed one year (±2months) after biological treatment initiation in 46.8% of the patients who formed the fCal-group (n = 87) whereas the remaining patients formed the non-fCal- group (n = 99). For the purposes of the analysis, only patients with follow-up period of at least 14 months were considered (fCal-group, n = 80; non-fCAL, n = 70).
Results: The study cohort consisted of patients aged on average 44.2 years, 58.0% male, CD duration of 10.0 years (sd 9.7) and follow-up period of 1249.5 days (range 429–2369) with no significant differences between fCal and non-fCal groups. The patients with and without fCal testing at 1 year had relatively similar disease location: ileal (20.0% vs 18.6%; p = 0.83), ileocolonic (58.8% vs 51.4%; p = 0.37) and colon (21.3% vs 30.0%; p = 0.22). There were no differences in prior biological exposure (33.8% vs 35.7%, p = 0.80) or number of previous biological treatments (0.38 vs 0.49; p = 0.29) in the compared groups. During the study period 44 (55.0%) and 37 (52.9%) composite events (surgical procedure, corticosteroid initiation, treatment failure or dose increase) occurred in fCal and non-fCal groups, respectively (p = 0.79) with no statistically significant differences in mean time to composite event from the biologic initiation (414.2 vs 368.8 days; p = 0.64) between groups. Nine surgical procedures were performed in each group during the follow-up. There were no statistically significant differences in mean time to surgery from biological initiation in patients with and without fCal-testing (526.1 vs 531.3 days). Patients with fCal testing at 1 year had overall more fCal-testing during the follow-up period (5.8 vs 3.7, $p < 0.001$). The difference remained significant also when the fCal test at 1 year was excluded for the fCal-group ($p < 0.05$). However, there were no differences in the proportion of patients with imaging (colonoscopy, ileal or perianal MRI, abdominal CT, esofagogastroduodenoscopy) 12 ± 2 months after biologic initiation (25.0%

and 34.3% of patients in fCal and non-fCal groups, p = 0.213). Treatment-site specific differences were observed for the use of imaging. In three study sites, proportionally more patients in non-fCal group underwent imaging at 1 year (39.6% vs 26.2%; p = 0.14; n = 109) even though the difference did not reach statistical significance, whereas the opposite was true for one site (22.7% vs 21.1%; p = 0.90; n = 41). Non-fCal patients had significantly lower leukocyte levels at baseline (6.89 vs 8.47, p = 0.004) and at 1 year (5.88 vs 6.78, p = 0.030) and higher haemoglobin values at 1 year (141.16 vs 135.13, p = 0.04).
Conclusion: This study showed only minor differences in long-term outcomes of CD patients with and without fCal measurement 12 ± 2 months after biological initiation in Finland. However, measuring fCal potentially decreases the use of imagining for assessing response to biological treatment in real-life setting.
Disclosure: Nothing to disclose

P1589 REAL-WORLD EFFECTIVENESS OF VEDOLIZUMAB AND ANTI-TUMOUR NECROSIS FACTOR ALPHA TREATMENT OVER 6 MONTHS IN CROHN'S DISEASE PATIENTS: A GERMAN RETROSPECTIVE CHART REVIEW

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Introduction: Vedolizumab (VDZ), an $\alpha_4\beta_7$ integrin antagonist, was approved in Germany in 2014 for the treatment of moderately to severely active Crohn's disease (CD). This study descriptively assessed the real-world effectiveness and safety of VDZ and anti-tumour necrosis factor-alpha (anti-TNFα) after VDZ was introduced in Germany.
Aims and Methods: A retrospective chart review (15 sites) investigated patients (pts) with CD who were biologic- (bio-) treatment naïve or had received one prior anti-TNFα at initiation of index treatment with VDZ or anti-TNFα between 15 July 2014 and 20 October 2015. Time to first chart-documented clinical remission (Harvey Bradshaw Index [HBI] < 5), abdominal pain (AP) resolution (score of 0 or 1), and liquid stools (LS) resolution (≤1.5 per day) were assessed using time-to-event Kaplan-Meier analyses over 26 weeks.
Results: The study investigated 69 VDZ (14% bio-naïve; 67% female) and 105 anti-TNFα (40 adalimumab, 65 infliximab; 62% bio-naïve; 55% female) pts. At baseline, pts' median age was 40 years (VDZ) vs 34 years (anti-TNFα); their median disease duration was 10 years (VDZ) vs 6 years (anti-TNFα); and 28% (VDZ) vs 26% (anti-TNFα) received a corticosteroid. The outcomes of interest were available in the medical chart for a subset of pts: HBI score in 57 VDZ (8 bio-naïve) and 70 anti-TNFα (41 bio-naïve) pts; AP in 57 VDZ (10 bio-naïve) and 70 anti-TNFα (41 bio-naïve) pts; and LS in 46 VDZ (7 bio-naïve) and 67 anti-TNFα (40 bio-naïve) pts. By Week 26, more VDZ vs anti-TNFα pts had AP resolution (63% vs 56%) whilst clinical remission (14% vs 33%) and LS resolution (30% vs 50%) were lower in VDZ pts (**Table**); however, differences were not statistically significant (log-rank test: clinical remission = 0.060; AP = 0.552; LS = 0.060). Proportionally, more bio-naïve vs one prior anti-TNFα pts who received VDZ achieved clinical remission (25% vs 13%) and AP resolution (69% vs 61%) by Week 26, although there was only a small bio-naïve VDZ sample (**Table**). A similar percentage of bio-naïve and one prior anti-TNFα pts who received anti-TNFα achieved clinical remission by Week 26 (34% vs 33%); symptom resolution was more likely in the bio-naïve cohort (AP: 58% vs 53%; LS: 53% vs 46%) (**Table**). Differences between cohorts by prior treatment history were also not statistically significant (log-rank test: clinical remission = 0.279; AP = 0.748; LS = 0.287). Adverse events occurred in 32% of VDZ vs 43% of anti-TNF pts.
Conclusion: This study included pts with CD who received VDZ shortly after launch and were mostly anti-TNFα failure pts of long disease duration, whereas pts treated with anti-TNFα were mostly bio-naïve and had shorter disease duration. The difference in pts' baseline status is a limitation of this study. Results revealed outcomes were similar between VDZ and anti-TNFα cohorts. Biologic treatments appear to be more effective in bio-naïve CD pts.
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P1590 THE SAFETY AND EFFICACY OF VEDOLIZUMAB IN THE ELDERLY – A RETROSPECTIVE ANALYSIS

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Introduction: The use of biologic agents in the elderly raises questions concerning their efficacy and safety in this particularly vulnerable population. Data regarding the gut selective drug vedolizumab (VDZ) in the elderly are scarce.
Aims and Methods: We aimed to evaluate the efficacy and safety of VDZ in elderly patients with inflammatory bowel disease (IBD). IBD patients over the age of 60 years completing a 14-week induction with VDZ were included. Patients were followed at the Tel Aviv Medical Center between 2015–2018. Clinical response and remission rates at weeks 14 and 52 were defined as a drop in Harvey-Bradshaw Index (HBI) of ≥3 or a score of ≤3, respectively, for Crohn's disease (CD), and as a drop in partial Mayo score of ≥2 or a score of 0, respectively, in ulcerative colitis (UC). Endoscopic assessment was performed using the Simple Endoscopic Score for CD (SES-CD) and the Mayo score for UC in those for whom the data was available. Clinical details, including response rates and side effects, were documented at each infusion and were retrieved from patients' files.
Results: A total of 31 patients (61% females) at an average age of 70 ± 7.8 [range 60–89] years and disease duration of 15 ± 11.2 [range 2–41] years, were included. Patients were followed up for 42 ± 16.3 (range 14 -52) weeks. Currently 20 patients reached the 52-week end-point.
HBI score at baseline (n = 16) was 8.25 ± 2.8 and the partial Mayo score (n = 15) was 4.5 ± 1.77. At week 14, remission and response in CD patients were 60% (n = 10) and 19% (n = 3), respectively. In the UC cohort, 47% (n = 7) achieved clinical response, however no UC patient achieved clinical remission. At week 52, remission and response in CD patients were 55% (n = 6) and 22% (n = 2), respectively, and 50% (n = 3) and 17% (n = 1) had endoscopic response and remission, respectively. In the UC cohort, 67% (n = 6) and 11% (n = 1) had clinical response and remission, respectively, and 30% (n = 2) had endoscopic response. Noticeably, the majority of patients (65%, n = 20) previously failed at least one anti-TNF, and 30% (n = 10) previously failed two anti-TNF agents. In the CD cohort at week 14, patients naïve to biologic therapy (n = 6) had higher response rates than those previously exposed to anti-TNF agents (n = 10), 80% vs 50% (P = 0.31) and significantly greater clinical remission rates, 60% vs 0% (P = 0.02). A similar trend towards greater week 14 response rates in anti-TNF naïve patients was observed in UC: 40% vs 60% (P = 0.3). However, at week 52, there were no differences in response or remission rates. Combined VDZ-immunomodulators at induction (16%, n = 5) was not associated with differences in response or side effects. Five patients (2 CD and 3 UC) stopped treatment: 4 due

Abstract No: P1589
Table 1: Kaplan-Meier Estimates of Responders Over 26 Weeks,% (standard error)

Follow-up Week	Outcome	Bio-naïve: Anti-TNFα	Bio-naïve: VDZ	Prior anti-TNFα: Anti-TNFα	Prior anti-TNFα: VDZ	Total: Anti-TNFα	Total: VDZ
Week 6	**Clinical remission**	2.8 (2.7)	0 (0)	3.6 (3.5)	2.9 (2.9)	3.2 (2.2)	2.5 (2.5)
Week 6	**AP resolution**	7.4 (4.1)	30.0 (14.5)	14.3 (6.6)	21.5 (6.0)	10.3 (3.7)	22.9 (5.6)
Week 6	**LS resolution**	5.1 (3.5)	0 (0)	11.9 (6.5)	3.1 (3.1)	7.8 (3.3)	2.6 (2.6)
Week 14	**Clinical remission**	20.4 (6.9)	25.0 (21.7)	28.2 (9.1)	7.6 (5.3)	24.0 (5.6)	9.9 (5.5)
Week 14	**AP resolution**	37.5 (7.7)	53.3 (16.6)	29.9 (8.9)	31.7 (7.1)	34.6 (5.9)	35.7 (6.7)
Week 14	**LS resolution**	27.8 (7.5)	25.0 (21.7)	28.7 (9.2)	10.5 (5.8)	28.2 (5.8)	12.4 (5.9)
Week 26	**Clinical remission**	33.7 (10.3)	25.0 (21.7)	33.0 (9.7)	13.0 (7.3)	32.8 (6.9)	14.4 (6.9)
Week 26	**AP resolution**	58.3 (7.9)	68.9 (16.8)	52.6 (10.3)	61.4 (8.6)	56.0 (6.3)	62.5 (7.7)
Week 26	**LS resolution**	53.3 (8.7)	25.0 (21.7)	45.8 (11.1)	29.7 (9.7)	50.3 (6.9)	29.9 (9.2)

to lack of response and 1 due to arthralgia. Additional side effects included a temporal flu-like illness after infusion (n = 2) and allergic reaction upon infusion (n = 2). Three patients were lost to follow-up.
Conclusion: Clinical response rates to VDZ in elderly IBD patients are similar to previous reports in younger patients. Anti-TNF naïve IBD patients may have greater response rates. VDZ has a favorable safety profile and is a valid and attractive option for this age group.
Disclosure: Nothing to disclose

P1591 REAL-WORLD EFFECTIVENESS AND SAFETY OF USTEKINUMAB FOR MODERATE-SEVERE CROHN'S DISEASE; A RETROSPECTIVE MULTICENTRE STUDY

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Introduction: Ustekinumab (UST), a monoclonal antibody targeting interleukin-12/23, has been shown in randomised clinical trials (RCTs) to be effective in inducing and maintaining clinical remission in Crohn's disease (CD).[1] However, as drug efficacy in a clinical setting may substantially differ from its effectiveness in the setting of a controlled RCT, real-world studies are necessary to assess clinical benefit. We retrospectively analysed patient records from 3 German IBD centres to evaluate the effectiveness and safety of UST in moderate to severe CD.
Aims and Methods: Patient records from one academic centre, one community hospital and one specialised outpatient unit in Germany from Dec 2016-Apr 2018 were retrospectively reviewed. Patients had moderate-severe CD and had previously shown intolerance, lack of response, or lost response to conventional immunosuppressive therapies or TNFα antagonists. UST was applied according to the German label; induction as infusion (6 mg/kg bw) at week 0, followed by s.c. injection (90mg) at week 8 and every 8 weeks thereafter. Effectiveness of UST was analysed by comparing CRP values prior to therapy and following the 3rd UST application, after ca. 17–22 wks. Patients were stratified in 2 groups according to inflammation prior to UST (CRP $\geq$5mg/L = active disease; CRP < 5mg/L = remission) and evaluated after therapy for remission (CRP < 5mg/L) or partial response (CRP decrease of $\geq$50% compared to baseline). Hypersensitivity reactions and drug-related adverse events (AEs) were assessed.
Results: Treatment data of 80 patients [59% female (F); mean age 40.02 ± 14.02yrs] were collected. Data sets of 52 patients [54% F; 39.50 ± 13.62yrs] were evaluable with respect to efficacy. 63.5% [33/52; 49% F; 40.4 ± 11.80 yrs] had active disease (CRP $\geq$5mg/L) prior to UST. In the active disease group, 36.4% (12/33) responded and 36.4% (12/33) showed partial response. Of those 36.5% [19/52; 63% F; 39.1 ± 15.01 yrs] in remission at baseline, 57.9% (11/19) maintained remission. In the active disease group, prior anti-TNF-treatment (in 15/33; 45.5%) had a significant positive effect on response (p = 0.029). Median baseline CRP values did not significantly differ between anti-TNF-naïv vs. -experienced patients. In contrast, prior anti-TNF therapy (10/19; 52.6%) had no significant effect on response (p = 0.260) in the remission group. Overall, UST was well tolerated, with no cases of anaphylaxis or acute hypersensitivity reactions. However, drug-related AEs occurred in 7/80 (8.75%), including dizziness, headaches, joint pain, vomiting, pruritis and psoriasis-like skin reactions (n = 3). Ustekinumab was discontinued in 10/80 (12.5%), primarily due to lack of response (n = 7). 3 patients received additional ''booster'' infusions due to unsatisfactory therapy response.
Conclusion: This study suggests that UST is generally well tolerated and has enduring long-term effectiveness in anti-TNF-experienced patients with active CD in a real-world setting. Our data suggest that in patients who do not respond to Ustekinumab within 24 weeks, additional treatment options should be evaluated and therapy optimised to increase the likelihood of long-term remission.
Disclosure: Jürgen Stein and Irina Blumenstein have received consultancy fees from Janssen-Cilag. All other authors have no conflicts of interest.

Reference

1. Feagan et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease; *N Engl J Med* 2016; 375:1946–1960. DOI: 10.1056/NEJMoa1602773.

P1592 EFFECTIVENESS, IMMUNOGENICITY, SAFETY AND PHARMACOECONOMIC ASPECTS FOLLOWING A SWITCH FROM REFERENCE INFLIXIMAB TO THE BIOSIMILAR SB2 IN INFLAMMATORY BOWEL DISEASE PATIENTS: A 6 MONTHS PROSPECTIVE COHORT STUDY

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Introduction: The anti-tumor necrosis factor (TNF) antibody SB2 is a biosimilar infliximab and has recently been approved in the European and US market for treatment of inflammatory bowel disease (IBD) patients. These are the first prospective data investigating clinical effectiveness, immunogenicity, safety and economic aspects over the course of 6 months following a switch from reference infliximab to SB2 in IBD patients.
Aims and Methods: This is a single-center, prospective, observational cohort study. We assessed clinical effectiveness, immunogenicity, safety and economic aspects regarding the switch from reference infliximab to the biosimilar SB2 in IBD. All patients receiving reference infliximab in the outpatient clinic for IBD at the University Hospital of Erlangen, Germany were switched to the biosimilar SB2 between February and April 2017 and prospectively assessed for 6 months. Harvey-Bradshaw Index (HBI) was used to determine clinical disease activity in Crohn's Disease (CD) and Partial Mayo Score (PMS) in Ulcerative Colitis (UC) patients. Trough-level (TL) and anti-drug antibodies (ADA) were measured at every SB2 application throughout the study period, using the Promonitor® test. The occurrence of adverse events was registered. Drug costs for SB2 were compared to the pricing of originator infliximab.
Results: In this analysis we report 114 IBD patients (72 CD, 42 UC) receiving reference infliximab who were enrolled and switched to SB2. The median age was 39.5 years (19–78) and the median duration of previous infliximab treatment before the switch was 131 weeks (range 2.9–478.3). Median disease activity for CD was a HBI of 3 (range 0–11) at baseline, 2 (0–13) at week 8, 2 (0–12) at week 16 and 2 (range 0–10) at week 24. Median disease activity in UC was a PMS of 0 (range 0–6) at baseline, 1 (range 0–6) at week 8, 1 (range 0–6) at week 16 and 1 (range 0–2) at week 24. TL for all IBD patients was a median of 6.3ug/ml (range $\leq$0.2–33.7) at baseline, 4.8ug/ml (range $\leq$0.2–31.1, comparison to baseline p = 0.07) at week 8, 5.3ug/ml (range $\leq$0.2–34.5, p = 0.11) at week 16 and 4.7ug/ml (range $\leq$0.2–33.4, p = 0.16) at week 24. Pre-existing ADA persisted in 7 patients over the follow-up period; 4 patients developed new ADA and 2 lost ADA positivity. Of all patients, 12 discontinued SB2 treatment (3 anaphylaxis, 1 recurrent infections, 6 secondary loss of response, 2 serious adverse events), 1 paused while nursing and 4 were lost to follow-up (1 change of physician, 3 unknown). Regarding serious adverse events, there was one malignancy (mamma carcinoma) diagnosed after the second and one ileocecal resection performed after the third SB2 application. Over 6 months the switching to SB2 led to a cumulative costs-saving of 354,137.88€ compared to the pricing of reference infliximab.
Conclusion: Our data demonstrate that in IBD patients switched from reference infliximab to the biosimilar SB2 no loss of effectiveness or increased immunogenicity was observed. SB2 was well tolerated and the switch resulted in substantial cost-saving in a real-life setting.
Disclosure: Biogen GmbH funded this research. The Investigators retained full control of scientific and analytic content, and had final editorial responsibility.

P1593 EVALUATION OF NEWLY REPORTED *NUDT15* SNPS (EXON1 AND 3) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH THIOPURINES

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Introduction: It is reported that the single nucleotide polymorphism (SNP) c.415C>T in exon 3 of *NUDT15* affects thiopurine-induced leukopenia in Asian patients with Crohn's disease (CD). Previously, we have reported that SNP c.52G>A and c.36_37insGGAGTC in exon1 also affect the thiopurine-induced leukopenia in patients with ulcerative colitis (UC) and CD (Kojima Y *et al. World J Gastroenterol* 2018; 24: 511–518).
Aims and Methods: In this study, we studied additional SNPs both exon1 and 3 in 123 patients, namely the newly reported SNPs in patients with acute lymphoblastic leukemia (Moriyama T *et al. Blood* 2017; 130: 1209–1212) including, c.37_42delGGAGTC, c.101G>C, c.103A>G in exon 1 and c.416G>A in exon 3.

One-hundred and twenty-three Japanese patients with UC and CD treated with thiopurines were enrolled. Genotyping for total seven SNPs of the *NUDT15* genes was performed using Custom TaqMan SNP genotyping assays or Sanger sequencing. The changes in WBC count, mean corpuscular volume (MCV), platelet count, hemoglobin, CRP, amylase, albumin, AST, ALT, and ESR were evaluated.

NUDT15	No. of Patients (%)	5/123 (4.1%)	3/123 (2.4%)	26/123 (21.1%)	89/123 (72.4%)
Exon 1	c.36_37insGGAGTC	+	–	–	–
Exon 1	**c.37_42delGGAGTC**	–	–	–	–
Exon 1	c.52G>A	–	+	–	–
Exon 1	c.101G>C	–	–	–	–
Exon 1	**c.103A>G**	–	–	–	–
Exon 3	c.415C>T	+	–	+	–
Exon 3	**c.416G>A**	–	–	–	–

[Number of Patients of Each Genotype of NUDT15]

Results: The results of SNP analysis of *NUDT15* were shown in Table (newly found SNPs were indicated in bold).

C.52G>A and c.36_37insGGAGTC in exon 1 were found in 3 (2.4%) and 5 (4.1%) of 123 patients, respectively. All five patients with c.36_37insGGAGTC in exon 1 were heterozygotes of c.415C>T in exon 3. Twenty-six patients (21.1%) had c.415C>T in exon 3 alone. Two were homozygote (T/T) and 24 were heterozygote (C/T). There were no cases with c.37_42delGGAGTC, c.101G>C, c.103A>G exon 1 and c.416G>A in exon 3. The WBC count gradually decreased after initiation of thiopurine treatment in the mutated cases (n=34) and was significantly lower at 8, 10, and 16 weeks (p=0.0036, 0.0048, and 0.017, respectively). Mean corpuscular volume (MCV) of RBC also increased after treatment of thiopurines started and was significantly higher in mutated cases at 10 weeks (p=0.0083). Three cases showed severe hair loss and two of three were homozygote of c.415C>T (T/T) and one of three was heterozygote of c.415C>T (C/T). Platelet count, hemoglobin, CRP, amylase, albumin, AST, ALT, and ESR did not differ significantly between the wild-type and mutated cases.

Conclusion: SNPs in exon 1 of *NUDT15* also affect thiopurine-induced leukopenia in patients with inflammatory bowel disease (IBD). Severe hair loss was observed in c.415C>T in exon 3. There were no cases with newly found SNPs c.37_42delGGAGTC, c.101G>C, c.103A>G in exon 1 and c.416G>A in exon 3 in Japanese patients with IBD.

Disclosure: Nothing to disclose

P1594 THE PREOPERATIVE USE OF ANTI-TNF α-ANTIBODIES IN IBD PATIENTS UNDERGOING RESECTIVE ABDOMINAL SURGERY HAS NO INFLUENCE ON PERI- AND POSTOPERATIVE COMPLICATIONS

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Introduction: There is still controversy whether the use of anti-TNF-α-antibody therapy (TNF-inhibitors) has an influence on the rate of postoperative complications and sometimes surgeries are delayed to wait for the reduction of antibody levels. Therefore, our aim was to assess the effect of preoperative TNF-inhibitors on the postoperative course in our IBD patients who received resective surgery.

Aims and Methods: A total of 176 patients with Crohn's disease (CD) or ulcerative colitis (UC) who underwent IBD related resective abdominal surgery at the hospital of the IBD-center-Munich between 2012 and 2016 were retrospectively analyzed. We recorded type, dosage and timing of application and identified patients who received TNF-inhibitors or not.

Patients were divided into 3 groups: Group 1 included patients who received TNF-inhibitors within one month before surgery, group 2 included patients treated with TNF-inhibitors more than 1 and less than 4 months and group 3 patients who have never received TNF-inhibitors. Postoperatively, we assessed the rate, type and time point of major and minor complications, reoperations and length of hospital stay. We defined early complications by appearance within 10 days and late complications within 11 to 90 days after surgery. We used Chi2-, Student's T- and Levene-test for statistical analysis.

Results: In 40 UC patients, proctocolectomy and ileo-pouch-anal anastomosis were performed in 92.5% (n=37), 7.5% (n=3) received other resections. 136 CD patients had ileocecal resections in 47.8% (n=65), anastomotic resections in 23.5% (n=32) and a combined resection of the small and large bowel in 28.7% (n=39). In CD 44.9% of patients received open laparotomy (in UC 20%), 47.7% were operated laparoscopically (in UC 77.5%) and in 7.3%, surgeons converted to open laparotomy (in UC 2.5%).

83 patients were assigned to group 1 (CD: 83%), 39 to group 2 (CD: 80%) and 54 to group 3 (CD: 76%). In groups 1 and 2, most patients received either infliximab (G1: 50.6%, G2: 89.7%) or adalimumab (G2: 43.3%, G2: 2.5%), only 6.0% and 7.6% of patients in both groups received golimumab or certolizumab.

The rates of proctocolectomies, ileocecal resections, and open laparotomies were comparable in all 3 groups, as well as disease duration and severity, age and sex distribution, the CD/UC ratio, median days of hospital stay, and reoperation rates.

	Group 1*	Group 2*	Group 3*
All complications*	**20.4%**	**30.7%**	**31.5%**
Major complications*	6%	10.2%	5.6%
Minor complications*	10.8%	12.8%	20.3%
Major plus minor complications *	3.6%	7.7%	5.6%

*[Rates of postoperative complications * differences statistically not significant]*

Late complications occurred more frequent in group 3 as compared to group 1 (14.9 vs. 3.5%, p < 0.01), early complications occurred similarly in all groups. Postoperative complications in CD correlated with the open laparotomy technique (p=0.003) and the prolonged duration of disease (p=0.004), independently from TNF-exposure.

Conclusion: Independently from the preoperative time interval, the use of TNF-inhibitors before surgery did not increase the risk of postoperative complications, reoperations or prolonged hospital stays as compared to patients without such preoperative therapy. Long disease duration was a risk factor for a complicated postoperative course.

Based on these data, the preoperative use of TNF-inhibitors might even exert a protective function. The introduction of infliximab and adalimumab biosimilars provides a chance to perform large prospective trials on strategies how we could best use TNF-inhibitors before surgery.

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P1595 PREDICTORS OF VEDOLIZUMAB RESPONSE TO INDUCTION: REAL-LIFE EXPERIENCE

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Introduction: Vedolizumab is a humanized immunoglobulin G1 monoclonal antibody (mAb) directed towards the integrin α4β7. Clinical trials have demostrated the efficacy and safety of vedolizumab (VDZ) in the induction and maintenance of Crohn's disease (CD) and ulcerative colitis (UC). We describe real-world treatment outcomes with VDZ in five tertiary Spanish hospitals.

Aims and Methods: EC treated with VDZ until october 2017 in five Spanish hospitals.

- Clinical response and remission were defined by Partial Mayo Score (UC) or Harvey Bradshaw Index (HBI) and were assessed after induction, at 6 and 12 months. We evaluated treatment persistence as well.
- We studied predictive factors of clinical benefit (response or remission) after induction in UC and CD patients.
- We evaluated if clinical benefit was different in UC and CD patients after exposure to one or more antiTNF agents.

Results: One hundred and three patients were included (52 female (50.5%), UC 40(38.8%), CD63(61.2%), median age 42.9±15.01 y, median disease duration 11.5±8.15 years). Median HBI was 7±3 and PMS was 6±2 at baseline. Majority of patients were refractory to antiTNF treatment: 22 patients (21.6%) had failed to 1 antiTNF and 71 (69.6%) to 2 or more antiTNF agents. Almost 60% of patients were using steroids during induction and 25 (24.5%) received concomitant immunomodulators. Median duration of VDZ treatment was 8.5±6.3 months. Clinical response after loading VDZ was achieved by 79 patients (77.5%). Clinical response and remission at 6 and 12 months were: 42.5%(25/59),33.9%(20/59),41.4%(12/29) and 41.4%(12/29), respectively. In October 2017, 72 patients (70,6%) were persistent on VDZ therapy. Clinical benefit (response or remission) was not associated to the number of antiTNF agents used previously or disease type (UC or CD). No factor (age, sex, disease duration, concomitant immunomodulators or steroids, smoking habit, disease type or severity of illness,) was associated to induction response in UC patients. Disease duration (67%<5 years vs 85.3% > 5 years, p=0.04) and baseline HBI (<7:96.3% vs >7:67.6%, p=0.05) were associated to induction response in CD patients. Thirty-five patients (34.3%) needed dose scalation.

Conclusion: VDZ is effective in IBD patients with long-term persistence of treatment in almost 70% of them. Severity of illness actvity and shorter time duration disease were associated to worse induction response in CD patients.

Disclosure: Nothing to disclose

P1596 LOWER RELAPSE RATES FOLLOWING A THERAPEUTIC DRUG MONITORING BASED STRATEGY FOR TNF ANTAGONIST DE-ESCALATION DURING INFLAMMATORY BOWEL DISEASE

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Introduction: There are limited data on infliximab therapy de-escalation for inflammatory bowel diseases (IBD). The aim of the study was to assess the rate of relapse following infliximab de-escalation in IBD patient in remission as well as predictors of the relapse including infliximab through level prior to de-escalation.

Aims and Methods: We performed a single-center study on 96 patients with IBD in clinical (Harvey Bradshaw Index <4 or Mayo Score <2) and biological (CRP $<$ 5mg/l) remission for whom the dose of infliximab was decreased or the infusion interval increased. The data were retrieved from a prospective IBD database (CNIL No. 1412467) between June 2012 and September 2017. The primary criterion was the relapse during the follow-up defined by the onset of clinical relapse associated with the need for infliximab optimization or biologic switch. Actuarial analysis was performed.

Results: A total of 146 de-escalations were performed in the 96 patients. There were 57 (53%) males with a median age of 36 at infliximab de-escalation. Regarding the 65 (68%) patients with Crohn's disease, 43(72%) were B1 according to the Montreal classification, 27 (28%) previously underwent surgery and 22 (14%) had perianal Crohn's disease. Seventeen of the 31 patients with UC had pancolitis. Among the 146 de-escalations, 54 (37%) were based on the clinical and biological remission only and 92 (63%) were based on a clinical remission associated with an infliximab through level above 7 mg/L. The type of de-escalation was mainly a dose reduction from 10 to 5 mg/kg (30(20%) de-escalations) and a prolonged interval between infusions of 2 weeks (90(62%) de-escalations). The cumulative probabilities of relapse following anti-TNF de-escalation were 16% and 47% at 1 and 2 years respectively. By multivariate analysis, smoking (HR $=2.2$, IC95[1,07–4,58], p $=0.03$), diagnosis of ulcerative colitis (HR $=2.9$, IC95[1,45–5.98], p $=0.0028$), absence of combination therapy at infliximab initiation (HR $=2.65$, IC95[1,34–5.1] increased the risk of relapse. Of note a strategy based on therapeutic drug monitoring decreased the risk of relapse (HR $=0.48$, IC95[0.24–0.96], p $=0.03$). Infliximab trough level above 3 mg/L following infliximab de-escalation was associated with less relapse. Pre- and post- infliximab trough level were well correlated (spearman correlation $\rho = 0{,}67$, p $< 0{,}0001$).

Conclusion: Infliximab dose de-escalation increase the risk of IBD relapse. The use of infliximab trough level to assess the feasibility of dose de-escalation seems a prerequisite to decrease the risk of relapse. Infliximab trough level post de-escalation may be predictable.

Disclosure: G. Bouguen declares COI with Abbvie, MSD, Takeda, Janssen, Ferring, Pfizer, Hospira, Diasorin

P1597 LONG-TERM EFFICACY OF VEDOLIZUMAB THERAPY ON CLINICAL AND ENDOSCOPIC ACTIVITY IN PATIENTS WITH ANTI-TUMOR NECROSIS FACTOR ALPHA RESISTANT INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab (VDZ) is the first gut-specific monoclonal antibody alternative to anti-tumor necrosis factor alpha (anti-TNF-alpha) therapy in patients with moderate-to-severe inflammatory bowel disease (IBD). It has been registered since 2016 in Hungary, but currently the high treatment costs are considerably limiting the availability of VDZ. All newly initiated VDZ therapy was individualized, it should be approved by the steering committee of five Hungarian IBD-specialist. The aim of our non-interventional retrospective study was to assess the efficacy of induction VDZ therapy on clinical and endoscopic activity in moderate or severe active IBD with previous anti-TNF failure or intolerance in real-life setting.

Aims and Methods: Anti-TNF-alpha therapy intolerant IBD patients who received VDZ therapy were enrolled between July 2016 and January 2017 in Hungary. The therapeutic response was assessed based on the changes of clinical (Crohn's Disease Activity Index [CDAI], Mayo score) and endoscopic (Simple Endoscopic Score for Crohn Disease [SES-CD], endoscopic Mayo score) scores. Clinical response was defined as >3 points decrease in the total Mayo score or >100 decrease in CDAI score from baseline. Remission was defined as Mayo score ≤ 2, with no individual subscores >1, or as CDAI score ≤ 150. Mucosal healing was defined as Mayo endoscopic subscore ≤ 1 or as SES CD score ≤ 4.

Results: 49 Crohn's disease (CD) and 73 ulcerative colitis (UC) patients received VDZ induction therapy after anti-TNF failure or intolerance. The mean age was 40.6 years (range 18–85; median 39) and the average disease duration was 10.3 years (range 1–36; median 9). Extraintestinal manifestations occurred in 32 patients (26.2%), and in 10 cases (8.2%) IBD was associated with primary sclerosing cholangitis (PSC). At the baseline the mean CDAI and SES-CD were 303 (range 40–430; median: 312) and 19.5 (range 6–37; median 18) in the CD group and mean Mayo and eMayo score were 9.59 (range 5–12; median 10) and 2.72 (range 2–3; median 3) in the UC group, respectively. Clinical response during the VDZ induction therapy was seen in 30 (61.2%) CD and 61 (83.6%) UC patients. The proportion of clinical remission and steroid-free remission was higher in the UC group compared with CD group (47.9% and 30.1% vs. 48.9% and 38.8%, respectively). In 51 cases the first-year VDZ treatment could have been completed during the study period, however in 20 cases (39.2%) primary non-response for induction therapy was observed. 31 patients received maintenance VDZ therapy. The rate of response, clinical remission and steroid-free remission were substantially higher in UC (55.0%, 41.4% and 41.4%) compared with CD (27.3%, 18.2% and 18.2%) by the end of first-year therapy. Significant difference was observed between UC and CD subgroups in terms of mucosal healing both by the end of induction and by the end of first-year therapy (48.3% and 51.7% vs. 9.1% and 13.6%).

Conclusion: Our results suggest that both induction and the one-year long maintenance VDZ therapy is effective and it is a safe therapeutic option in anti-TNF-alpha failure or intolerant IBD patients with moderate or severe disease activity, however significant difference was observed between the UC and CD subgroups. Mucosal healing was achievable in every second UC and in only every fifth CD patients both by the end of the induction and by the end of first-year treatment in this difficult-to-treat population.

Disclosure: Nothing to disclose

P1598 LONG-TERM PROGNOSIS OF CROHN'S DISEASE OF THE POUCH

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Introduction: The occurrence of signs of Crohn's disease (CD) such as fistula and stricture in ulcerative colitis (UC) patients after total proctocolectomy ileal pouch anal anastomosis (TPCIPAA) is called Crohn-like disease (CLD), or Crohn's disease of the pouch. The aim of this study is to investigate long-term prognosis and risk factors of CLD.

Aims and Methods: The records of patients who underwent TPIPAA operation between 2000–2017 were investigated. The criterion for inclusion in the study was the histopathological diagnosis of UC in the operation material. CLD was defined as ulcer morphology similar to CD detected in the pouch or afferent loop, or fistula or stricture developed during postoperative period. Two groups of patients were included as control groups. The first group who had pouchitis and / or cuffitis after TPCIPAA without signs of CD is named "diseased control group". The second control group consists of UC patients without complaints after TPCIPAA operation. Data about age at the diagnosis, age at the operation, smoking habits, family history of CD, preoperative colonoscopy and CT findings were recorded. The demographic, clinical and laboratory data of all three groups were compared using the Pearson Chi-Square test, the Fisher Exact test and the Kruskal Wallis test for the comparison of parameters between groups.

Results: A total of 1166 records of UC patients were examined, we found 57 patients who underwent TPCIPAA operation, 9 patients were excluded. From remaining 48 patients, 16 were grouped as CLD, 15 were in the diseased control group, and 17 were in the control group. The rate of inadequate examination of the terminal ileum before the operation in CLD, diseased control and control group were 31.2%, 26% and 11.8% respectively. The difference between three groups was not statistically significant. There were 6 patients (37.5%) In CLD group with fistula, including 5 with perianal fistula and 1 with pouch – vaginal fistula. The mean time of the appearance of the fistula after operation was 44 ± 13.5 months. All patients with fistula had also cuffitis. Three of these patients had permanent ileostomy. In one patient, fistula flow stopped after ileostomy, but in the remaining 5 patients, fistulas were still active. Obstructive complications were present in 6 patients (37.5%). The stenosis was in the cuff and the afferent loop in 3 patients for each. Two of these patients underwent endoscopic balloon dilation. The remaining 6 patients without fistula or stricture had pouchitis and/or ileitis, and none were in remission despite medical treatment. During the follow up period with the mean of 69 ± 45.8 months, none of 16 patients with CLD were in remission except one patient who had permanent ileostomy. Comparisons of the three groups revealed that the age at the time of operation in CLD group was less than that of other two groups and that

18.7% (3/16) of patients with CLD had ulcer morphology suggesting CD in the preoperative colonoscopy. Any of patients in the diseased control and the control group had endoscopic findings suggesting CD.
Conclusion: CLD is more common in patients who had an inadequate preoperative investigation of terminal ileum. To detect ulcers on colonoscopy before surgery with morphological aspects suggesting CD is a risk factor for CLD, even if the ileum is normal. In CLD mucosal remission could not be achieved in any patient despite combined immunosuppressive therapy. Fistula rate was about 40% in CLD patients, and 3 of 6 patients with fistula in our series required permanent ileostomy.
Disclosure: Nothing to disclose

P1599 THE EFFECT OF PROBIOTIC LACTOBACILLUS CASEI ON MITOTIC AND APOPTOTIC ACTIVITY, HISTOPATHOLOGICAL SCORE AND MORPHOMETRIC PARAMETERS IN PORCINE EXPERIMENTAL INFLAMMATORY BOWEL DISEASE INDUCED BY DEXTRAN SODIUM SULFATE

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Introduction: Gastrointestinal injury caused by dextran sodium sulfate (DSS) is a suitable and reliable porcine experimental model of inflammatory bowel disease (IBD).
Aims and Methods: The purpose of this study was to evaluate effect of probiotic *Lactobacillus casei* DN 114001 (LC) on DSS-induced experimental IBD. Eighteen experimental mature female pigs (*Sus scrofa* f. domestica; weight: 33–36 kg, mean 34.3 ± 1.0; age: 4–5 months), were enrolled into the study: controls with no treatment (n = 6); DSS (n = 6) and DSS+LC (n = 6). LC was administrated to fasting animals in a dietary bolus in the morning on day 1–7 (4.5*10^10 live bacteria/day), DSS (Sigma-Aldrich) simultaneously on day 3–7 (0.25 g/kg/day). All animals were fed twice a day (standard assorted A1 food of equal amounts). On day 8, the pigs were sacrificed (after 24 hours of fasting) by means of pharmacological euthanasia (i.v. embutramide, mebezonium iodide and tetracaine hydrochloride; Intervet International BV) and exsanguinated. Immediate autopsy was performed and specimens for structural and morphometric analysis were taken. Specimens of the stomach, small and large intestine were routinely processed, formalin-fixed, and tissue sections 5 μm thick were cut (Microtome model SM2000 R, Leica). Sections were stained with haematoxylin-eosin (Merck) and evaluated using a BX-51 microscope (Olympus) equipped with image analysis software ImagePro plus 7 (Media Cybernetics). Histopathology score (from 0 to 11) was measured (according to Ref. 1): by summing scores of loss of mucosal architecture (0, 1, 2 or 3), cellular infiltration (0, 1, 2 or 3), muscle thickening (0, 1, 2 or 3), crypt abscess formation (0 or 1), and goblet cells depletion (0 or 1). The length of crypts (all segments) and length and width of villi (small intestine only) were assessed. The grade of mitosis, conveyed as mitotic index [mitotic index (%) = number of mitotic figures * 100 / number of all evaluated cells] and the grade of apoptosis, conveyed as apoptotic index [apoptotic index (%) = number of apoptotic cells * 100 / number of all assessed cells] were evaluated. Apoptotic activity was also assessed immunohistochemically by detection of activated caspase-3 (Cell Signaling Technology) and standard peroxidase technique. Kruskal-Wallis test was used for statistical analysis (software IBM SPSS Statistics, version 22, IBM).
Results: Histopathology score was increased significantly only in the large intestine, from 0 (controls) to 3.80 ± 1.47 (DSS; $p = 0.007$) and 3.60 ± 1.36 (DSS+LC; $p = 0.015$). The length of jejunal villi and crypts were significantly different in controls (293.1 ± 93.1; 312.1 ± 60.5 μm), DSS group (307.7 ± 84.9; 439.8 ± 87.9; $p = 0.023$; $p < 0.001$) and DSS+LC group (282.0 ± 108.7; 385.2 ± 101.2; $p > 0.05$; $p < 0.001$). The length of ileal crypts was 281.8 ± 62.3 (controls), 347.0 ± 78.4 (DSS; $p < 0.001$) and 323.3 ± 73.3 (DSS+LC; $p < 0.001$), respectively. The length of villi in the ileum increased from 251.3 ± 85.3 (controls) to 291.5 ± 127.9 (DSS; $p = 0.047$) and 244.8 ± 93.7 (DSS+LC; $p = 0.015$). The length of colonic crypts increased from 421.0 ± 65.8 (controls) to 660.0 ± 124.9 (DSS; $p < 0.001$) and 659.3 ± 119.7 μm (DSS+LC; $p < 0.001$). Mitotic index of the colonic mucosa was 1.19 ± 0.33% (controls), 3.10 ± 1.82 (DSS; $p = 0.009$) and 2.40 ± 1.17% (DSS+LC; $p = 0.049$), respectively. Other changes, including apoptotic activity at any investigated segment of the gastrointestinal tract, did not reach any statistical significance.
Conclusion: Treatment with probiotic strain LC reduced morphological changes in DSS-induced experimental IBD.
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Disclosure: Nothing to disclose

Reference

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P1600 AN INTRODUCTION TO LUCID; LIVING WITH ULCERATIVE COLITIS; IDENTIFYING THE SOCIOECONOMIC BURDEN IN EUROPE

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Introduction: The need for newer therapies remains an important challenge to properly manage patients with Ulcerative Colitis (UC). Colectomy still remains the last resort faced by patients that are non-responsive to current medical therapies. The increasing incidence of UC and the advent of biological drugs ultimately generated a new economic burden associated with UC that remains to be explored. To date there is little evidence about direct and indirect medical and societal costs across Europe. Although Health-related quality of life (HRQoL) outcomes are crucial to assess UC treatment benefits, it is still poorly reported in the literature.
HCD Economics in conjunction with the University of Chester (UoC) UK, are undertaking a pan-European burden of illness study (LUCID) across 10 countries (Denmark, France, Germany, Italy, Norway, Poland, Romania, Spain, Turkey and the UK) including 377 physicians and 3,582 patients.. LUCID is governed by an expert review group consisting of charity, academic, medical and health economist representatives.
Aims and Methods: The primary objective is to quantify UC-related costs from a societal perspective. The secondary objective is to determine the impact on patient's HRQoL.
The study population includes adult patients diagnosed with UC at least 24 months prior to the index date (date of clinical consultation). The study cohort comprises two arms: Arm 1: patients with moderate or severely active UC at initiation of documentation period, Arm 2: patients with prior moderate or severely active UC who had achieved mild UC or remission.
Data are to be collected by means of two questionnaires: physician on-line clinical record form (CRF), and written public and patient involvement engagement form (PPIE). The CRFs collect information on direct medical resource utilisation over the 12 month documentation period. The PPIE form covers out-of-pocket expenses and work loss (direct non-medical and indirect costs), as well as quality of life, disability and work-related activity (EQ-5D-5L, IBD-DI and Work Productivity and Activity Impairment Questionnaire, WPAI).
Full ethical approval is being sought from the UoC Faculty of Health and Social Care Research Ethics Committee.
Results: This study will enable the generation of a granular database comprehensively detailing the wide variety of costs that accompany living with UC. Per-patient costs are calculated by multiplying the quantities of the resource use collected in the study with the national unit price of each resource. Costs associated with temporary and long-term work absence (including early retirement) are valued using the traditional human capital approach.
Conclusion: The LUCID burden of illness study aims to comprehensively contribute to the evidence base for socioeconomic burden of UC. This study adds value to all stakeholders including: academics, patients, carers, government/payers and the pharmaceutical industry. The intent is to publish the findings in peer review publications to inform the international community.
Disclosure: Nothing to disclose

P1601 USE OF ANTI-TNF AGENTS FOR PRIMARY PREVENTION OF POSTOPERATIVE RECURRENCE OF CROHN'S DISEASE: A NATIONWIDE, REAL-LIFE STUDY. RESULTS FROM THE SPANISH ENEIDA REGISTRY

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Introduction: Anti-TNF and thiopurines are the only drugs that demonstrated efficacy in preventing postoperative recurrence (POR) in Crohn's disease (CD). There are only two large RCTs in this setting assessing the efficacy of infliximab (IFX) or adalimumab (ADM). Moreover, real-life experience has been scarcely reported.

Aims and Methods: All CD patients in whom anti-TNF agents were prescribed for primary prevention of POR within the first 3 months after ileocecal or ileocolonic resection with anastomosis were identified from the ENEIDA registry (a large, prospectively maintained database of the Spanish Working Group in IBD - GETECCU-). Only those patients who had at least one endoscopic assessment within 18 months after surgery were included. Clinical and endoscopic features were collected before and within 18 months after surgery. Endoscopic POR was defined by a Rutgeerts score >i1 and advanced endoscopic POR by >i2. Clinical POR relied on the criteria of the treating physician. Surgical POR was defined by the need of the new intestinal resection during follow-up.

Results: A total of 152 patients were included, 55 treated with IFX and 97 with ADM. Concomitant use of immunosuppressants was prescribed in 39%, of which 83% thiopurines and 17% methotrexate. 44% received an additional 3-month course of metronidazole after surgery. Anti-TNF was started after a median time of 32 days (IIQ13–44) from surgery. Regarding risk factors for POR: 23% were active smokers, 44% had prior resections, 44% had penetrating CD behaviour, and 28% had a history of perianal disease. In total, 27 (18%) had none, 59 (39%) had only 1, and 66 (43%) had >1 risk factor for POR. 82% had been exposed to anti-TNF prior to the index surgery (73% within the last 6 months). Median time of follow-up on anti-TNF was 29 months (IIQ 13–48). 121 patients (80%) had one endoscopic assessment within 18 months of follow-up and 31 patients (20%) had more than one endoscopic assessment in this period time. Overall, 34% had endoscopic POR and 14% advanced endoscopic POR. Additionally, 30% presented clinical POR as considered by the treating physician and 3% developed surgical POR, with no differences between IFX and ADM. Treatment was dose-escalated in 24% of patients, being similar for IFX and ADM. Endoscopic or clinical POR were the main reason to dose-escalate anti-TNF. In the univariate logistic regression analysis perianal disease, prior exposure to anti-TNF, concomitant immunosuppressant therapy and penetrating behaviour were associated to endoscopic POR. In the multivariate analysis only the perianal disease was associated with endoscopic POR (OR 3.11, 95% CI 1.46–6.61).

Conclusion: Use of anti-TNF agents for the prevention of POR in real practice is markedly different from RCTs: they are more frequently used in combination with immunosuppressants and/or a 3-month course of metronidazole, a great proportion is anti-TNF experienced, and meet high-risk criteria for POR. In this setting, although anti-TNFs prevent POR in a large proportion of patients (particularly advanced endoscopic lesions), still one-third of patients develop early endoscopic lesions.

Disclosure: Nothing to disclose

P1602 EVALUATION OF TREATMENT ADHERENCE AMONG INFLAMMATORY BOWEL DISEASE PATIENTS FROM ARGENTINA: A MULTICENTER STUDY

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Introduction: Poor treatment adherence is a common problem among chronic diseases such as inflammatory bowel disease (IBD). Since treatment adherence may be closely related to the risk of symptomatic relapse in IBD patients, identifying potential features associated with the lack of adherence may be useful for relapse prevention.

Aims and Methods: We aimed to determine lack of adherence to oral and parenteral treatments among IBD patients from Argentina and to identify factors associated with non-adherence.

A multicenter cross-sectional study involving seven referral centers from three cities of Argentina was undertaken. Patients with a diagnosis of ulcerative colitis or Crohn's disease were invited to answer an anonymous online survey which included the 8-item Morisky Medication Adherence Scale, a 5-point Likert Scale to evaluate adherence to biologic therapy, and a questionnaire that contemplated the following variables: age, gender, years from diagnosis, education level, type of medical insurance, smoking, history of surgery and/or hospitalizations due to IBD, number of annual visits to a gastroenterologist, perception of easy communication with the gastroenterologist, use of e-mail for consultation, overall satisfaction with medical attention, use of other chronic medications. Univariate analyses were performed for aminosalicylate adherence, thiopurine adherence and biologic adherence. Multivariate analyses looking for independent variables associated with lack of adherence were furtherly performed in each case.

Results: Overall, 447 ulcerative colitis and 135 Crohn's disease patients were enrolled. Median age was 37 years (range 21–72), 39.86% were male; median time from diagnosis was 6 years (0.5–35). When analyzing treatment adherence, 91.41% were under treatment with at least one oral medication. According to the Morisky Scale results, 50.37% of these patients reported a low adherence to their oral medications. Ulcerative colitis patients had a lower risk of low adherence when compared to Crohn's disease subjects [OR 0.57 (0.37–0.87)]. Low adherence was more prevalent when considering aminosalicylate consumption (52.21% had a score compatible with low adherence). Independent variables significantly associated with low aminosalicylate adherence were use of other chronic medication [OR 1.49 (1.01–2.25)] and the lack of perception of easy communication with the gastroenterologist [OR 1.67 (1.1–2.95)]. Low adherence to thiopurines was reported in 40.25% of patients who were under that treatment; lack of perception of easy communication with the gastroenterologist [OR 1.2 (1–5.8)] and smoking [OR 3.75 (1.53–9.17)] were significantly associated with thiopurine low adherence. When considering biologic treatment, 21.8% reported low adherence; subcutaneous administration instead of intravenous was significantly associated with low adherence to biologics [OR 4.8 (1.57–14.66)].

Conclusion: Low treatment adherence is common among IBD patients, especially among aminosalicylate consumers. Clinical features were found to be associated with an increased odds of poor adherence to medications that are potentially modifiable and thus efforts should be directed towards that aim.

Disclosure: Nothing to disclose

P1603 INFLIXIMAB DOSE-REDUCTION IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS IN PROLONGED DEEP REMISSION: POTENTIAL IMPLICATIONS ON DE-ESCALATION STRATEGIES IN A REAL-LIFE CLINICAL SETTING WITHOUT A THERAPEUTIC DRUG MONITORING (TDM) APPROACH

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Introduction: An increasing number of IBD patients are treated with Infliximab (IFX). Potential costs and safety concerns encourage de-escalation strategies particularly in patients with low risk of relapse. Few studies have investigated the impact of increasing dose intervals on maintenance of remission whereas a dose-reduction strategy has been reported in IBD patients only in conjunction with a TDM approach.

Aims and Methods: The aim of this study was to evaluate the effect of Infliximab dose-reduction on clinical remission in IBD patients in deep remission.

In this retrospective single-centre study, patients treated with IFX monotherapy every 8 weeks and in composite deep remission for at least 1 year had a dose reduction of their infusion from 5 mg/kg to 3 mg/kg. Patients were followed up every 3 months and relapse was defined by composite markers of clinical, biological and endoscopic recurrence. IFX was increased at 5 mg/kg in patients with relapse and infusion reaction or intolerance to IFX was recorded. Statistical analysis was perfomed by SPSS package.

Results: Fifty-seven patients (17F, 40M) were included (33 Crohn's disease [CD] and 24 ulcerative colitis [UC]) with a mean follow-up after dose reduction of 12.7 ± 8.5 months. Mean duration of IFX before dose reduction was 45.8 ± 28.4 months. Overall, 14 (24.5%, 6 UC and 8 CD) patients relapsed during the follow-up. Cumulative probability of relapse free survival was $74.9\% \pm 0.06\%$ at 1 year and $69.2\% \pm 0.08\%$ at 2 years. Patients with relapse had an IFX re-escalation to 5 mg/kg dose with clinical response in 11/14 (78.5%). None of the patients

reported adverse events during maintenance with dose reduction whereas one patient (1/14, 7.1%) reported an infusion reaction after re-escalation to 5 mg/kg. No difference in the mean duration of IFX before dose reduction was observed in patients with relapse compared to patients maintaining remission (45.2 ± 28.6% months vs. 44.8 ± 28.2% months, p = 0.1). In CD patients there was a trend of association between duration of IFX before dose reduction < 36 months and the risk of relapse, although not statistically significant (OR = 2.07; CI 95% 0.3–12.4, p = 0.4).

Conclusion: In a real-life clinical setting, IFX dose reduction is feasible and safe in IBD patients with composite deep remission with a relatively low risk of relapse at 2 years. More than three-quarters of patients who relapsed regain remission after IFX re-escalation. In CD patients an IFX use > 36 months seems to be associated with a lower risk of relapse after dose reduction.

Disclosure: Nothing to disclose

P1604 RESCUE THERAPY WITH ANTI-TNF AGENTS FOR ESTABLISHED POST-OPERATIVE RECURRENCE OF CROHN'S DISEASE. A MULTICENTRE, RETROSPECTIVE, NATIONWIDE STUDY

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Introduction: Thiopurines are the treatment of choice for the prevention of post-operative recurrence (POR) in Crohn's disease (CD) in high-risk patients, whereas those at low risk should be monitored and treated only in case POR occurs. Endoscopic assessment of POR is recommended within the first year following surgery in all patients. With this strategy, up to 50% of patients will develop POR within 6–12 months after surgery. In patients with established POR, anti-TNF agents may be of benefit, but scarce data on this are available.

Aims and Methods: Our aim was to evaluate the rate of endoscopic remission and improvement of mucosal lesions under rescue therapy with anti-TNF for established POR. Retrospective, multicentre, nationwide study in CD patients who received therapy with anti-TNF agents because of established POR as defined by a Rutgeerts' endoscopic score >i1. Epidemiological, clinical, biological and endoscopic features were collected before and after starting anti-TNF. Endoscopic improvement and remission were defined by a reduction in the baseline Rutgeerts' score and by a score <i2, respectively. Clinical POR was defined by the presence of 2 out of the following 3 criteria: weight loss, increase in stool frequency, and new onset of abdominal pain, in the setting of POR at endoscopy or MRI enterography.

Results: 287 CD patients treated with infliximab (n = 126) or adalimumab (n = 161), 70% in combination with immunosuppressants, because of established POR were included. Table 1 summarizes the baseline characteristics of the patients. Endoscopic assessment was available in 190 patients (66%) after a median time of anti-TNF treatment of 16 months (IQR 11–31). Among these patients, 114/190 (60%) had endoscopic improvement and 82/190 (43%) achieved endoscopic remission (Rutgeerts i0-i1). Of the 82 patients with clinical POR at anti-TNF start, 60 patients (73%) achieved clinical remission. Median time of follow-up on anti-TNF treatment was 45 months (IQR 20–75). During this time, 44 patients (15%) developed clinical POR and 17 patients (7%) developed surgical POR. Univariable and multivariable logistic regression model showed that combination therapy with thiopurines and treatment with infliximab were the only factors associated with a higher rate of both endoscopic improvement (OR 2.97; 95%CI 1.6–5.7, and OR 2.23; 95%CI 1.2–4.2, respectively), and endoscopic remission (OR 2.28; 95%CI 1.2–4.3, and OR 2.65; 95%CI 1.5–4.8, respectively).

Conclusion: Rescue therapy with anti-TNF is efficient for the treatment of established POR, even in patients in whom endoscopic POR occurs while on azath.

	Overall (n = 287)	Infliximab (n = 126)	Adalimumab (n = 161)	p value
Female sex	135 (47)	49 (39)	86 (53)	0.01
Penetrating behaviour	107(37)	47 (37)	60 (37)	0.99
Perianal disease	53 (18)	25 (20)	28 (17)	0.59
Intestinal resections prior to index surgery	51 (18)	21 (17)	30 (19)	0.66
Active smoking	123 (43)	59 (47)	64 (40)	0.23
>1 known risk factor for POR	97 (34)	46 (37)	51 (32)	0.39
Anti-TNF exposure prior to surgery	102 (36)	38 (30)	64 (40)	0.10
Preventive thiopurines for POR	142 (49)	65 (52)	77 (48)	0.53
Advanced POR (Rutgeerts score i3-i4) at anti-TNF start	173 (60)	76 (60)	97 (60)	0.99
Clinical POR at anti-TNF start	82 (29)	36 (29)	46 (29)	1.00
Concomitant thiopurines with anti-TNF	182 (63)	87 (69)	95 (59)	0.08

[Table 1.]

Disclosure: Nothing to disclose

P1605 STOPPING 5-AMINOSALICYLATES IN ULCERATIVE COLITIS PATIENTS STARTING BIOLOGIC THERAPY DOES NOT INCREASE THE RISK OF ADVERSE CLINICAL OUTCOMES

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Introduction: 5-aminosalicylates (5-ASA) are commonly used in the treatment of ulcerative colitis (UC). The benefit of continuing 5-ASA in UC patients who initiate anti-tumor necrosis factor alpha (anti-TNF) biologics is unknown.

Aims and Methods: We aimed to compare clinical outcomes in UC patients already on 5-ASA who started anti-TNF and then either continued or stopped 5-ASA. Our primary outcome was any adverse clinical event defined as a composite of new corticosteroid use, hospital admission, or colectomy. We utilized two national databases: the United States (U.S.) Truven MarketScan health claims database and the Danish National Patient Register linked with the Danish National Prescription Register. Patients with UC who started anti-TNF after having been on oral 5-ASA for at least 90 days were included. Patients were classified as stopping 5-ASA if therapy was discontinued within 90 days of starting anti-TNF. Analyses were performed using multivariable Cox regression models controlling for age, sex, disease duration, 5-ASA treatment duration, and baseline healthcare utilization. Hazard ratios (HR) with 95% confidence intervals (95% CI) are reported comparing stopping 5-ASA with continuing 5-ASA (reference group).

Results: Of 4,363 U.S. anti-TNF-treated UC patients, 1,667 (38.2%) stopped 5-ASA and 2,696 (61.8%) continued 5-ASA. Among 699 anti-TNF-treated Danish UC patients, 225 (32.2%) stopped 5-ASA and 474 (67.8%) continued 5-ASA. In both cohorts, the incidence rates of adverse outcomes were similar in those who continued or stopped 5-ASA and there were no significant differences in the risk of adverse outcomes in adjusted analyses (Table 1).
Conclusion: In two separate national databases, stopping 5-ASA in UC patients starting anti-TNF therapy did not increase the risk of adverse clinical events including corticosteroid use, hospitalizations, and colectomy. These results should be validated in a prospective clinical trial.

	Continue 5-ASA IR (95% CI), per 100 person-years	Stop 5-ASA IR (95% CI), per 100 person-years	Stop versus continue 5-ASA Adjusted HR (95% CI)	P value
United States Cohort				
New Steroid Use	32.9 (30.3–35.7)	37.8 (33.7–42.4)	1.04 (0.88–1.23)	0.7
Hospitalization	14.2 (12.6–16.0)	15.1 (23.8–17.9)	0.97 (0.76–1.23)	0.8
Surgery	2.5 (1.9–3.3)	2.1 (1.4–3.3)	0.72 (0.40–1.30)	0.3
Composite	***44.7 (41.6–48.1)***	***51.2 (46.3–56.7)***	***1.04 (0.90–1.21)***	***0.6***
Denmark Cohort				
New Steroid Use	22.9 (19.0–27.6)	21.7 (16.1–29.3)	1.05 (0.71–1.55)	0.8
Hospitalization	13.0 (10.2–16.6)	22.2 (16.4–30.1)	1.35 (0.88–2.08)	0.2
Surgery	6.2 (4.4–8.7)	10.2 (6.7–15.5)	1.36 (0.75–2.46)	0.3
Composite	***37.5 (32.0–43.8)***	***42.0 (33.2–53.1)***	***1.09 (0.80–1.48)***	***0.6***

[Table 1. Risk of Adverse Outcomes in Patients Who Continue or Stop 5-ASA]
Disclosure: Nothing to disclose

P1606 TARGET CELLS OF VEDOLIZUMAB IN PERIPHERAL BLOOD AND GUT MUCOSAL CELLS FROM IBD PATIENTS

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Introduction: The new biological vedolizumab (anti-a4b7) blocks the migration of leukocytes from the vasculature into the gut. It leads to sustained steroid-free remission in about 30% of Crohn's disease (CD) and ulcerative colitis (UC) patients. In UC, this remission is reached much faster (47% after 6 weeks) than in CD (15% after 6 weeks), rendering treatment with vedolizumab much more cost-efficient in UC than in CD[1]. Deeper insight into the immunological effects of vedolizumab is necessary to explain differences between the mechanistic impact of vedolizumab therapy in CD and UC.
Aims and Methods: The aim of this study was to determine the binding capacity of vedolizumab to both immune cells in blood and to isolated mucosal cells from the inflamed ileal and colonic mucosa. We collected peripheral blood and intestinal biopsies from patients with CD and UC prior to vedolizumab treatment, and peripheral blood from healthy controls. Intestinal biopsies were dissociated into cell suspensions from the epithelial layer and lamina propria separately. We engineered fluorescent-labeled vedolizumab and assessed the percentage of vedolizumab-bound cells as well as the level of vedolizumab binding per cell type, using flow cytometry.
Results: Vedolizumab binds a large variety peripheral blood immune cells (*i.e.* $CD4^+$T cells, $CD8^+$ T cells, B cells, eosinophils, NK cells and monocytes). Vedolizumab binds nearly all eosinophils (median 91% [IQR 83–94]) and gut mucosa directed $CD4^+CD38^+CD62L^{neg}$ T cells[2] (median 82% [IQR 68–91]), at high levels. Vedolizumab also binds the majority of B cells (median 84% [IQR 75–92]), $CD8^+$ T cells (median 70% [IQR 60–80]) and $CD4^+$ T cells (median 55% [IQR 48–61]), at intermediate levels. Vedolizumab binds to 37% (IQR 21–50) of NK cells and to only 5% (IQR 2%-10%) of monocytes, at intermediate levels. The highest level of binding was observed on the gut directed $CD4^+CD38^+CD62L^{neg}$ T cells, which was significantly higher than on $CD4^+$ T cells, $CD8^+$ T cells and B cells ($P < 0.0001$). Before vedolizumab treatment, no significant differences in percentage of vedolizumab-bound cells or levels of vedolizumab binding were observed between patients with CD, UC, and similar to healthy controls.
Within the intestinal mucosa, vedolizumab preferably binds lamina propria cells, at moderate levels, and in particular $CD8^+$ T cells from the terminal ileum (median 64% [IQR 28–94]). These lamina propria $CD8^+$ T cells from the terminal ileum also showed the highest levels of vedolizumab binding.
Conclusion: Vedolizumab binds to a large variety of immune cells in both peripheral blood and intestinal mucosa. Indeed, the highest level of binding was observed on a specific subset of gut directed $CD4^+$ T cells. Pretreatment percentages of vedolizumab-bound cells or levels of vedolizumab binding do not explain differences between mechanistic impact of vedolizumab therapy in CD and UC. These results provide baseline data for correlating vedolizumab binding capacities to clinical response in IBD patients.
Disclosure: Nothing to disclose

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P1607 SYSTEMIC CYTOMEGALOVIRUS INFECTION IS A RELEVANT FACTOR AFFECTING SHORT AND LONG-TERM OUTCOMES OF PATIENTS WITH ACUTE SEVERE ULCERATIVE COLITIS: AN 11-YEAR EXPERIENCE

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Introduction: Acute severe ulcerative colitis (ASUC) remains a life-threatening condition. Short and long-term clinical outcomes are still highly variable despite the widespread use of Oxford protocol and the current availability of infliximab (IFX) or cyclosporine (CyA) as rescue therapies. We aimed to report our single-center experience on clinical outcomes of patients with ASUC and the factors affecting its course.
Aims and Methods: We retrospectively collected data from 202 consecutive hospital admissions (106 patients) for ASUC from January 2006 to July 2017. The response to intravenous steroids and rescue therapy, and the occurrence of toxic megacolon (TM) were assessed as short-term outcomes, whereas long-term outcomes included remission after one year from the episode of ASUC and colectomy free-survival along the entire follow-up.
Results: The overall response rates to intravenous steroids and rescue therapy were 47.5% and 91.8% (IFX: 74/79, 93.7%; CyA: 16/19, 78.9%), respectively, while TM occurred in 24 cases (11.9%). After one year from the episode of ASUC, only 25.4% of patients were in continuous clinical remission. After a median follow-up of 37 months (IQR 9.25–98 months), 28 patients (26.4%) underwent colectomy. Colectomy-free survival rates at 3 months and 1 year were, respectively, 82.1% and 77.4%. At multiple mixed-effect regression analysis, systemic CMV infection (defined by blood positivity for CMV-DNA or pp65 antigenemia) was an independent predictor of nonresponse to IFX rescue therapy (OR 0.12, CI 0.02–0.78, $p = 0.031$), occurrence of TM (OR 4.21, CI 1.35–13.12, $p = 0.013$), and colectomy (OR 4.56, CI 1.41–14.55, $p = 0.010$), together with TM (OR 4.77, CI 1.70–13.35, $p = 0.003$). Semi-parametric survival Cox analysis confirmed systemic CMV infection (HR 3.54, CI 1.47–8.51, $p = 0.005$) and TM (HR 3.00, CI 1.35–6.65, $p = 0.007$) as independent risk factors for colectomy.
Conclusion: Detection of CMV in blood – but not on rectal biopsies – is an independent risk factor affecting the main clinical outcomes of patients with ASUC.
Disclosure: Nothing to disclose

P1608 HIGH ANTI-TNF DRUGS TROUGH LEVELS ARE NOT ASSOCIATED WITH THE OCCURRENCE OF ADVERSE EVENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: In Inflammatory Bowel Disease (IBD) patients treated with anti-tumour necrosis factor (TNF) drugs there is approximately 40% per year likelihood of experiencing secondary loss of response (LOR). In these patients, an increase of the dose of the drug is often carried out in order to restore disease response, and as a fact, higher drug trough levels (TL) are associated with a better disease outcome and a lower likelihood of LOR. However, there are no data concerning drug TL and adverse events (AEs).
Aims and Methods: To evaluate the possible association between drug TL and AEs in IBD patients treated with adalimumab (ADA) and infliximab (IFX).
We included in this analysis 113 patients (65 males, 86 Crohn's Disease, 27 Ulcerative Colitis) treated with IFX (50, 44%) or ADA (63 56%). Twenty-seven patients (24%) were in combo therapy with an immunomodulatory drug. We considered the TL only if it was concomitant (*plus/minus* 1 week) to the occurrence of the AE. TL were measured using a homogeneous mobility shift assay (Prometheus Laboratories, San Diego, United States).
Results: During a median follow up of 16 months (range, 1–144) we observed 103 AEs, mainly infections (n = 81, 79%), followed by dermatologic reactions

(n = 13, 13%). TL were available during 88 AEs (85%): 61 samples from patients in monotherapy and 27 from those in combo-. There was no statistical difference in median TL at the time of AEs occurrence in patients in combo- *vs.* monotherapy (6.9 mcg/mL [range 0.0–20.3 mcg/mL] *vs.* 6.2 mcg/mL [range 0.0–36.2 mcg/mL, $P = 0.42$). Moreover, considering a cut off of 7 mcg/mL for IFX TL ($P = 0.57$) and 5 mcg/mL for ADA TL ($P = 0.75$), we observed no statistical difference in terms of AE occurrence. Moreover, even considering a higher cut off of 15 mcg/mL for IFX TL and 10 mcg/mL for ADA TL, we still did not observe any statistically significant difference in terms of occurrence of AEs experience.

Conclusion: IBD patients with higher anti-TNF TL do not seem have a greater risk of occurrence of AEs as compared to patients with lower TL, independently of mono or combo therapy. Physicians' decision to increase anti-TNF dosage should be based on clinical evaluation and should not be influenced by concerns regarding the potential for AEs occurrence.

Disclosure: Nothing to disclose

P1609 EFFECTIVENESS AND SAFETY OF USTEKINUMAB 90 MG EVERY FOUR WEEKS IN CROHN'S DISEASE

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Introduction: The most commonly drug regimen for ustekinumab in Crohn's disease (CD) is 90 mg every 8 weeks. Some patients will partially respond to ustekinumab or will experience a secondary loss of response. These patients might benefit from shortening the interval between injections. The efficacy and safety of ustekinumab 90 mg every 4 weeks (90mg q4W) is unknown.

Aims and Methods: All patients with active CD, as defined by CDAI > 150 and one objective sign of inflammation (CRP > 5 mg/L and/or fecal calprotectin > 250 ug/g and/or radiologic and/or endoscopic evidence of disease activity) who required ustekinumab dose escalation to 90mg q4W for loss of response or inadequate response to ustekinumab 90mg q8W were included in this retrospective multicentre cohort study.

Results: Sixty-nine patients, with a median age of 33 years (interquartile range (IQR), 27–42) and median disease duration of 11 years (IQR, 7–16) were included. Optimization was performed after a median of 5.4 months (IQR, 3.2–7.8) of ustekinumab treatment initiation. Ustekinumab was associated with corticosteroids and immunosuppressants in respectively 36% (n = 25/69) and 33% (n = 23/69) of cases. Clinical response was observed in 68% (n = 41/69) after a median of 2.1 months (IQR, 1.0–3.0). Among the 23 patients with colonoscopy during follow-up, 9 had mucosal healing. At the end of follow-up (median 6.8 months (IQR, 3.7–10.8), 45% (n = 31) were still treated with ustekinumab, 22% (n = 15) were hospitalized, and 15% (n = 10) underwent surgery. Adverse events were reported in 10% (n = 7) of patients, including two serious adverse events (pneumonitis, infectious colitis). In multivariate analysis, colonic location (L2) (Hazard Ratio (HR), 4.6 (95%CI, 1.8–8.4); p = 0.047), inflammatory behavior (B1) (HR, 9.1 (95CI%, 1.2–16.5); p = 0.015) and duration of ustekinumab therapy before optimization (HR, 3.2 (95%CI, 1.2–5.4); p = 0.043) were associated with clinical response at 2 months.

Conclusion: This is the first study that evaluates the efficacy and safety of ustekinumab optimization 90mg q4W in CD. Two-thirds of patients recaptured response following treatment optimization. Colonic location, inflammatory behavior and duration of ustekinumab therapy before optimization were associated with clinical response at 2 months

Disclosure: MF: lecture fees, advisory bord for Janssen

P1610 RADIOLOGICAL OUTCOMES IN PERIANAL FISTULISING CROHN'S DISEASE TREATED WITH ANTI-TNFA THERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Management of perianal fistulising Crohn's Disease (pfCD) remains a significant challenge. While the advent of biological agents has led to improvement in clinical outcomes, their effect on MRI endpoints is less well-established. This is despite MRI being a more accurate measure of treatment success, given the possibility of persistence of fistula tracts despite clinical improvement (1).

Aims and Methods: We performed a systematic review to assess rates of fistula improvement on MRI pelvis, following biological therapy. Online databases MEDLINE, EMBASE and Cochrane were searched until February 2018, for randomised controlled trials, cohort and case control studies that reported on MRI outcomes following biological therapy in the adult population (2). 8 papers met this criterion, all of which administered an anti-TNFa (Infliximab or Adalimumab) as the biologic. All 8 papers examined clinical outcomes, with heterogeneity in endpoints. 7 defined remission as closure of all baseline draining fistulas and "response" as ≥50% reduction; 2 of these studies required this at a single time point and 6 across two consecutive visits. One study defined clinician-reported decrease in fistula drainage as "response". Radiologically, "healing" was defined as disappearance of tracts on T2-weighted sequences. Degree of radiological improvement was assessed in 4 papers, defined as decrease in T2-hyperintensity (2 papers), decrease in number of tracts/collections (1 paper), or decrease in number or volume (≥10%) of tracts/collections (1 paper). Endpoints ≤12 weeks post treatment commencement were considered short-term, and those >12 weeks long-term.

Results: Of 208 unique papers identified in the search, 8 met the inclusion criteria, with a total sample size of 233. 67 patients received a post-treatment MRI ≤12 weeks of induction therapy. 6/67 (9%) achieved radiological healing of the underlying fistula tract, 11/22 (50%) had improvement and 9/22 (41%) had no improvement. 146 patients underwent MRI >12 weeks post induction. 33/146 (23%) achieved healing, 20/45 (44%) had improvement and 15/45 (33%) had no improvement. The odds ratios of MRI healing compared to clinical was 0.14 (95% CI, 0.03–0.54) in the short-term and 0.34 (95% CI, 0.21- 0.58) in the long-term, demonstrating the relative infrequency of radiological healing.

Van Assche score findings varied, with some reporting significant differences between clinical responders and non-responders (3–5), and pre- and post-treatment (6), while others reported no significant difference (7).

Conclusion: There are discrepancies between clinical and MRI outcomes in pfCD, following biological treatment. Lack of consensus on the definition of MRI improvement, or a universally accepted grading system, has led to variability of endpoints assessed and heterogeneity in reported rates of improvement. Further studies assessing recurrence rates in patients who do achieve healing, and variables which prognosticate for radiological healing, will aid management of pfCD.

Disclosure: Nothing to disclose

Abstract No: P1610

Table 1: Clinical and Radiological Outcomes

Study	Number of pf CD patients	Induction with anti-TNFα	Maintenance with anti-TNFα	Short-term clinical remission	Long-term clinical remission	Short term MRI healing	Long term MRI healing	Short-term Odds Ratio	Long-term Odds Ratio
Bell et al	7	7	–	4/7 (57%)	–	2/7 (29%)	–	0.3 (0.03–2.76)	–
Van Assche et al (Part 1)	8	8	–	4/8 (50%)	–	0/8 (0%)	–	0.06 (0.00- 1.36)	–
Van Assche et al (Part 2)	7	7	7	4/7 (57%)	–	0/7 (0%)	2/6 (33%)	–	–
Tougeron et al	26	26	16	13/26 (50%)	11/16 (69%)	–	2/14 (14%)	–	0.08 (0.01–0.47)
Savoye-Collet et al	20	20	20	–	7/20 (35%)	–	2/20 (10%)	–	0.21 (0.04–1.16)
Karmiris et al	59	59	–	–	24/59 (41%)	3/29 (10%)	5/38 (12%)	–	0.22 (0.08–0.65)
Horsthuis et al	16	16	–	6/16 (38%)	–	1/16 (6%)	–	0.11 (0.01–1.07)	–
Tozer et al	41	41	41	–	4/19 (21%)	–	6/19 (32%)	–	1.73 (0.40–7.51)
Thomassin et al	49	–	49	–	26/49 (53%)	–	16/49 (33%)	–	0.43 (0.19–0.97)
Totals	233	184	192	31/64 (48%)	72/163 (44%)	6/67 (9%)	33/146 (23%)	0.14 (0.03–0.54)	0.34 (0.21- 0.58)

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P1611 GOLIMUMAB IMPROVES PATIENT-REPORTED WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH ULCERATIVE COLITIS: INTERIM RESULTS FROM A NON-INTERVENTIONAL TRIAL IN GERMANY

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Introduction: No prospective data evaluating work productivity and activity in real world practice are available in patients with moderate to severe ulcerative colitis (UC) treated with Golimumab (GLM) for more than 3 months. The aim of this study is to assess the change of work productivity, activity and quality of life (QoL) in UC patients treated with GLM for 1 year in an observational real-world setting in Germany.

Aims and Methods: The validated WPAI-questionnaire (**W**ork **P**roductivity **A**ctivity **I**mpairment Questionnaire) was used for the primary analysis. The change of work productivity and ability for daily activities at 3 months and 12 months versus baseline visit was evaluated.

The 4 subscores of WPAI were assessed: disease-related absence from work (absenteeism), working while sick (presenteeism), total work productivity impairment (TWPI) and activity impairment. TWPI was the primary endpoint. To assess disease-specific quality of life the IBDQ (**I**nflammatory **B**owel **D**isease **Q**uestionnaire) was used. Analysis population included all treated pts (N = 287) and patients who completed the WPAI and were employed at baseline (N = 203).

Results: 287 UC patients were included in the study. At baseline, 61% had moderate UC, 18% had severe UC by global physician's assessment. Slightly less than half of the population were male (48%). 75% of the subjects were either employed full-time or part-time. 269 patients completed the WPAI and 203 were analyzed for the primary efficacy endpoint, as these were employed at baseline.

12 months after start of treatment all WPAI subscores showed significant improvements compared to baseline. Similarly significant improvements were detected in the IBDQ.

	Change from BL Mo 3(%)	Change from BL Mo 12 (%)
WPAI		
TWPI [mean ± SD]	−16.6 ± 32.1 (N = 99)*	−20.2 ± 29.2 (N = 53)*
Absenteeism [mean ± SD]	−−14.9 ± 38.6 (N = 132)*	−20.1 ± 41.4 (N = 77)*
Presenteeism [mean ± SD]	−14.1 ± 28.6 (N = 100)*	−19.3 ± 28.2 (N = 56)*
Activity impairment [mean ± SD]	−13.5 ± 28.2 (N = 149)*	−25.9 ± 29.5 (N = 92)*
	Change from BL Mo 3	Change from BL Mo 12
IBDQ	26.0 ± 35.7 (N = 191)*	41.2 ± 38.7 (N = 121)*

*[*comparison vs baseline: $p < 0.001$]*

Conclusion: GLM treatment results in significant improvement of work productivity and daily activities in patients with UC up to 12 months after start of treatment. Patients also experience a significant improvement in their QoL in terms of IBDQ.

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P1612 DRUG-INDUCED TOXICITY AND IMMUNE-INFLAMMATORY DISORDERS OF HEPATO-PANCREATO-BILIARY SYSTEM IN IBD PATIENTS: A DIAGNOSTIC CHALLENGE

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Introduction: Drug-induced toxicity by commonly used therapeutics, aminosalicylates (ASA) and azathioprine (AZA), in patients with inflammatory bowel disease (IBD) have been described in a literature, with AZA-induced pancreatitis occurring more frequently in IBD patients than in other AZA-treated patients. IBD are also often accompanied by extraintestinal immune-inflammatory diseases, frequently involving hepato-pancreato-biliary system.

Aims and Methods: To investigate frequency and clinical presentation of drug-induced toxicity and its association with extraintestinal diseases in IBD patients treated with common therapeutic protocols.

Patients with verified IBD (endoscopy and histopathology) were included in the retrospective study. For each subject we collected general and anamnestic data, laboratory and other diagnostic findings, data regarding application of therapeutic protocols, clinical response to applied therapy and the presence of extraintestinal immune-mediated diseases, drug-induced toxicity and disease complications. Drug-induced toxicity was confirmed empirically (symptom withdrawal after drug cancellation).

Results: Out of 258 IBD patients (male 55%, female 45%, mean age 40.8 yrs), 51.6% had ulcerative colitis and 48.4% had Crohn's disease. Extraintestinal and/or concomitant autoimmune disease was present in 21.3% of IBD patients. Drug-induced toxicity occurred in 16.3% IBD patients, AZA-induced more frequently than ASA-induced (69% and 31%). The incidence of AZA-induced toxicity was 18%, while ASA-induced toxicity was 5%. Drug-induced toxicity manifested as hepato-pancreato-biliary disorders in 21/42 patients (50%), including: toxic pancreatitis (43%), more frequently AZA-induced than ASA-induced (66.7% vs. 33.3%, $p < 0.05$) and toxic hepatitis (7%) presented only in ASA treated patients. The incidence of toxic pancreatitis was 7.3% among AZA treated IBD patients. The second most frequent drug-induced toxicity were hematologic disorders (11/42, 26%), which were all AZA-induced, with the incidence of 6.7% in IBD patients. Patients with extraintestinal disease and/or concomitant autoimmune disease more often developed drug-induced toxicity ($p < 0.05$).

Conclusion: Suspicion of drug-induced toxicity in IBD patients requires multidisciplinary diagnostic approach in order to differentiate drug-induced toxicity from immune-inflammatory extraintestinal manifestations, especially when they are presented as hepato-pancreato-biliary disorders.

Disclosure: Nothing to disclose

P1613 EFFICACY AND SAFETY OF BIOSYMILAR INFLIXIMAB CT-P13 IN PATIENTS WITH CROHN'S DISEASE WHO WERE NAïVE TO ANTI-TNF THERAPY: PRELIMINARY RESULTS FROM POLIBD STUDY

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Introduction: CT-P13 biosimilar monoclonal antibody to infliximab (IFX) approved for the same indications as its IFX counterpart in Poland.

Aims and Methods: The purpose of the study was to evaluate the efficacy and safety of biosimilar infliximab in Crohn's disease (CD) in patients from Subcarpathian Region (South- Eastern Poland). 93 patients with CD naïve to anti-TNF therapy were enrolled (30 females/63 males); aged from 18 to 69 years, treated with CT-P13 in the Department of Gastroenterology between years 2010 and 2017. 7 (7.5%), 43 (46.2%) and another 43 (46.2%) of patients had ileal, ileo-colonic and colonic CD respectively. All patients received standard immunosuppression with no additional steroid nor antibiotic therapy.

Results: In 56% of the patients clinical remission was achieved (CDAI score < 150). Response to treatment (CDAI score reduction of ≥70 points) was noticed in 31% patients, and 13% patients worsen. Secondary loss of treatment in 5 patients (5.4%) was observed. Among those with ileal CD, clinical remission

was achieved in 3 patients (43%), 2 patients responded to the therapy (28.5%) and another 2 patients did not respond. Among those with colonic CD, clinical remission was achieved in 25 patients (58%), 13 responded to the therapy (30%) and 5 patients did not respond (12%) Among those with ileo-colonic CD, clinical remission was achieved in 24 patients (56%), 14 responded to the therapy (32.5%) and 5 patients did not respond (11.5%).
11 out of 70 patients (12%) had adverse events (AEs); 8 of them (8.5%) had serious adverse events (SAEs) that forced the withdrawal of treatment: sepsis (1 patient 1%), allergic reactions (6 patients 6.5%), peritonsilar abscess (1 patient 1%) Other AEs were perianal abscess (3 patients 3.2%).
Conclusion: In analyzed population, biosymilar IFX CT-P13 seems to be effective and safe in patients with CD who are naïve to anti-TNF therapy.
References: not applied
Disclosure: nothing to diclosure

P1614 DE-ESCALATING THERAPY IN PATIENTS WITH CROHN'S DISEASE RECEIVING ADALIMUMAB: A SUBGROUP ANALYSIS OF THE CALM STUDY

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Introduction: This analysis evaluated the impact of de-escalating therapy on mucosal healing 48 weeks (wks) after randomisation in patients with Crohn's disease (CD) in the CALM study.
Aims and Methods: In CALM, adult patients with moderate to severe CD naïve to immunomodulators and biologics were randomized 1:1 to a tight control (TC) or clinical management (CM) group after ≤ 8 wks of prednisone therapy. Treatment was escalated from no treatment to ADA induction+40 mg every other wk (EOW) to 40 mg ADA every wk (EW) to 40 mg ADA EW+2.5 mg/kg azathioprine (AZA)/day at 12, 24, and 36 wks after randomisation based on specific failure criteria (CD Activity Index [CDAI] ≥200 or decrease < 70 points (1 wk prior to randomisation) or < 100 points compared with baseline (at wk 11, 23, 35) and prednisone use for the CM group, and CDAI ≥150, C-reactive protein ≥5 mg/L, faecal calprotectin ≥250 µg/g, and prednisone use for the TC group). At 24 and 36 wks, if failure criteria were not met, patients de-escalated ADA EW dose to 40 mg ADA EOW. Patients would re-escalate to 40 mg ADA EW if the failure criteria were met at the following visit. In this subgroup analysis, the primary endpoint (mucosal healing [CD Endoscopic Index of Severity < 4] and no deep ulcers at 48 wks after randomisation) was evaluated in patients who de-escalated treatment. Analyses were performed in patients who completed the study and did not move to rescue therapy. Non-responder imputation was used for missing data.
Results: 15 patients in the CM group and 31 patients in the TC group de-escalated treatment during the study (CM, n = 15 from 40 mg ADA EW to 40 mg ADA EOW; TC, n = 21 from 40 mg ADA EW to 40 mg ADA EOW; TC, n = 10 from 40 mg ADA EW+2.5 mg/kg AZA/day to 40 mg ADA EOW+2.5 mg/kg AZA/day). Of those, 2 patients in the CM group and 8 patients in the TC group re-escalated to 40 mg ADA EW. Overall, 54% (7/13) of patients in the CM group and 61% (14/23) of patients in the TC group who de-escalated to 40 mg ADA EOW ± AZA achieved the primary endpoint (Table). Of the patients who re-escalated to ADA EW, 0% in the CM group, and 75% (6/8) in the TC group achieved the primary endpoint (Table). The overall adverse event rates in CALM have been previously reported.[1]
Conclusion: Our data suggest that repeated dose optimization (ADA de-escalation and re-escalation) based on tight control is a more refined approach resulting in mucosal healing compared with CM. Larger data sets are needed to confirm our observation on repeated dose optimization.

	CM n/N (%)	TC n/N (%)
De-escalated and remain de-escalated		
40 mg ADA EW to ADA EOW	7/13 (53.8)	7/13 (53.8)
40 mg ADA EW +2.5 mg/kg AZA/day to ADA EOW +2.5 mg/kg AZA/day	0	7/10 (70.0)
Re-escalated		
40 mg ADA EW to ADA EOW to ADA EW	0/2	6/8 (75.0)
*mITT, patients who completed the study and did not move to rescue therapy, NRI analysis		

[Proportion of patients with CDEIS < 4 and no deep ulcers at 48 weeks in patients who de-escalated and/or re-escalated treatment]*

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P1615 ATTITUDES TOWARDS TREATMENT WITHDRAWAL IN IBD

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Introduction: A recently published ECCO topical review on exit strategies in inflammatory bowel disease (IBD) has underlined the role of treatment withdrawal in selected cohorts with stable disease. As the disease course in IBD varies greatly, certain patients may well be over-treated with immunosuppressive agents. Identifying which patients can safely stop their treatment remains a challenge. Little is known regarding patients' own attitudes towards stopping long-term immunosuppressive treatment.
Aims and Methods: We invited patients undergoing immunosuppressive therapy, attending either out-patients or the infusion suite, during a 6-week period in March-April 2018, to participate in this prospective observational study. Participants were asked a series of questions regarding their disease and treatment history, compliance with treatment, awareness of risks of immunosuppression, concerns regarding long term treatment, concerns regarding treatment withdrawal and willingness to switch to generic medication.
Results: In total, 151 (female = 77, 51%) patients participated. The mean age was 41.5 years, with a range of 19–82 years. The majority of patients had a diagnosis of Crohn's disease (n = 117, 77%). The mean duration of disease was 12.2 years, with a range of 0.5–46 years. The breakdown of current treatments was as follows: 28% Adalimumab, 26% Infliximab, 22% combination therapy, 14% Imumunomodulator, 4% Ustekinumab, 4% Vedolizumab, 1% Golimumab, 1% Certolizumab. The mean duration of therapy was 4.67 years, with a range of 0.5–18 years. At least one course of glucocorticoids had been taken by 35% (n = 43) in the previous 12 months. Amongst the cohort there were 32 active smokers (21%) and 52 (34%) former smokers. Missed doses were reported most frequently for oral medications (80% IMM) and subcutaneous injections (78%). There were less missed doses in the intravenous treatment group (35%). Overall for the group the mean HBI was 6.3, with a range of 1–26, and the mean partial Mayo score was 1. There was very good awareness of the effect of therapy on the immune system (n = 147, 97%), with 100 (65%) expressing concern regarding same. There was general acceptance of life-long therapy (n = 115, 77%), however many (n = 91, 60%) would be happy to stop treatment if advised so by their Physician, particularly if the decision were based on suboptimal drug levels (n = 142, 93%). In terms of switching to a biosimilar drug, the majority (n = 111, 73%) had no objection. The main concerns expressed regarding treatment withdrawal included the risk of relapse (68%), loss of response (16%) or none (16%).
Conclusion: There is a good understanding amongst patients regarding the risks of long-term immunosuppression. Despite a long duration of disease and treatment, patients would be willing to stop immunosuppressive therapy if advised to do so. Objective measures such as drug levels may provide one tool to guide treatment withdrawal in patients with suboptimal levels. The main concern for patients when considering treatment withdrawal is the risk of future relapse.
Disclosure: Nothing to disclose

Reference

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P1616 CLINICAL TRIAL: HIGH-DOSE VITAMIN D TREATMENT TO CROHN'S DISEASE PATIENTS WITH DISEASE ACTIVITY, A RANDOMIZED PLACEBO-CONTROLLED DOUBLE-BLINDED STUDY (MIRVIDIC)

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Introduction: Vitamin D treatment may reduce the risk of disease activity in Crohn's disease (CD) [1]. Longitudinal studies have shown that vitamin D levels above 75 nmol/l are associated with reduced disease activity score, need for hospitalisation and surgery [2]. Yet it is unknown if CD patients with disease activity would benefit from high-dose vitamin D treatment and if it is well tolerated.

Aims and Methods: To investigate whether high-dose vitamin D treatment alone or combined with infliximab induction treatment to patients with active CD decreases inflammation markers and activity score compared to placebo.

Forty CD patients with disease activity were included. Patients were randomized to: 1) infliximab and high dose vitamin D (N = 8), 2) infliximab and placebo vitamin D (N = 8), 3) placebo infliximab and high dose vitamin D (N = 16), 4) placebo infliximab and placebo vitamin D (N = 8). Infliximab was given as 5 mg/kg week 0, 2 and 6 and vitamin D was given as 5 mg bolus week 0 followed by 0.5 mg/day in up to 7 weeks. Patients underwent colonoscopy week 0 and 7 and a Crohn's disease index of severity (CDEIS) score was measured. C-reactive protein (CRP), faecal calprotectin, leucocytes and Harvey Bradshaw Index (HBI) were measured week 0, 2 and 6.

After the 7 weeks of project treatment all patients were treated open with infliximab 5 mg/kg. Therefore during follow up the four groups were assembled into 2 groups: initial vitamin D treatment (group 1 and 3) or initial placebo-vitamin D treatment (group 2 and 4). Mixed model was used to test if the mean curves of the inflammation markers in the four groups were parallel. If the mean curves were not parallel, differences between respectively group 1 and 2 and group 3 and 4 were examined.

Results: During 26 weeks of follow up patients who had received high-dose vitamin D treatment during the project period had significantly less disease activity illustrated by 2.89 times lower calprotectin mean curves compared to placebo vitamin D (95% CI: 1.26–6.67, $p = 0.012$), and 2.19 times lower CRP mean curves compared to placebo vitamin D (95% CI: 1.11–4.32, $p = 0.024$).

During the 7 weeks of project treatment combined infliximab and vitamin D treatment reduced the CDEIS score compared to placebo (group 1 delta median -12.5, group 4 delta median -0.9, p = 0.04). However, single therapy with infliximab (group 2) did not reduce the CDEIS score significantly compared to placebo ($p = 0.11$). During the 7 weeks of project treatment the mean curves of the four groups differed over time regarding CRP ($p = 0.0024$), calprotectin ($p = 0.001$), HBI ($p = 0.045$), and leucocytes ($p = 0.028$). Single treatment with high dose vitamin D (group 3) decreased the leukocytes count compared to placebo (group 4) ($p = 0.039$), but significant differences were not reached regarding CRP, calprotectin and HBI.

Seven weeks of high-dose vitamin D treatment alone and combined with infliximab increased the calcium-ion levels over time compared to placebo-vitamin D treatment ($p = 0.013$) but within normal range of calcium. Phosphate levels were unaffected by treatments.

Conclusion: Patients who initially received high-dose vitamin D treatment had lower calprotectin and CRP levels during 26 weeks of follow up compared to placebo-vitamin D treatment.

Seven weeks of combined infliximab and high-dose vitamin D treatment reduced the CDEIS score compared to placebo. In patients with active CD, high-dose vitamin D treatment is safe and well tolerated and reduces the leukocytes count compared to placebo but not calprotectin and CRP.

Disclosure: Nothing to disclose

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P1617 SECONDARY LOSS OF RESPONSE TO VEDOLIZUMAB: EXPERIENCE FROM A SINGLE UNIVERSITY CENTRE

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Introduction: Vedolizumab (VDZ), a humanised monoclonal anti-$\alpha 4\beta 7$ integrin antibody, is effective for inducting and maintaining remission in both Crohn's disease (CD) and ulcerative colitis (UC). Secondary loss of response (LOR) can occur but there is limited information on its frequency and timing.

Aims and Methods: The aim was to assess the rate and timing of secondary LOR in patients with inflammatory bowel disease (IBD) treated with VDZ in a routine clinical practice at a large single university centre. A retrospective case-note review was undertaken of all patients who had received at least one infusion of VDZ from March 2015 – January 2018. Patients received VDZ 300mg intravenous infusion therapy at 0, 2 and 6 weeks and then 8 weekly for maintenance. Harvey-Bradshaw index (HBI) for CD and Simple Colitis Activity Index (SCAI) for UC were documented at each infusion. Clinical remission was defined as HBI < 5/SCAI < 3 and clinical response as a reduction in HBI/SCAI ≥3. Secondary LOR was defined as response followed by one of: an increase in HBI/SCAI ≥3, loss of clinical remission or treatment alteration required by: worsening of symptoms/radiological/endoscopic findings attributable to IBD. Chi square analysis was used to compare rates of response, LOR and recapture of response between those with CD and UC.

Results: 156 patients (102 CD, 50 UC, 4 IBD-unclassified (IBD-U) received VDZ. Two patients with IBD-U were grouped with CD and 2 with UC based on endoscopic and histological findings. Thirteen patients still in induction were excluded from analysis. 68/143 were on systemic corticosteroids at week 0 (37 CD, 31 UC). 138/143 had previous exposure to tumour necrosis factor (TNF) antagonists, 9 of these had not experienced failure of TNF antagonists. Twenty-one patients (16 CD, 5 UC) were in clinical remission at week 0. 122/143 patients (78 CD, 44 UC) were not in remission on starting VDZ and of these 56/78 (71.8%) patients with CD and 36/44 (81.8%) with UC responded. Of the 113 patients (72 CD, 41 UC) who showed response or were in remission on starting VDZ, secondary LOR occurred in 41/72 (56.9%) patients with CD (median 5 doses; 26 weeks (range 2–102)) and 21/41 (51.2%) patients with UC (median 6 doses; 41 weeks (range 5–98)). LOR occurred between weeks 0 and 16 in 18 (29.0%) patients, weeks 17 and 34 in 19 (30.6%), weeks 35 and 52 in 11 (17.7%) and after week 52 in 14 (22.6%). LOR tended to occur later in patients not on steroids at baseline (median 6 vs 5 doses and 36.5 vs 26.5 weeks). Clinical response was recaptured in 22 (53.7%) patients with CD, median of 1 dose and 8 weeks (range 1–54): 7 (31.8%) had a reduction in the dose interval, 5 (22.7%) received steroids and 10 (45.5%) had no treatment alteration. Clinical response was recaptured in 13 (61.9%) patients with UC, median 2 doses and 14 weeks (range 5–53): 7 (53.8%) had a reduction in the dose interval, 1/13 (7.7%) received steroids, 1 (7.7%) had both and 1 (7.7%) had a reduction in dose interval and azathioprine. There was no significant difference between CD and UC in rates of response, secondary LOR and recapturing of response.

Conclusion: LOR with VDZ occurred in over 50% of patients with IBD, median duration 5–6 doses in both CD and UC. However, clinical response could be recaptured without drug withdrawal in most patients. Early apparent LOR may represent relapse after steroid withdrawal and different mechanisms may be associated with later LOR. Further studies are required to understand mechanisms by which this occurs, including studies of antidrug antibodies.

Disclosure: Lobo AJs conflicts of interest are: speaker fees, advisory board membership or consultancy for Takeda, MSD, Vifor, Shield Therapeutics, Abbvie, Pfizer, Janssen, Medtronic

P1618 VEDOLIZUMAB TROUGH LEVELS DURING AND AFTER INDUCTION CORRELATE WITH CLINICAL AND ENDOSCOPIC OUTCOMES IN INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab is an alpha4beta7 integrin antagonist for the treatment of inflammatory bowel disease (IBD). The role of drug monitoring, based on the assessment of Vedolizumab trough levels (VTL) and anti-Vedolizumab antibodies (AVA) has not been clarified.

Aims and Methods: Consecutive IBD patients who started therapy with Vedolizumab were prospectively enrolled. Clinical activity was evaluated by Harvey Bradshaw Index (HBI) and partial Mayo score (pMayo). Endoscopic assessment was performed at baseline and during follow-up. VTL and AVA were assayed by ELISA (Theradiag) at weeks 6 and 14. Limits of detection for VTL and AVA were 2 ug/ml and 35 ng/ml, respectively. Clinical response was defined as at least 30% reduction of activity scores from baseline and remission was defined as HBI < 5 or pMayo < 2. Mucosal healing was defined as a Mayo score of 0 for ulcerative colitis (UC) and absence of ulcers for Crohn's disease (CD). Endoscopic response was defined as a reduction of at least 1 point of Mayo score for UC and improvement in mucosal inflammation for CD compared to baseline. Statistics was performed by Mann Whitney test, Spearman's rho, ROC curve analysis.

Results: We included 66 patients (mean age 46.1 y; male 61%) with CD (n = 32) and UC(n = 34). 87% of patients were anti TNF-alpha experienced. Baseline median C-reactive protein (CRP) levels was 6.7 mg/dl (cut-off < 5 mg/l). The median follow-up was at 59 week. Follow-up endoscopy was performed in 45 patients after a median of 50 weeks.

Median VTL measured at week 6 were significantly higher in clinical responders as compared to non-responders (41.3 vs 26.9 ug/ml, p = 0.003), and in patients in clinical remission at week 14 (45.9 vs 27.9 ug/ml, p = 0.03) and at week 22 (46 vs 27.6 ug/ml p = 0.009) compared to non-remitters. By ROC curve analysis we identified a cut-off value for VTL of 40,3 ug/ml for clinical response at week 6 (AUC 0.714, sensitivity 52%, specificity 85%, p = 0.0009). For remission at week 14 the identified cut-off was 24.4 ug/ml (AUC 0.682 sensitivity 93%, specificity 40%, p = 0.03) while for remission at week 22 the cut-off was 44.3 ug/ml (AUC

0.722 sensitivity 56%, specificity 82%, p = 0.005). Week 14 VTL were also significantly higher in patients being in clinical remission (20.6 vs 15.1 ug/ml p = 0.009) and also in remitters at week 22 (20.6 vs 15.4 ug/ml, p = 0.01). The cut off of week 14 VTL for week 14 and week 22 remission was 18 ug/ml (AUC 0.729 sensitivity 80% specificity 68%, p = 0.005 for week14; AUC 0.721 sensitivity 80% specificity 69%, p = 0.075 for week 22). Remission and response at later time points were not correlated with earlier VTL. AVA were detected in 1.5% of patients at week 6 and in 3% at week 14 and were not correlated with VTL and clinical response. Week 6 and 14 VTL were not predictive of mucosal healing. However, week 6 VTL were higher in those patients who obtained an endoscopic response (median of responders 40.3 vs 27.2 ug/ml, non-responders, p = 0.037). By ROC curve analysis a cut-off for week 6 VTL of 38.6 ug/ml was detected for week 50 endoscopic response. Week 6 but not week 14 VTL were negatively correlated with CRP levels.
Conclusion: Our data suggest that VTL at week 6 are correlated with early clinical response and remission and with endoscopic response. Week 14 VTL are correlated with clinical remission at week 14 and 22 and the identified cut off is 18 ug/ml. Immunogenicity of Vedolizumab is low in our patients.
Disclosure: Nothing to disclose

P1619 TOLERANCE OF THIOPURINES IN PATIENTS WITH CHRONIC INFLAMMATORY BOWEL DISEASE (IBD)

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Introduction: Thiopurines, represented by azathioprine (AZA) and 6-mercaptopurine (6-MP), are among the first treatments used in inflammatory bowel diseases (IBD). Their therapeutic effectiveness is perfectly established with, in particular, a major role of corticosteroid savings and a maintenance of the effect over time. However, nearly 20% of patients cease taking thiopurines because of its side effects.
Aims and Methods: The objective of this study is to evaluate the frequence of adverse effects of azathioprine (AZA) and 6-mercaptopurine (6-MP) in patients with IBD.
This is a retrospective and descriptive study conducted in the gastroenterology department of our hospital including 100 patients with chronic inflammatory bowel disease (IBD) treated with thiopurines (AZA or 6-mercaptopurine). The inclusion criteria are: age > 16 years, with a follow-up period of 3 months after the initiation of treatment.
Results: One hundred (100) patients with IBD were included, 64 patients (64%) had Crohn's disease. 24 (24%) ulcerative ulcerative colitis. And 12 (12%) indeterminate colitis. The average age was 36 years old [16–76]. The sex ratio M / F was 0.8, with an average duration of follow-up after the beginning of immunosuppressive treatment of 19 months [3–48]. 52 patients were on 6 mecartopurine and 48 were on azathioprine. The main indications for the prescription of thiopurines in Crohn's disease were: maintenance treatment after a first flush requiring corticosteroid therapy in 32% of cases, after severe acute colitis in 8.1%, postoperatively in 21.6%% of cases, ano-perineal lesions in 16% of cases, upper gastrointestinal tract involvement in 8.1% of cases, and corticodependence in 13.5% of cases. In ulcerative colitis the main indications were: treatment maintenance after severe acute colitis, inefficacy of 5-ASA, corticodependence with respectively: 50%, 33% and 16% of cases. Complete clinical and biological remission at 3 months was obtained in 65% of cases (65 patients). 32 patients experienced side effects with thiopurines (32%) occurring beyond six months of treatment in 45% of cases, they were mainly hematologic in 47.05% of cases (26% lymphopenia and 21% anemia), liver abnormalities in 41.16% of cases, and acute pancreatitis in 5.8% of cases. The occurrence of adverse effects resulted in discontinuation of treatment in 11% of cases
Conclusion: Our study has objectified a remission rate of 65%, which proves that the thiopurines still keep their place in the treatment of IBD at the same level of anti- TNF especially in our contexts.
Disclosure: Nothing to disclose

P1620 A MULTICENTER RANDOMIZED PROSPECTIVE STUDY ASSESSING THE EFFICACY OF SINERGIN IN INDUCTION AND MAINTAINING REMISSION IN MILD-MODERATE IBD

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Introduction: The role of the gut microbiota, in addition to genetic factors, in the inititation and perpetuation of inflammatory processes is well established. There are studies that showed that the association between oligo-fructose and inulin (OF-IN) has the ability to modulate not only the composition of the intestinal microbiota but also its activity in a beneficial way, increasing the butyrate concentrations, which exhibits immunomodulatory and anti-inflammatory properties.
Aims and Methods: The main purpose of this multicentric prospective study was to highlight the anti-inflammatory effect of OF-IN (Sinergin) in patients with mild and moderate forms of active IBD. The patients were randomized into 2 groups as follows: group 1 received conventional therapy associated with 10 g/day of Sinergin and group 2 received only conventional therapy.
Clinical manifestations, CRP, faecal calprotectin were assesed in each patient at entry and at 3, 6, 11 months or in case of a flare. Colonoscopy was performed only when considered necessary.
Results: 82 eligible patients entered the prospective study (April 2017-March 2018) from which 8 of them abandoned the trial before the first control visit (3 months), one was excluded due to pregnancy and another due to severe flare, so a total of 72 patients were assessed. The studied group was divided almost even (37 patients without Sinergin vs 35 patients with Sinergin). There are 10 patients that underwent 6 months evaluation (4 with sinergin and 6 without). 25 patients underwent the 3 months evaluation (10 in group 1 and 15 in group 2). At 3 months there is no significant difference between the calprotectine drop down percentage from group 1 and 2 (36% vs 35%), but at the 6 months assessment we found a difference of 5% (45% vs 40%)(p < .05).
Conclusion: Group 1 (with OF-IN) maintained constant values of fecal calprotectin at 3, 6 months and registered a general decrease in CRP values
Group 2 (without OF-IN) has heterogenous results at 3,6 month-evaluation
The complex of oligofructose and inulin plays an important role on the long term in preventing high inflammatory flares in IBD.
Disclosure: Nothing to disclose

P1621 HIGHER ADALIMUMAB LEVELS DURING MAINTENANCE TREATMENT FOR CROHN'S ARE ASSOCIATED WITH DEEP REMISSION: RESULTS FROM A LARGE PROSPECTIVE CROSS-SECTIONAL COHORT

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Introduction: Adalimumab (ADA) is a well-established treatment for Crohn's disease (CD). Despite this limited data are available regarding the relationship of serum ADA levels, and antibodies to ADA (ATA) with clinical outcomes.
Aims and Methods: We performed a prospective cross-sectional study to investigate the association of serum ADA levels with deep remission (HBI < 5, CRP < 5mg/L and faecal calprotectin ≤200mcg/g). Inclusion criteria were a diagnosis of CD and minimum of 12 weeks therapy. Patients were written to in advance of their next clinic visit and advised to omit their ADA dose if due within 48 h from their appointment. Harvey Bradshaw Index (HBI), serum ADA levels / ATA, CRP and faecal calprotectin (FC) were simultaneously collected at clinic. Biochemical remission was defined as FC < 200 μg/g in addition to CRP < 5 mg/l.
Results: At the time of drug level testing, 259 patients were on ADA maintenance therapy. A total of 195 samples were available for analysis from 178 patients; matched HBI, FC and CRP were available for 171 patients. Median duration of ADA therapy was 2.4 years (IQR 1.2–4.3) with 37/178 (20.8%) patients receiving concomitant immunosuppression. Median ADA levels were higher in patients receiving weekly (n = 55) (14.0 μg/ml, 8.0–17.4) vs. fortnightly dosing (n = 123) (11.0 μg/ml, 7.0–14.5, p = 0.0095). 29/178 (16.3%) patients were positive for ATA. A clear negative correlation was observed between ADA levels and ATA (Spearman's r = −0.567, p < 0.0001). Median ADA levels were 11.4 μg/ml (8.0–15.0), 5.0 μg/ml (4.0–6-6) and 1.0 μg/ml (0.8–2.0) at ATA of < 10 AU/ml, 10–50 AU/ml and > 50 AU/ml, respectively (p < 0.0001). Patients in biochemical remission (n = 81/171; 47.4%) had significantly higher ADA levels (12.0 μg/ml, 10.0–15.7) than those with active disease (8.0 μg/ml, 4.8–12.5, p < 0.0001). ROC analysis revealed a positive correlation between ADA levels and biochemical remission [AUC (95% CI) 0.71 (0.63–0.79), p < 0.0001]. An optimum ADA level of > 8.8 μg/ml was identified for predicting biochemical remission (82.7% sens, 55.6% spec, positive LR 1.86). ADA levels but not ATA independently predicted biochemical remission in a multivariate logistic regression model.
Conclusion: Higher ADA levels were independently associated with biochemical remission; levels of > 8.8 μg/ml, higher than previously suggested, might be an appropriate target in the maintenance treatment of CD.
Disclosure: Speaker fees / travel support from Abbvie.

P1622 INFLAMMATORY BOWEL DISEASE MANAGEMENT AND SEXUAL HEALTH ISSUES – DO EXPERTS IN THIS FIELD ADDRESS SEXUAL PROBLEMS IN ROUTINE PATIENT TREATMENT YET ? RESULTS OF THE IGLS-VIENNA-SEXMED-SURVEY ON EXPERTS IN IBD, BAD ISCHL, SEPTEMBER 2017

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Introduction: Sexual health is part of the holistic WHO-concept of health. The World Health Association, WAS, defined in §7 "the right to the highest attainable standard of health, including sexual health". Thus, sexual health as well as dysfunction have to be respected and integrated in patients' treatment and disease management programs. Inflammatory bowel disease patients' quality of life is compromised including social engagement, sexual health, intimacy as well as fertility and reproduction caused by medication's side-effects, surgical procedures, reduced control of body function (enterostoma). Therefore, medical doctors were asked whether these aspects are integrated in routine medical treatment by addressing the topic in disease-management.
Aims and Methods: A 3-part questionnaire on health professionals' patient-treatment, health care structures as well as professional profile was distributed at the annual Austrian Crohn and Colitis symposium, Bad Ischl, September 2017. 50 of 190 congress-participants returned the questionnaire (26.3%).
Results: 58% of the health professionals addressed in up to 20% of the patients sexual health problems. 68% were asked by at most 20% of the patients about sexual issues. 46% of the participants assumed that up to 20% of their patients had troubled sexuality, 32% of the participants in even up to 40% of the patients but left the patients un-asked.
38% of the participants did not offer any help for troubled sexuality, 32% referred the patients to specialists such as internal medicine (70%), urologists (50%), gynecologists (48%), 30% evaluated the impact of medication on sexual dysfunction. 44% of the participants stated that lack of sexual-medicine expertise decreases the success of disease-management.
54% of the participants were male, 40% female. 52% of the participants worked in public hospital. 28% were clinically experience more than 21 years, 26% had between 10 and 20 years of clinical experience.
Conclusion: The participants of this survey were experienced in the field of inflammatory bowel disease. Despite this they did not integrate sexual health issues in routine treatment and disease-management-program so far: in up to 80% of the patients' sexual health including intimacy, fertility and reproduction-issues were left unaddressed and thus not treated. Sexual medicine competence was one of the aspects to increase the likelihood of successful disease management. Sexual medicine therefore may be an emerging field for experts in inflammatory bowel disease to be integrated in the near future.
Disclosure: Nothing to disclose

P1624 MULTIDISCIPLINARY TEAM CARE AT THE EMERGENCY DEPARTMENT CONTRIBUTES TO IMPROVED MANAGEMENT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: A substantial component of disease burden in patients with inflammatory bowel diseases (IBD) is due to frequent emergency department (ED) visits and hospitalizations. We hypothesized that an intervention by a dedicated IBD-nurse accompanied by a multidisciplinary team (MDT) at the ED may improve management and reduce admission rates.
Aims and Methods: We aimed to estimate the impact of proactive MDT care in the ED of a tertiary medical center. IBD-ED visits between November 2017 and April 2018 were identified by the ICD-9-CM codes. IBD patients that were proactively assessed by the MDT (intervention group) were compared to those not approached by the team (standard-ED group). Hospitalizations, exposure to CT scans, and recurrent admission rates within the first 30 days were detected.
Results: A total of 155 IBD patients' visits in the adults ED were identified. Of those, 50 patients (32.2%) were managed by the IBD-nurse and the MDT; average age at index ED visit: 36.1 ± 14.4 years (18–85), M/F 31/19 patients, disease duration 8.3 ± 9.0 years, 37/50 patients had Crohn's disease of whom 10 had a history of perianal involvement. The most common chief complaint (88%) was abdominal pain. Most patients (86%) were either referred by their primary care physician or self-referred. Seventeen patients (34%) underwent CT scan in the ED. MDT management was associated with ED discharge in 28/50 patients (56%). After discharge, most patients (26/28) were shortly followed by a phone call with the IBD-nurse (within 1–7 days), and then seen in the IBD clinic (median 5 [IQR 1–12] days post discharge). Nineteen out of 22 hospitalizations were directly IBD related. Of those, 12 (63.1%) were because of a surgical complication: either an obstruction or an abscess, requiring surgery in 7 patients (58%). The median duration of hospitalization was 3 days (IQR 1–6). Significant decrease in ED revisit within the first 30 days after discharge was observed in the intervention compared with the standard ED group (2% vs 18%, $P = 0.009$). However, there were no differences in rates of hospitalizations or CT scanning (44% vs 52.4%, P = NS, and 34% vs 20%, P = NS, respectably). Notably, patients in the standard ED group were older (36.1 ± 14.4 vs 50.1 ± 20.1, years $P = 0.001$). However, in logistic multivariate analysis the age at index ED visit was not associated with 30-days ED revisit (OR = 0.986, 95% CI 0.961–1.012, $P = 0.292$). In contrast, MDT intervention was associated with decreased ED revisit rates (OR = 0.77, 95% CI 0.01–0.607, $P = 0.015$).
Conclusion: MDT intervention for patients with IBD in the ED, improves patients management and reduces ED readmission in the first 30 days after discharge. This may suggest that MDT management should be a part of the care for patients with IBD visiting the ED.
Disclosure: Nothing to disclose

P1625 CHARACTERISTICS OF ANTI-TNF ALPHA THERAPY FOR ULCERATIVE COLITIS BETWEEN 2010–2016 IN HUNGARY

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Introduction: Anti-TNF therapy showed high efficacy in induction and maintain of remission in ulcerative colitis.
Aims and Methods: Study design: Retrospective data analysis using the National Health Insurance Fund social security databases including inpatient-, outpatient care, medications as well as the special drug reimbursement database of patients with the diagnosis of ulcerative colitis (UC) from 2010 to 2016. This is an observational / non-interventional, retrospective, epidemiological study. **Study population:** All of the adult – over 18 years of age – UC patients between 2010 and 2016. **Eligibility criteria:** Patients who have at least two events in all of relevant health care services or at least 1 inpatient event only with UC diagnosis (ICD codes: K51) K50 (Crohn's disease-CD) and K51 (UC) occurrence together: 80:20 distribution ratio. **Primary endpoint:** Analyze patient characteristics and therapeutic outcome of UC patients treated with anti-TNF agent in Hungary.
Results: 0.24% of total Hungarian population suffered from UC in 2016. This is more than 23.000 patients. The median age of the patients with UC is 51 (male 49, female 53) in the examined period. 1095 UC patients were treated with biologicals between 2010–2016. Annual prevalence of biological therapy was increasing continuously from 1.1% to 2.1%; 497 patients with UC were on anti-TNF alpha therapy at the end of 2016. The onset of biological therapy in UC is between 20 and 39, the average age is 37 years. This is 16 years less compared to the average age of total UC population.
Frequency of any type of extraintestinal manifestation was 29.8% among UC patients on biological therapy. The prevalence of different agents was 1.2% for infliximab and 1.1% for adalimumab in 2016. Anti-TNF alpha therapy was started within 3 years after the diagnosis in 35% of the patients, while disease duration was more than 10 years in every third cases. Primary non-response was observed in 9.7% of anti-TNF therapy. Ratio of dose escalation was 13.6%. Dose escalation was equally common among patients on infliximab and adalimumab therapy; however it occurred significantly later in case of infliximab. Frequency of switch was 15.7% and 83.1% of switch was performed after dose escalation. Ratio of adalimumab to infliximab switch was only 11%. Although frequency of hospitalization was as high as 71.7%, surgical intervention was needed in only 11.2% of patients on anti-TNF.
Conclusion: Both the prevalence and incidence of UC are high in Hungary. 3.4% of the UC population was treated with biological therapy in the last year of examination. Patients receiving biological therapy are typically from the younger part of the total UC population. Prevalence of using infliximab and adalimumab were the same in 2016. Primary non-response was observed about 10% of the cases, while ratio of loss of response was 16.3% (dose escalation 13.6% + 2.7% of switch without previous dose escalation). Need of surgical intervention was relatively low among Hungarian UC patients on biological therapy.
Disclosure: Nothing to disclose

P1626 VEDOLIZUMAB RESULTS IN REDUCED HOSPITALISATIONS AND STEROID USE AT 1 YEAR: RESULTS FROM THE SCOTTISH VEDOLIZUMAB COHORT

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Introduction: The GEMINI trials and an increasing body of real-world data have demonstrated the effectiveness and safety of vedolizumab (VDZ) in IBD. However, there is limited available data about its effect on hospitalisations and steroid use. Our aim was to address this in a large real-world cohort of IBD patients from across Scotland.
Aims and Methods: A multicenter retrospective cohort analysis of medical records was performed across 7 Scottish healthcare trusts. Primary outcomes were hospitalisation rates and overall steroid use in patients remaining on VDZ. Secondary outcomes were safety and intention to treat steroid free remission rates in patients with active disease. All data were prospectively collected as part of routine clinical care. Baseline demographics, clinical scores (HBI or Partial Mayo), faecal calprotectin (FC), endoscopy and radiology at 3, 6 and 12 months was recorded where available. Active disease was defined as endoscopic or radiographic evidence of disease or FC >200 mcg/g. Clinical remission was defined as HBI <5 or Partial Mayo <2. Biochemical remission was defined as FC <200 mcg/g.
Results: 340 (137 UC and 203 CD) patients were included in the primary analysis with a median follow-up of 9.4 months. Hospitalisation rates per patient-year were 0.60, 0.67, 0.36 and 0.16 at baseline, 3, 6 and 12 months of treatment respectively. Total number of hospitalisations reduced by 52.5% from 204 (12 months prior to VDZ) to 97 (12 months after VDZ). Proportion of patients on concomitant steroids reduced from 39.7% to 16.7% (n = 332), 8.1% (n = 270), 9.3% (n = 194) at 3, 6 and 12 months respectively. In patients with active CD (n = 153, 75.4%) steroid free clinical and steroid-free biochemical remission rates were; 54.4% and 30.2% at 3 months; 47.7% and 32.1% at 6 months; 28.6% and 33.9% at 12 months. In patients with active UC (n = 112, 81.8%) steroid-free clinical and steroid-free biochemical remission rates were; 57.4% and 40.9% at 3 months; 51.6% and 39.1% at 6 months; 37.5% and 41.2% at 12 months. Our cohort received >2066 VDZ infusions, 2 (0.6%) patients developed infusion reactions, 9 (2.6%) patients developed serious infections and 17 (5.0%) serious adverse events.
Conclusion: VDZ is associated with reduced hospitalisation and steroid use over 1-year. Steroid-free remission rates and safety profile is in keeping with the published literature.
Disclosure: Speaker fees and travel support Takeda

P1627 AZATHIOPRINE INDUCES HYPERBILIRUBINEMIA IN INFLAMMATORY BOWEL DISEASE: A HOSPITAL-BASED COHORT STUDY

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Introduction: Intestinal mucosal injury is supposed to cause liver disease and abnormal liver function tests are frequently observed in inflammatory bowel disease (IBD) patients.
Aims and Methods: We investigated the hepatic biochemistry abnormality and change during the treatment in IBD patients. IBD patients who were newly diagnosed and followed up in our hospital up to 2017 with the results of hepatic biochemistries at the both time points of diagnosis (before IBD treatment) and then at two years later (after IBD treatment) were enrolled. The biochemical profiles including aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TB), direct bilirubin (DB), alkaline phosphatase (ALP), Gamma-glutamyltransferase (GGT) were analysed.
Results: One hundred forty-six (77 patients of Crohn's disease and 69 ulcerative colitis) patients were enrolled. HBs Ag positivity was found in 9 (6.2%) patients and anti-HCV antibody in 1 (0.7%). Radiologic diagnosis of fatty liver was found in 15 (10.2%) patients and gallbladder stone in 10 (6.8%). Within first year, 85 (58.2%) patients started and maintained azathioprine (AZA) therapy. At diagnosis, 45 (30.8%) patient revealed at least one abnormal hepatic biochemistry. AST was elevated than upper limit of normal (ULN) in 9 (6.2%) patients, ALT in 11 (7.5%), TB in 14 (9.5%), DB in 16 (11%), ALP in 21 (14.6%) and GGT in 15 (10.3%). At two years later, 59 (40.4%) patients showed at least one abnormal hepatic biochemistry. TB was elevated compared to baseline ($P < 0.001$) and absolute abnormal elevation of TB (>0.5 mg/dL) was significantly related with AZA ($P = 0.006$). In the AZA therapy group, hyperbilirubinemia (>1.2mg/dL) was found in 6 (7.1%) patients at initial diagnosis, but 19 (22.4%) patients at two years later. In this group, absolute TB abnormal elevation was found in 63 (64.1%) patients. Eighteen (21.2%) patients were within normal TB level at diagnosis and experienced newly developed hyperbilirubinemia after AZA therapy.
Conclusion: Abnormal hepatic biochemistry profiles were observed in nearly one-third of IBD patients at diagnosis. AZA therapy is related with elevation change of TB during the treatment of inflammatory bowel disease.
Disclosure: Nothing to disclose

P1628 TARGETING DETECTION OF FISTULA TISSUE LEVELS OF ANTI-TNF – A POTENTIAL BIOMARKER OF TREATMENT RESPONSE?

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Introduction: Anti-TNF therapy is recommended as the first line for treatment of patients with Crohn's anal fistula. However, significant proportion of patients either fail initial trial or lose response to anti-TNF therapy. Reasons for this are likely multifactorial and related to metabolism of the drug as well as the development of antidrug antibodies. Currently, it is unknown whether fistula tissue levels play a role in this process.
Aims and Methods: We undertook a pilot study to measure fistula tissue levels of anti-TNF medication (infliximab and adalimumab) using a sensitive technique for peptide detection following trypsin digestion i.e. ultraperformance liquid chromatography mass spectrometry (UPLC-MS). Biopsies from two patients with infliximab and five patients on adalimumab for Crohn's anal fistula were obtained under general anaesthetic. The protein present in fistula's samples were extracted and digested by trypsin to obtain peptide fragments specific to each drug.[1] These were then analysed by UPLC-MS. The anti-TNF drug analysis was performed by ACQUITY UPLC (Waters Ltd., Elstree, UK) coupled to either a 'Xevo TQ-S' mass spectrometer (Waters, Manchester, UK). The MS system was equipped with an electrospray ionization source operating in positive ion mode (ESI−). The targeted UPLC-MS/MS detection and quantification method implemented was previously validated.[1] The chromatographic conditions were shortened to 7.2 min and consisted on mobile phase A (Acetonitrile with 0.1% formic acid) and mobile phase B (H2O with 0.1% formic acid) using a ACQUITY BEH 130 C18 1.7um 2.1×150 mm. MS parameters were optimised to detect specific peptide sequences from each drug. These multiple reaction monitorings (MRMs) also aimed to quantify the anti-TNF present in fistula tissue samples.
Results: The limit of detection (LOD) and linearity range of the method was assessed for each drug. Infliximab and Adalimumab were respectively with LOD of 0.096 and 1.92 mg/mL for linearity range over 4-fold. The peak area for each drug were normalised according to the weight of the fistula samples. Idiopathic (cryptoglandular) tissue samples were analysed as negative controls and anti-TNF drugs were spiked to these samples as positive controls.
Duplicated idiopathic and fistula samples were analysed. The anti-TNF drugs were not detected in fistula samples.
In addition, to validate the result samples were concentrated (x10) and still no detection of the drug was observed in the test samples.
Conclusion: Recent evidence suggests that higher infliximab trough levels are associated with perianal fistula healing in patients with Crohn's disease. In this study we have shown absence of detection of adalimumab / infliximab in all fistula biopsy samples from patients with Crohn's anal fistula. Furtherwork is required in greater numbers of patients biopsies to validate the findings observed and understand the correlation of tissue levels with serum levels of anti-TNF and clinical outcome.
Disclosure: Nothing to disclose

Reference

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P1629 USTEKINUMAB EFFICIENCY IN ASSOCIATION WITH SERUM LEVELS IN COMPLICATED REFRACTORY PATIENTS WITH CROHN'S DISEASE

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Introduction: Ustekinumab (UST) is an anti-IL-12/23 monoclonal antibody used for treatment of Crohn's disease (CD). We evaluated response to UST in a cohort

of patients with complicated course of disease and its association with serum trough levels (TLs).
Aims and Methods: Data from consecutive CD patients who previously failed at least one biologic agent and started UST with an i.v. dose between March and December of 2017 were included. Disease activity was assessed by Physician's Global Assessment (PGA) score as 0 (remission), 1 (mild disease), 2 (moderate disease) or 3 (severe disease) at week 0 and every following 8 weeks up to week 24 in a retrospective manner. At week 24, patients were considered as complete responders (CR) with PGA drop of at least 2 points, partial responders (PR) with drop of 1 PGA point or no responders (NR) with zero or negative decrease in PGA. C-reactive protein (CRP), fecal calprotectin (FC) and UST TLs were measured at every visit.
Results: Twenty-nine CD patients (37.9% males, 62.1% females) with mean age of 35.9 years were included. Mean disease duration was 15.2 years with 37.9% of patients classified as A1 according to Montreal classification. Proximal disease was present in 24.1% of patients and the same proportion of patients suffered from perianal disease. At least one previous surgery was performed in 86.2% of patients. In median, UST was administered as a 3rd biologic agent. Over half of patients had concomitant immunomodulators and 31% corticosteroids at week 0. At baseline, 20.7% of patients had severe disease activity, 62.1% had moderate and 17.2% mild or no current disease activity. Severe activity was present in 10.7% of patients, 50% had moderate and 39.3% mild or no activity at week 8. At week 24 the proportions were 8.7%, 47.8% and 43.5%, respectively, however, there was no decrease in mean CRP and FC between the two timepoints (CRP 11.2 ± 15.5 mg/L vs. 12.6 ± 16.5 mg/L, $p = 0.8838$; FC 1724 ± 1718 µg/g vs. 1611 ± 1830 µg/g, $p = 0.9277$). Patients with moderate to severe disease activity had significantly lower UST TLs at both week 8 and 24 (12.9 ± 10.1 µg/mL vs. 23.2 ± 11.8 µg/mL, $p = 0.0090$ at week 8 and 3.9 ± 1.9 µg/mL vs. 7.1 ± 3.8 µg/mL, $p = 0.0351$ at week 24). Fifty-two percent of patients experienced at least PR according to PGA decrease between baseline and week 24, while 48% didn't respond. There was no difference, and thus no predictive value, in UST TLs at week 8 between patients who did and didn't respond at week 24, however responders had significantly higher week 24 UST TLs (7.5 ± 3.7 µg/mL vs. 3.8 ± 1.9 µg/mL, $p = 0.0145$). Most frequent adverse events registered included fevers or arthralgias after application and there were 2 cases of periorbital rash at week 8. One patient developed demyelinating polyneuropathy during the follow-up, however, no patient had discontinued the treatment.
Conclusion: Despite no decrease in inflammatory markers, over 50% of the refractory CD patients experienced clinical benefit from ustekinumab after 24 weeks which was associated with its higher serum trough levels. No adverse event requiring the treatment to be terminated was registered.
Disclosure: Nothing to disclose

P1630 POTENTIAL THERAPEUTIC EFFICACY OF CURCUMIN IN THE TREATMENT OF EXPERIMENTAL COLITIS. MODULATORY ROLE OF PROSTAGLANDINS, NITRIC OXIDE, HYPOXIA INDUCIBLE FACTOR-1ALPHA AND INTESTINAL MICROBIOTA

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Introduction: Curcumin, a bioactive pleiotropic component derived from a rhizome of the *Curcuma longa* plant, exhibits antioxidant, anti-inflammatory, antiproliferative, analgesic and chemopreventive efficacy against various GI-tract disorders, however, its role in pathogenesis of IBD with respect to experimental colitis in animal models has been little studied. The potential proitective mediators such as prostaglandins, nitric oxide (NO) and the alterations in intestinal microbiota have been little determined.
Aims and Methods: We compared the effect of vehicle and curcumin on the intensity of inflammation in experimental colitis induced by TNBS (15 mg/kg per rectum) in rats with inhibited cyclooxygenase (COX)-1 and COX-2 activity by daily treatment with indomethacin (2 mg/kg i.p.), SC-560 or celecoxib (both at 5 mg/kg i.g.), and the inhibited NO-synthase activity by L-NNA (10 mg/kg i.p.). At day 9 upon TNBS administration, rats were euthanized with isoflurane and the macroscopic and microscopic damage and the colonic blood flow (CBF) was determined by disease activity index (DAI) and laser Doppler flowmetry, respectively, blood was withdrawn for the determination of the plasma proinflammatory cytokines IL-1b, TNF-a, IL-6, IL-13 and IL-17 by Luminex Multiplex platform and the accompanying alterations in mucosal MPO activity and the expression of mRNA and protein of proinflammatory and antioxidazing factors HIF-1α, IL-1β, TNF-α, HO-1 and SOD 2 were analysed by RT-PCR and Western blot. The composition in the intestinal microflora was determined by NGS in faecal samples.
Results: Intrarectal administration of TNBS resulted in macroscopic and microscopic colonic lesions accompanied by the significant fall in CBF, and the significant increase of colonic tissue weight, MPO and plasma IL-1b, TNF-a, IL-17, IL-6 and IL-17 levels ($p < 0.05$) and these effects were significantly increased by co-treatment with indomethacin (2 mg/kg i.p.), SC-560 or celecoxib (both at 5 mg/kg i.g.) ($p < 0.05$). Treatment with curcumin (20–200 mg/kg i.g.) dose-dependently reduced DAI and significantly raised the CBF suppressed MPO and plasma IL-1β, TNF-α, IL-6 and IL-17 levels ($p < 0.05$). The curcumin-induced reduction of DAI was mitigated by treatment with indomethacin, SC-560 or celecoxib and L-NNA, and further restored by concurrent treatment with 16, 16 dm PGE_2 (1 µg/kg i.g.) and L-arginine (200 mg/kg i.g.), the substrate for NO-synthase ($p < 0.05$ vs respective controls). In fecal samples, curcumin-treated rats had a higher ratio of phyla *Firmicutes* and *Bacteroidetes* and lower intestinal phylum levels of *Proteobacteria* compared to vehicle-control TNBS-treated rats. Curcumin downregulated mRNA and protein expression of Hif-1α, IL-1β and TNF-α and upregulated HO-1 and SOD 2 and these effects were reversed by L-NNA and further restored by co-treatment of L-NNA with L-arginine.
Conclusion: We conclude that 1) curcumin accelerates the healing of TNBS-induced colitis due to its antioxidazing and anti-inflammatory activities, possibly mediated by endogenous PG and NO, the inhibition of mRNA and protein expression of HIF-1α, IL-1β and TNF-α and the activation of HO-1 and SOD 2 expression and 2) curcumin caused changes in the distribution and structure of intestinal microflora and partially reversed changes in the diversity of gut microbiota in colitis.
Disclosure: Nothing to disclose

P1631 ACTIVE SUBSTANCES IN CHAMOMILE FLOWER AND COFFEE CHARCOAL EXTRACT CONTRIBUTE TO THE ANTISPASMODIC AND CYTOKINE/CHEMOKINE-INHIBITING ACTIVITY OF A TRADITIONAL HERBAL MEDICINE

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Introduction: The herbal medicinal product Myrrhinil-Intest®, a combination of myrrh (*Commiphora molmol* E.), chamomile flower (*Matricaria chamomilla* L.) and coffee charcoal (*Coffea Arabica* L.) is used for the treatment of gastrointestinal complaints. Clinical data suggest its use for the maintenance therapy of inflammatory bowel disease [1]. Pharmacological investigations further revealed antispasmodic and immune-modulating activities of the herbal combination [2]. However, information regarding active substances remain insufficient.
Aims and Methods: The present investigation aimed to identify potential active components in the herbal combination with regard to their antispasmodic and ant-inflammatory activity.
Thus, HPLC/LC-MS analysis was performed to identify main plant compounds. Subsequently, the influence of the single compounds apigenin (API), trigonelline (TRI), caffeine (CAF), chlorogenic acid (3-CQA) and its isomers cryptochlorogenic (4-CQA) and neochlorogenic acid (5-CQA) on intestinal motility was determined using isometric tension measurement in isolated rat small intestinal preparations. Furthermore, cytokine (TNFα; IL-6) and chemokine (MCP-1) release from LPS-challenged human macrophages (THP-1) was investigated using an ELISA test system. Nimodipine and budesonide served as positive control for the antispasmodic and anti-inflammatory effect respectively.
Results: A spasmolytic effect indicated by inhibition of acetylcholine-induced contractions in rat small intestinal preparations was confirmed for apigenin ($IC_{50} = 31.1$ µM; 15.7% max. inhib.). Furthermore, cytokine TNFα and IL-6 as well as chemokine MCP-1 release from LPS-challenged human macrophages was inhibited concentration-dependently after apigenin incubation (IC_{50}-TNF$\alpha = 14.3$ µM, 2.9% max. inhib.; IC_{50}-IL6 = 12.79 µM, 5.7% max. inhib.; IC_{50}-MCP-1 = 10.43 µM, 23.4% max inhib.). Cryptochlorogenic acid (4-CQA) led to an inhibition of cytokine TNFα ($IC_{50} = 20.7$ µM, 7.9% max. inhib.) and IL-6 ($IC_{50} = 43.3$ µM, 30.7% max. inhib.) as well as chemokine MCP-1 (IC_{50}: 4-CQA = 13.9 µM, 22.5% max. inhib.) release. 3-CQA and 5-CQA were less effective (3-CQA: IC_{50}-TNF$\alpha = 51.0$ µM, 30.5% max. inhib.; 5-CQA: IC_{50}-TNF$\alpha = 14.3$ µM, 21.3% max. inhib.; no influence on IL6 or MCP-1).
Conclusion: Apigenin and 4-CQA – single components of chamomile flower and coffee charcoal – inhibited acetylcholine-induced contractions in rat small intestinal preparations and cytokine/chemokine release from activated human macrophages. These data reinforce the use of the traditional herbal medicinal product (Myrrhinil-Intest®) for the treatment of inflammatory intestinal disorders and the application of apigenin and 4-CQA as active markers for the antispasmodic and anti-inflammatory activity.
Disclosure: Authors LW and CV are employed by and Author KHG is shareholder of Repha GmbH Biologische Arzneimittel.

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WEDNESDAY, OCTOBER 24, 2018 09:00–14:00
Other Lower GI Disorders III – Hall X1

P1632 HUMAN MILK OLIGOSACCHARIDES IMPACT THE MICROBIOTA COMMUNITY AND ASSOCIATED BACTERIAL METABOLITES OF IBS PATIENTS

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Introduction: Irritable bowel syndrome (IBS) is one of the most common clinical problems in gastroenterology with an estimated prevalence of between 10 to 25%

(1). Common co-morbidities include psychiatric disorders and both IBS and these comorbidities are associated with the gut microbiota and their metabolites (2,3). In particular there are compositional differences in the intestinal microbiota of IBS patients relative to healthy individual, and a depletion of faecal and mucosal bifidobacteria (4,5,6). Further, IBS patients have been reported to have a compromised gut barrier which may be linked to the microbiota and metabolites (7). Diet is one of the greatest determinants of gut microbiota composition and may offer a promising avenue for management of IBS. The challenge is to identify dietary modifiers of the microbiota which are specific. Human Milk Oligosaccharides (HMOs) are a family of complex carbohydrates found in high concentrations in human milk. In clinical studies, in both infants and adults, HMOs powerfully and specifically modulated the gut microbiota by increasing bifidobacteria and reducing certain detrimental bacteria (8,9). Further, beneficial metabolites such as short chain fatty acids are produced, which can improve gut barrier function, and potentially influence the pathogenesis of IBS and co-morbidities.

Aims and Methods: The aim of this study is to assess the *in vitro* mechanisms of i) the impact of HMOs on the microbial community and associated metabolites, and ii) the consequential improvement of gut barrier function. *In vitro* gut models were used to examine the impact of HMOs on the microbiota and bacterial metabolite production using faecal samples from healthy donors and IBS patients. Samples were analysed using flow cytometry coupled with fluorescent in-situ hybridization (FISH) for microbial composition and NMR spectroscopy for metabolite profiling. Intestinal cell lines were used to examine the impact of fermented HMOs on gut barrier permeability and immune response.

Results: The study showed (i) the microbiota of healthy and IBS patients to be different, (ii) a clear change in microbial composition and bacterial metabolites in IBS samples during HMO fermentation, (iii) an increase in bifidobacteria in the IBS samples to levels closer to healthy donors; and (iv) differential modulation of gut barrier function. Multivariate analysis on the NMR data revealed that the main cause of variation during the HMO fermentation was short chain fatty acids.

Conclusion: The results indicate that HMOs favourably impact the gut microbiota composition and associated bacterial metabolites of IBS patients and parameters of gut barrier function *in vitro*. This suggests HMOs as potential candidates for the dietary management of functional gastrointestinal diseases like IBS and associated comorbidities.

Disclosure: Louise Kristine Vigsnæs and Bruce McConnell are employed at Glycom A/S, Denmark, which funded this study.

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P1633 DAY-TO-DAY VARIABILITY IN FECAL MICROBIAL RICHNESS AND ITS ASSOCIATION WITH STOOL CONSISTENCY: DO WE NEED MULTIPLE SAMPLE COLLECTION?

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Introduction: Stool consistency has been associated with the fecal microbial composition. Temporal instability in stool consistency and microbial composition has been demonstrated in irritable bowel syndrome (IBS), raising the question of whether day-to-day variability in microbial composition and stool consistency should be taken into account in IBS microbiota studies.

Aims and Methods: We aimed to evaluate within-subject (day-to-day) variability in fecal microbial richness and its association with stool consistency in IBS patients and healthy subjects, over a period of seven days. Twelve IBS subjects (IBS) and 12 age- and sex-matched healthy subjects (HC) collected fecal samples once daily during seven consecutive days. Samples were frozen directly after collection. Microbial richness, as assessed by the observed number of species and Chao1 index (*i.e.*, alpha diversity), was analyzed by 16S rRNA gene sequencing. Fecal dry matter percentage, as a measure of stool consistency, was determined for each sample. Linear mixed-effects models were used to evaluate the association between microbial richness and stool consistency. To evaluate the within-subject variability in microbial richness, inter-item correlations and intra-class correlations (ICC) were calculated.

Results: Using linear mixed-effects models, significant associations were observed between stool consistency and microbial richness over time. However, regression coefficients were small for both Chao1 index (B:1.231, 95%-CI: 0.835;1.628) and observed species (B:1.066, 95%-CI: 0.725; 1.407), indicating a small change in alpha diversity per unit increase in stool consistency. Furthermore, in IBS and HC, microbial richness was highly correlated between subsequent samples (inter-item correlations >0.8; ICCs >0.850), for both measures of alpha diversity.

Conclusion: The small, but significant association between stool consistency and alpha diversity over time suggests that day-to-day variability in microbial richness might be influenced by stool consistency. The low within-subject variability in alpha diversity, however, indicates that the microbial richness of one single fecal sample is representative for a period of seven days and therefore, we consider collecting multiple fecal samples unnecessary.

Disclosure: Nothing to disclose

P1634 ENTEROTOXIN BACTEROIDES FRAGILIS PREDICTES COLORECTAL CANCER PROGNOSIS

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Introduction: Human intestinal flora play an important role in the homeostasis of gastrointestinal tract. As one of the human intestinal commensal bacteria, Enterotoxin *Bacteroides fragilis* (ETBF) is an anaerobic Gram-negative bacterium which produces *Bacteroides fragilis* toxin (BFT). It has been found that ETBF colonization increases in colorectal cancer patients, and it may be associated with tumorigenesis.

Aims and Methods: We aimed to investigate the association between ETBF and the prognosis and chemotherapeutic effect of colorectal cancer. 242 cases of colorectal mucosa biopsy or resection, which had been made into paraffin tissue, were collected from Southern Medical University Affiliated Nanfang Hospital. These samples were divided into colorectal adenoma group (112 cases), colorectal cancer group ($n=80$) and mild inflammation group ($n=50$). Clinical data were collected from these patients, including sex, age, history antibiotics use within one week, radiotherapy history, chemotherapy history, biopsy location, pathology diagnosis, parenteral infection, carcinoembryonic antigen (CEA), C-reactive protein (CRP), white blood cell count (WBC), lymphocyte count (LYM), neutrophil count (NEU), monocyte count (MO), etc. Patients with colorectal cancer were followed up for one year and their clinical data such as surgery, chemotherapy, TNM staging, imaging data, relapse and death were collected. The total DNA(including host DNA and commensal bacteria DNA) from each group of paraffin tissues was extracted and then the endotoxin gene segment of ETBF were amplified by polymerase chain reaction. Then we analyze the relationship between ETBF infection and clinical data we collected.

Results: The positive rate of ETBF in colorectal adenoma group and colorectal adenocarcinoma group were both significantly higher than that in mild inflammation group ($p=0.008$, $p<0.000$). Positive rate of ETBF in biopsy from right colon was significantly higher than that from left colon ($\chi^2=14.13$, $P<0.000$). TNM tumor staging in patients with ETBF-positive colorectal cancer was significantly higher than that in ETBF-negative patients ($Z=-3.322$, $p=0.001$). There was no significant difference in inflammation index, such as WBC, LYM, NEU and MO between ETBF-positive and negative group ($p>0.05$). But the quantitative of CRP in ETBF-positive group was significantly higher than that in ETBF-negative group ($p<0.000$). The depth of tumor invasion ($Z=-2.892$, $p=0.004$) and distant metastasis of ETBF-positive patients ($Z=-2.881$, $p=0.004$) were significantly worse than ETBF-negative patients. There was no significant difference of recurrence and death within one year between ETBF-positive colorectal cancer patients and negative ones ($\chi^2=3.878$, $p=0.078$; $\chi^2=3.374$, $p=0.151$). Lymphatic metastasis, distant metastasis were significantly higher in ETBF-positive patients ($Z=-2.892$, $p=0.004$; $Z=-2.881$, $p=0.013$). Tumor-free survival rate of ETBF-positive patients was significantly lower than that of ETBF-negative ones ($\chi^2=12.836$, $p<0.000$). But there was no significant difference in tumor infiltration depth ($Z=-1.885$, $p=0.064$). Chemotherapy efficacy of ETBF-positive patients was significantly worse than ETBF-negative ones ($\chi^2=5.437$, $p=0.020$).

Conclusion: The ETBF infection was more prevalent in colorectal neoplasms patients. The higher colorectal cancer TNM stage, the higher positive rate of ETBF was. Prognosis and chemotherapeutic effect of colorectal cancer were worse in ETBF-positive patients, which may make ETBF detection an indicator of poor prognosis and chemotherapy efficacy.

Disclosure: Nothing to disclose

P1635 CHANGES OF HUMAN GUT MICROBIOTA FUNCTIONAL POTENTIAL AFTER HELICOBACTER PYLORI ERADICATION THERAPY

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Introduction: Changes in human gut microbiota composition are often observed after the antibiotic therapy. Most of studies published recently paid attention to specific bacterial content, but there is limited data concerning functional roles of altered microbiota.
Aims and Methods: The aim of the study was to evaluate the influence of *H.pylori* eradication therapy on different functional groups of bacteria in the gut microbiota immediately after the eradication therapy and one month later.
Stool samples were collected from 83 patients before and immediately after eradication therapy (amoxicillin 1000 mg, clarithromycin 500 mg, proton pump inhibitor, bismuth subsalicylate 240 mg bid for 14 days), also 14 stool samples were collected one month after eradication therapy from the same patients. Samples were analyzed using shotgun metagenomic sequencing (SOLiD 5500 Wildfire platform). Relative abundance of bacterial groups in the gut microbiota was evaluated.
Results: We identified 5 functional groups of bacteria: butyrate-producing (*Eubacterium rectale, Roseburia hominis, Roseburia intestinalis, Roseburia inulinivorans, Eubacterium hallii, Faecalibacterium prausnitzii, Butyrivibrio crossotus, Coprococcus comes, Coprococcus eutactus, Subdoligranulum variabile*), propionate-producing (*Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides vulgatus, Veillonella parvula, Dialister succinatiphilus, Phascolarctobacterium succinatutens, Akkermansia muciniphila, Coprococcus catus, Megasphaera elsdenii, Roseburia inulinivorans, Ruminococcus gnavus, Ruminococcus torques*), hydrogen-utilizing (*Ruminococcus bromii, Blautia hydrogenotrophica, Blautia hansenii, Desulfovibrio piger, Methanobrevibacter smithii*), lactate-producing bacteria (*Bifidobacterium spp., Lactobacillus spp., Collinsella aerofaciens, Eubacterium rectale, Faecalibacterium prausnitzii, Roseburia spp., Bacteroides spp.*) and bacteria involved in vitamins biosynthesis (*Bacteroides thetaiotaomicron, Bacteroides vulgatus, Bifidobacterium longum*) as the most important for the maintenance of functional stability of the gut microbiota.
Significant reduction in the relative abundance of butyrate-producing and hydrogen-utilizing bacterial groups was observed immediately after eradication therapy compared to the baseline level: $(24.87 \pm 18.59)\%$ vs. $(32.81 \pm 16.77)\%$ ($p = 0.0048$) and $(1.6 \pm 2.74)\%$ vs. $(2.5 \pm 3.89)\%$ ($p = 0.0053$), respectively. One month after eradication therapy the relative abundance of hydrogen-producing bacteria almost completely returned to initial level, $(2.15 \pm 3.3)\%$ vs. $(2.5 \pm 3.89)\%$ ($p = 0.9878$). A tendency of increasing of the relative abundance of butyrate-producing bacterial group was also observed one month after the therapy, without significant differences compared to the initial level, $(25.21 \pm 13.69)\%$ vs. $(32.81 \pm 16.77)\%$ ($p = 0.2829$), but their number was still less than before the initiation of therapy.
No significant changes were observed in the relative abundance of bacteria involved in vitamins biosynthesis, as well as propionate-producing and lactate-producing bacterial groups immediately after eradication therapy as well as one month after the eradication.
Conclusion: So *H.pylori* eradication therapy leads to significant reduction of butyrate-producing bacteria abundance in human gut microbiota with a slight tendency to return to the initial level within one month after the end of treatment. This fact should be taken into account when prescribing eradiation therapy and predicting possible adverse events of therapy.
Disclosure: Nothing to disclose

P1636 FECAL MICROBIAL ECOSYSTEM IS DISTINCT IN IRRITABLE BOWEL SYNDROME ACCORDING TO SUBTYPES

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Introduction: Much evidence suggests the contribution of intestinal microbiota in the pathophysiology of irritable bowel syndrome (IBS). We characterized the intestinal microbial ecosystem (IME) by means of 16s ribosomal RNA (rRNA) gene profiling in fecal samples of IBS subtypes collected during a multicentre intervention trial with *Lactobacillus paracasei* CNCM I-1572 in IBS
Aims and Methods: To characterize the IME, we inluded in the study a total of 40 patients with IBS according Rome III criteria (12 IBS-C; 14 IBS-D; 11 IBS-M; 3 IBS-U). Biological specimens were collected every four weeks for five consecutive time points. Metagenomics DNA was extracted from about 200 mg of feces using the PowerSoil® DNA Isolation Kit. Subsequently, the bacterial community structure was profiled by 16s rRNA gene profiling, amplicons were sequenced using Illumina MiSeq System and the results were managed by means of the bioinformatic pipeline Quantitative Insights Into Microbial Ecology with the GreenGenes database.
Results: The taxonomic overview of the fecal sample analyzed revealed that the first 7 most abundant genera belong to the Firmicutes Gram positive order. Clostridiales accounted for about 75% of detected bacteria, while the relative abundance of members of the order Bacteroidales was lower than 10%. The analysis of median profiling data revealed 26 significantly different operational taxonomic units (OTUs) between IBS-M and IBS-C, while 19 OTUs distinguished IBS-M from IBS-D. Interestingly, the highest number of dissimilarities was found between IBS-C and IBS-D: 85 OTUs had, in fact, a significantly different relative abundance. Most of the discriminating OTUs were ascribed to the order Clostridiales; IBS-C were distinguished from IBS-D by numerous Clostridiales-associated OTUs belonging to the families Ruminococcaceae (in particular, the genus Ruminococcus) and Lachnospiraceae. Two OTUs ascribed to *Bifidobacterium adolescentis* were increased in IBS-C whereas OTUs associated to the order Bacteroidales and to the Firmicutes species *Eubacterium biforme* were enriched in IBS-D samples.
Conclusion: Our results indicate that the fecal microbiota of IBS-C and IBS-D is characterized by a different distribution of Clostridiales, whereas IBS-M samples possesse compositional features intermediate between IBS-C and IBS-D. The distribution of bacteria inside the Gram-positive order Clostridiales distinguishes the microbial ecosystem of IBS subtypes, suggesting that distinct therapeutic approaches targeting microbiota should be developed according to IBS subtypes.
ClinicalTrials.gov Identifier: NCT02371499
Disclosure: Nothing to disclose

P1637 CHARACTERIZATION OF GUT MICROBIOTA IN A COHORT OF NORMAL ITALIAN SUBJECTS; RESULTS FROM A CROSS-COUNTRY POPULATION STUDY

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Introduction: The composition of intestinal microbiota is gaining importance in human health studies since there is increasing evidence that bacteria play a role in disease etiology. The composition of the gut microbiota is relatively stable throughout adult life, but can be transiently or permanently altered as a result of bacterial infections, antibiotic treatment, lifestyle, surgical, and a long-term change in diet.
Aims and Methods: To characterize normal Italian gut microbiota and identify factors shaping its composition, we conducted 16S rRNA analysis using GA-map™ Dysbiosis Test[1] of fecal samples collected from normal Italian adults residing in 3 regions of Italy (Milan, Rome, Palermo). Participants were recruited from subjects coming to the clinic for colonoscopy in connection to the national screening program, with no abnormal findings. Each participant also completed a 16-question questionnaire.
The GA-map™ Dysbiosis Test[1] is composed of 54 pre-selected highly specific 16S rRNA gene-targeted single nucleotide primer extension (SNuPE) probes, detecting at least 300 bacteria on different taxonomic levels, for detection and characterization of dysbiosis. The test reports a Dysbiosis Index (DI), where DI = 1–2 is considered normobiosis, and DI = 3–5 is dysbiosis. Fecal-Calprotectin (FCal) analysis was performed using BÜHLMANN fCAL® ELISA with a cut-off of ≤200mg/kg. Chi-square test was used to determine differences in proportions, with $p < 0.05$ for significance.
Results: We collected fecal samples from 78 normal Italian adults (39 females, 39 males; median age, 55; range age, 24–73; median FCal, 37; range FCal 6–190; median BMI, 23.4; range BMI, 18.4–28.4). 27 (35%) of study participants were smokers.
In total 60% (47/78) of normal Italian adults were determined to be normobiotic, 36% (28/78) were determined to have mild dysbiosis, and 4% (3/78) were determined to have severe dysbiosis. However, no subjects were found to have the highest degree of dysbiosis with DI = 5. Site-wise, the results show 58% normobiosis in Milan, 68% in Rome, and 38% in Palermo.
Of note, 15 (56%) of 27 smoking subjects versus 16 (31%) of 51 non-smoking subjects were determined to be dysbiotic ($p = 0.04$). No significant difference in proportion of dysbiosis between sites ($p > 0.01$) or gender ($p = 0.8$).
We observed high variability in the profiles of fecal microbiota among the Italian adults. The profiles were generally dominated by Actinobacteria (mainly the genus Bifidobacterium), Firmicutes (with diverse representation from numerous genera), Verrucomicrobia (*Akkermansia muciniphila*), and Bacteroidetes (mainly Bacteroides and Prevotella).
Conclusion: We used GA-map™ technology to characterize the gut microbiota in normal Italian adults. The present study showed that the composition of the fecal microbiota of normal Italian adults at the national level, while highly variable, was not strongly associated with subjectś area of residence or gender. However, smoking was found to be associated with dysbiosis. Altogether, our results indicate a 40% proportion of dysbiosis in normal Italian adults, which may possibly be caused by environmental factors such as dietary or smoking habits, as we observe a 25% higher proportion of dysbiosis among smokers as compared to non-smokers.
Disclosure: MKK and CC are employees of Genetic Analysis.

Reference

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P1638 A TEXT-MINING TOOL TO DETECT THE MANAGEMENT OF ANTITHROMBOTICS BEFORE COLONOSCOPY – A ANALYSIS OF 656 PATIENTS

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Introduction: The use of antithrombotics (antiplatelet agents and anticoagulants) is increasing with an ageing global population, there is lack of data and system to evaluate adherence to international practice guidelines and standard instructions prior to colonoscopy.
Aims and Methods: We aim to develop an automatic text-mining system to assess the instructions of antithrombotic medications in a retrospective cohort of patients who used antithrombotics and underwent elective colonoscopy in a large teaching hospital. The system first determined whether the clinician has ordered colonoscopy for a patient. If colonoscopy was arranged, the algorithm would search for keywords indicating modification of anti-thrombotic therapy. A list of keywords was created that carries the meaning of ''withholding'', such as ''stop'', ''withhold'' and its abbreviation ''w/h''. We matched these keywords with a list of relevant drug names, e.g. aspirin, warfarin and their abbreviations. Regular expressions were developed to extract the stoppage information using these concepts. Two investigators manually reviewed all consultation notes to determine whether instructions on modifying anti-thrombotic therapy were given. The manual review findings were used as a gold standard to assess the performance of the automated text-mining system.
Results: There were a total of 656 patients and 1,907 consultation notes identified. Manual review identified 108 relevant instructions in the notes. The text-mining system had an accuracy of 0.936, sensitivity of 0.843, specificity of 0.954, and an F1-score of 0.813. The computational and manual effort had 53 out of 656 patients with different results. Because of this discrepancy, the staff went through the consultation notes of those patients with different results. 42 patients were correctly labelled by the manual method but incorrectly labelled by the computational process; the sum of 42 came from false negative (FN)+ false positive (FP).
Conclusion: The computational text-mining tool was able to achieve a high accuracy of 93.6% in this pilot experiment. We can apply this automated tool to screen a larger population to understand the quality of instructions offered to patients. We can also relate this result of detection of drug stoppage instruction to other clinical outcomes, e.g. bleeding complications of the procedures and reversal instruction in future studies.
Disclosure: Nothing to disclose

P1639 READMISSION OF GASTROINTESTINAL BLEEDING IN THE EMERGENCY DEPARTMENT

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Introduction: Gastrointestinal bleeding (GIB) is one of the main causes of admission to the Emergency Department (ED) and with hospitalizations, responsible for health burden.
Aims and Methods: We studied all the readmissions by GIB in a tertiary hospital A retrospective study of all GIB admissions was made in the adult population during the year 2016. All patitents were caracterized by comorbilities and medication. Data was analized by Excell and SPSS.
Results: They were admitted to the ED with suspected GIB 690 episodes, reporting to 622 patients. A total of 68 readmissions, by 55 patients, 69% male and 31% female, the mean age being 62.58 ± 16.81 years. Using the Manchester triage protocol 75% of the patients were screened as urgent and 25% as very urgent. The presentation forms were: 43% Rectorragias, 24% Hematemesis, 23% Hematochesis and 10% melenas. In most readmissions (65%), the clinical form of presentation was different from the previous presentation, and agreement was observed in 35% of cases. Throughout the year, most (80%) of patients were readmitted only once, 16% 3 times and 2 patients 4 times. We found readmissions were 64.75 ± 73.17 days. In 50% of the cases were <30 days, with a average of 10.74 days. Analytically mean hemoglobin admission was 10.64 g / dL, with substancial loss at readmission 9,99 g / dL ($p = 0.035$). The hospitalization rate at readmission was 38% with a mortality rate of 15%.
Conclusion: Readmissions by GIB presented with clinical signs of severity, since in all cases they were stratified as urgent or very urgent by the Manchester triage. Taking into consideration that 50% of cases there was an early readmission (average time -10 days), we suggest a schedule reassessment of the most severe cases within 1 week after discharge.
Disclosure: Nothing to disclose

P1640 A NOVEL SCORING SYSTEM FOR LOWER GASTROINTESTINAL BLEEDING: A MULTI-CENTRE COMPARISON OF RISK ASSESSMENT TOOLS

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Introduction: Lower Gastrointestinal bleeding (LGIB) is common and its incidence is increasing. There are well-validated predictive scoring models for upper gastrointestinal haemorrhage Rockall, Glasgow Blatchford Score (GBS) and AIM 65. There have been several attempts at identifying risk factors for developing severe LGIB. The BLEED criteria by Kollef et al[1] has not been found to be useful clinically. Strate et al[2] validated risk factors, triaging patients into low, moderate and high-risk groups. Unfortunately, the risk factors are likely to lack the sensitivity to be useful particularly at the low-risk end of the spectrum.
Aims and Methods: The aim of this multicentre review was to identify risk factors that predict adverse outcomes from LGIB. We retrospectively reviewed all patients admitted with LGIB from three large centres in the Midlands, UK between 2010 and 2017. Parameters collected included those that make up GBS, Rockall and AIM65 (Gender, age, co-morbidities, admission haemoglobin (Hb), Urea, Albumin, INR, blood pressure/heart rate, presence of melena, syncope and altered mental state). Adverse outcomes include red cell transfusion, endoscopic intervention, CT angiography, surgery, re-bleeding and mortality. Using regressional analysis all statistically feasible combinations of factors were used to predict adverse outcomes (both multivariate and univariate logistic regression models were fit) with cross-validation method repeated 100 times each combination. The model which exhibited the highest average AUROC value was identified. The factors with 95% CI for ORs containing value 1 were excluded. Then a multivariate logistic regression was fit again on the identified factors. Estimates of the Area Under the Receiver Operating Curve (AUROC) were calculated using a cross-validation method repeated 100 times.
Results: 473 patients were included. Admission Haemoglobin (Hb $<$ 72g/L 14 points, 73–95g/L 10points, 96–117g/L 7 points, 118–139g/L 4 points, $>$140 0 point, altered mental state 1 point, admission BP (Systolic blood pressure $<$ 90mmHg 1 point) and male gender (1 point) were the strongest predictors of the requirement of blood transfusion achieving an AUROC of 0.92 (95% CI 0.90–0.94), therefore giving The Birmingham Score (table 1).
This performed better than the Glasgow-Blatchford score (AUROC 0.89).
When predicting the risk of re-bleeding, the admission haemoglobin was the strongest predictor achieving an AUROC of 0.66 (0.60–0.72). Age, gender, co-morbidities, admission Hb/urea/albumin/INR, blood pressure and syncope predict a length of stay of more than four days with an accuracy of 80%.
Conclusion: Our study shows that admission haemoglobin, altered mental state, male gender best predict the need for blood transfusion after admission with LGIB, giving a novel LGIB score termed The Birmingham Lower GI bleed score. Therefore, this may act as a guide to initiate a more intensive treatment regimen and guide admission.

Score	Probability of requiring blood transfusion
≥12	≥90%
11	70%
9–10	45%
8	30%
6–7	15%
5	6%
≤4	≤3%

[The Birmingham score]
Disclosure: Nothing to disclose

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P1641 OAKLAND SCORE IS NOT BETTER THAN HAEMOGLOBIN FOR PREDICTING OUTCOMES IN LOWER GASTROINTESTINAL BLEEDING

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Introduction: The incidence of acute lower gastrointestinal bleeding (LGB) is increasing in Western countries. Recently the Oakland score has been developed for predict safe discharge after LGB.

Aims and Methods: The aim of this study was to compare the accuracy of Oakland score (OakS) with haemoglobin alone (Hb) for predicting outcomes after LGB. Safe discharge was the main outcome predicted by OakS. It was defined as the absence of all the following: a) rebleeding (need for additional red blood transfusion or a further decrease in haematocrit concentrations of 20% or more after 24 hours of clinical stability); b) red blood cell transfusion; c) therapeutic intervention (endoscopic therapy, vascular embolization or surgery); d) readmission with further LGB within 28 days and e) in-hospital death.

A retrospective study was performed from January 2013 to December 2015 in a university tertiary care hospital. Patients with acute LGB were identified using the International Classification of Diseases (9th Revision) and Clinical Modification codes for admission diagnosis. OakS was retrospectively calculated according to clinical reports data. Area under the receiver operating characteristic curve (AUROC), were calculated for OakS and Hb value. AUROCs were compared with the DeLong method by using STATA 14.1 software (StataCorp.2015).

Results: A total of 258 consecutive patients admitted to the hospital with acute LGB were identified retrospectively. Median age was 76.4 years (range 31.7–96.5), 178 (69%) of patients were older than 70 years, 54.3% were men. 154 (57.7%) patients were safely discharged. Six patients (2.3%) died, 50 (19.4%) rebleed, 84 (32.6%) needed transfusion, 20 (7.8%) were readmitted, 28 (11.2%) needed endoscopic treatment and 3 (0.8%) transcatheter arterial embolization. No patient required surgery.

The comparison of the AUROC for OakS and Hb are shown in table 1. Hb was equal or better than OakS for predicting all outcomes but readmission. AUROC were >0.8 for clinical intervention, transfusion, rebleeding and death for Hb and for clinical intervention, transfusion and death for OakS.

Conclusion: Hb seems non-inferior or even superior to OakS for predicting safe discharge, transfussion, rebleeding, haemostatic intervention or dead. OakS was better only for predicting readmission, but the predictive value for this outcome was low for both Hb and OakS.

	Oakland Score AUROC (95%IC)	Haemoglobin AUROC (95%IC)	P value
Safe Discharge n = 154; 59.7%	0.80 (0.74–0.86)	0.82 (0.77–0.88)	0.1516
Transfusion n = 84; 32.6%	0.87 (0.82–0.92)	0.90 (0.87–0.94)	0.0236
Rebleeding n = 50; 19.4%	0.76 (0.68–0.83)	0.81(0.75–0.87)	0.0409
Readmission n = 20, 7.8%	0.68 (0.55–0.77)	0.62(0.48–0.77)	0.0374
Haemostatic intervention n = 31; 12%	0.67 (0.55–0.77)	0.70 (0.61–0.80)	0.3852
Death n = 6; 2.3%	0.84 (0.73–0.95)	0.82 (0.72–0.91)	0.5066

[Table 1]

Disclosure: Nothing to disclose

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P1642 THE USE OF NSAIDS, PAAS AND OACS IN HEMORRHAGE ASSOCIATED WITH DIVERTICULAR DISEASE

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Introduction: Diverticular Disease (DD) is one of the most frequent benign gastrointestinal condition in older adults, is an asymptomatic condition, however, complications can occur in 5% of cases. The increasing use of non-steroidal anti-inflammatory drugs (NSAIDs), platelet anti-aggregators (PAAs) and oral anticoagulants (OACs) in this population raises the probability of hemorrhage associated with DD.

Aims and Methods: The aim of this study is to evaluate if the use of NSAIDs, PAAs and/or ACOs influence the presentation and the course of hemorrhage episodes associated with DD.

Retrospective analysis of patients admitted for DD complicated with hemorrhage between January 2015 and December 2017. Demographic, clinical, analytical and number of days of hospitalization were evaluated. Statistical analysis was performed using SPSS v24.

Results: 68 patients were included; average age was 80.85 ± 9.49 (53–97) years and 57.4% were male. At the entrance, average hemoglobin was 95.4 ± 25.1 (46–150) mg/dL, systolic blood pressure 115.10 ± 18.64 (80–159) mmHg and heart rate 79 ± 10.7 (50–99) bpm. The mean days of hospitalization was 6.56 ± 5 (2–40) days and the mean hemoglobin at discharge was 104.6 ± 16.9 (81–142) mg/dL. 22.1% of the patients were on NSAIDs; 45.6% PAAs and 42.7% on ACOs. Differences were found between patients with PAAs and ACOs and the highest INR (p-0.0 and p-0.00, respectively), as well as those with OACs with a higher number of days of hospitalization (p -0.036). In the categorization of the variables, it was verified that the patients who performed ACOs had HR at entry > 80bpm and > 6 days of hospitalization (OR 0.22, 95% CI 0.075–0.67, p-0.007 and OR 3.68, 95% CI 1.34–10.13, p-0.012, respectively). The use of NSAIDs did not present statistical significance in the influence of those variables.

Conclusion: The use of OACs influences the presentation and evolution of hemorrhage and is associated with a greater number of days needed for surveillance and treatment. Given the increasing use of these drugs, it is important to rethink the indications as well as the risk-benefit of use.

Disclosure: Nothing to disclose

P1643 CAN METABOLIC AND LIFESTYLE RISK FACTORS PREDICT COLONIC ADENOMATOUS POLYPS?

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Introduction: Recent studies have suggested that metabolic and lifestyle risk factors (including metabolic syndrome, obesity, diabetes mellitus and tobacco smoking) may increase the risk of developing colonic adenomatous polyps.[1–2] Strong evidence pointing towards an association between metabolic syndrome and colonic adenomas, may lead to new recommendations in colonic screening.

Aims and Methods: We analysed whether metabolic and lifestyle risk factors are associated with colonic adenomas. A prospective study on patients over the age of 50 undergoing a screening colonoscopy at Mater Dei Hospital was performed. Exclusion criteria included a history of inflammatory bowel disease, family history of colorectal cancer and previous colonic malignancy. We collected data on weight, body mass index (BMI), waist circumference, history of hypertension, diabetes and hyperlipidaemia, smoking, level of exercise done (using the Godin Leisure-Time Exercise Questionnaire), fasting glucose, triglyceride and HDL cholesterol level. A BMI ≥25 was considered as 'overweight.' The National Cholesterol Education Program (NCEP) Adult Treatment Panel III criteria were used to define 'metabolic syndrome.' Statistical analysis was performed using Fisher's exact test. *P*-value ≤ 0.05 was considered statistically significant. The presence or absence of colonic adenomatous polyps at colonoscopy was documented.

Results: 72 patients were recruited (51.4% were male). 40.3% of patients had one or more colonic adenomas. 40.3% patients had metabolic syndrome. 81.9% patients were categorized as overweight. 29.2% patients had diabetes mellitus. 18.1% patients were active smokers. 51.3% of patients had a sedentary or insufficiently active lifestyle (total leisure activity score < 14). See table 1.

Conclusion: Our study did not confirm the previously documented associations between metabolic and lifestyle risk factors and colonic adenomas. Further data from large screening centres may help establish the risk of adenomatous polyp formation in patients with metabolic syndrome.

Risk Factor	Present	Not present	Fisher exact test statistic value
Metabolic syndrome	10 (13.9%)	19 (26.4%)	0.47
Overweight	22 (30.6%)	7 (9.7%)	0.35
Diabetes mellitus	9 (12.5%)	20 (27.8%)	0.8
Active smokers	4 (5.6%)	15 (20.8%)	1
Sedentary lifestyle	15 (20.8%)	14 (19.4%)	0.81

[Table 1: Table showing the number of patients who had adenomas compared to the presence or absence of risk factors]

Disclosure: Nothing to disclose

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P1644 HOW OLD IS OLD IN COLORECTAL CANCER

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Introduction: How old is really old is a controversial topic in colorectal cancer. Whether the old patients did have different outcomes comparing with younger CRC.

Aims and Methods: Our study aims to determine an optimal cutoff age of defining older patients in CRC, and present a real-world impact of the factor of old on CRC, which could provide more evidence in future clinical practices.

A total of 76,858 eligible patients from Surveillance, Epidemiology and End Results (SEER) database were included in the study. Cox proportional hazards regression model and chow test were used to explore the suitable cutoff age. The propensity score matching method was performed to adjust the heterogeneity between the groups. Kaplan-Meier survival curves were plotted. Competing risk regression model was used to explore the impact of age on cancer-specific death (CCSD) and non-CSD. An external validation was performed based on the data from 1998 to 2003 from SEER database.

Results: The age of 70 years was determined as the optimal cutoff value. Based on the cutoff value, patients was divided into younger group ($n = 51,915$, < 70 years of old) and older group ($n = 24,943$, ≥ 70 years of old). Compared with younger patients, older patients were related with high rate of male, Caucasians, right CRC, mucinous carcinoma, poorer differentiated grade, and more likely to have less lymph nodes sampled, less possibility to receive chemotherapy and radiotherapy. After adjustment for covariates and propensity score weighting, older patients (age ≥ 70 years) remained associated with decreased CSS (HR, 1.67 95 CI, 1.60–1.74, $p < 0.001$). To account for competing risks (non-CCSD), the competing analysis indicated that older group did have more CCSD as well as increased non-CCSD. The external validation consistently showed that age of 70 years was a suitable cutoff value and older patients have poorer prognosis.

Conclusion: The age of 70 was a suitable cutoff value for defining "young". Old Ptients with CRC was not only associated with more non-CCSD but also more CCSD. Old patients might receive extra strengthened treatment if possible.

Disclosure: Nothing to disclose

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P1645 ENDOSCOPIC FINDINGS IN A COLORECTAL SCREENING PROGRAMME BELOW THE THRESHOLD OF 100 NG/ML (50–99 NG/ML)

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Introduction: The colorectal screening programmes based on the detection of FOBT (FIT – Faecal Immunological Test) in asymptomatic subjects between 50–69 years old, has proved its efficacy in the reduction of incidence and mortality of colorectal cancer (CRC). The established threshold in this context is 100 ng/mL. Given that values over 50 ng/mL are considered positive outside of the screening programme, there might be a percentage of asymptomatic individuals with values between 50–99 ng/mL that could have undetected lesions.

Aims and Methods: We aimed to analyse the endoscopic findings in patients included in the CRC screening programme with values of FIT between 50–99 ng/mL.

We retrospectively analysed the FIT results (OC-SENSOR, Biogen®) received at our hospital in the first round of screening between the years 2014–2016. We selected those patients with results between 50–99ng/mL that underwent a colonoscopy as indicated by their GP as screening. As a control group we used subjects from the same programme with FIT$\geq$100.

Results: A total of 989 subjects between 60–69 years old presented FIT results ranging from to 99ng/ml. 70 (7%) of them underwent colonoscopy. We detected adenomas in 32 (45.7%), high-risk adenomas in 14 (20%) and CRC in 2 (2.9%). In the table, we present the results comparing with the control group. Stratifying the analysis by sex, the% of adenomas (54.9%vs74.9%; $p = 0.13$) and high-risk adenomas (32.3%vs57.3%; $p = 0.05$) in male individuals differ with statistical significance from the control group.

Conclusion: The threshold of FIT established in the CRC population screening programme is efficient but can increase the percentage of false negatives. It is necessary to evaluate these results with wider series to find the risk factors associated to the false negatives and propose changes in the threshold or in the screening intervals.

	Screening group (FIT$\geq$100)	FIT 50–99	p-value
n	1270	70	
Age (years)	65.27	65.47	0.705
Sex (male)	744 (58.6%)	31 (44.3%)	0.018
Complete colonoscopy	1248 (98.3%)	69 (98.6%)	0.849
Adenomas	879 (69.2%)	32 (45.7%)	0.00
Male	557(74.9%)	17 (54.8%)	0.13
Female	322(61.2%)	15(38.5%)	0.05
High risk adenomas	608 (47.9%)	14 (20%)	0.00
Male	426 (57.3%)	10 (32.3%)	0.05
Female	182(34.6%)	4 (10.3%)	0.01
CRC	105 (8.3%)	2 (2.9%)	0.074
Male	71 (9.3%)	1 (3.3%)	0.212
Female	34 (6.5%)	1 (2.6%)	0.285

[Comparative of endoscopic findings FIT 50–99 vs FIT > 100 (control group)]

Disclosure: Nothing to disclose

P1646 COLORECTAL CANCER INCIDENCE AND MORTALITY REDUCTION IN THE CZECH REPUBLIC – EFFECT OF THE NATIONAL SCREENING PROGRAM?

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Introduction: The organized non-population based National Colorectal Cancer (CRC) Screening Program in the Czech Republic has been running since year 2000. In January 2014, the transition to population-based setting has been implemented. Currently, the annual immunochemical FOBT (FIT) is offered at the age 50–54, followed by FIT+ colonoscopy, if positive. In age of 55, there is a choice of either FIT biannually or screening colonoscopy in 10-years interval.

Aims and Methods: The main target lesions of the CRC screening program are the adenomas and early cancers. Therefore, the relation between number of colonoscopies/endoscopic polypectomies and CRC incidence and mortality decrease was evaluated. The analysis was based on the aggregate data from the Health Insurance Companies Databases, Preventive Colonoscopies Database and National Oncology Registry.

Results: Between years 2000 and 2015, there was significant reduction of the CRC incidence (18.4%) and mortality (32.4%) observed. The number of colonoscopies and endoscopic polypectomies has been raising continuously every year. In 2015, there were 264,399 colonoscopies performed from the following indications: 227,905 (86.2%) symptoms, follow-up and therapy; 23,463 (8.9%) FIT positivity and 13,031 (4.9%) screening at age $\geq$ 55. In the same year, overall 60,120 endoscopic polypectomies were done (22.7% of all colonoscopies) in following age groups: 5,272 in age $<$ 50; 5,627 in age 50–54 and 49,221 in age $\geq$ 55. In 36,494 colonoscopies performed within the organized CRC screening program in year 2015, there were 14,085 (38.6%) adenomas and 969 (2.7%) cancers diagnosed. 40.0% of the adenomas were advanced ($\geq$ 10 mm, villous component, high-grade dysplasia). Majority of the cancers found were in stage I (45%) and II (18%).

Conclusion: There is a very likely connection between the high number of diagnostic/therapeutic colonoscopies and CRC incidence and mortality reduction. To assess the benefit of the screening program to this effect, the comprehensive individual data from the new National Registry of Reimbursed Health Services needs to be evaluated.

References: Supported by the Czech Ministry of Health grant No. 17-31909A and projects MO1012 and Progres Q28/LF1.

Disclosure: Nothing to disclose

P1647 RIGHT-SIDED LESIONS CHARACTERISTICS AND SURVIVAL IN A POPULATION-BASED COLORECTAL SCREENING PROGRAMME

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Introduction: Colorectal cancer (CRC) is one of the most frequent cancer entities in Europe and most cases of CRC arise through malignant transformation of benign adenomas known as the adenoma-to-carcinoma-sequence. Screening colonoscopy is less effective in reducing the incidence of proximal compared to distal colorectal cancer, presumably because of missed adenomas and advanced lesions during

endoscopy. Thus, effectiveness and success of colorectal cancer (CRC) screening programs depend decisively on the quality of the endoscopic procedures.
Aims and Methods: We aimed to provide a detailed analysis of the epidemiology and survival of right-sided detection lesions (adenomas and CRC) in a population based screening programme with a high participation and colonoscopy compliance rates. We collected data retrospectively from 42,267 colonoscopies, 4,823 patients with adenomas and 2,180 with CCR were diagnosed, from January 2009 to December 2014. Data of clinical characteristics of patients, screening history, endoscopic procedure and histology results were collected.
Results: During the study period, 2,145 screening cancers (SCRC), 16 post-colonoscopy interval cancers (PCICRC) and 19 surveillance cancers (PCSCRC) were diagnosed. The rate of post-colonoscopy cancer (PCCRC) for the right-sided was 0.3% and for left-sided 0.6%. 20% of the SCRCs were located in the right colon. The mean age was 62.6 ± 5.4 years, slightly lower than left-sided, being 46.4% in the age range 64–69 years. 62.8% were men compared to 66.4% in left-sided. We did not find differences in the distribution in the deprivation index, nor in the stage at the diagnosis time. In the right-sided 68.1% were in early stage. The median µg Hb/g faeces detected by the immunochemical test in the right-sided was 234.9 (IQR = 1428), finding a significant difference with left-sided, 526.0 (IQR = 2105); $p < 0.0001$. The degree of differentiation was also different: 93.5% well-moderate in right-sided and 95.9% in left-sided; $p = 0.043$. We did not find difference in endoscopists adenoma detection rates (ADT). The 5-year survival for right-sided was 87.2% with an average of 7.86 years and 90.8% for left-sided with an average of 7.90 years; $p < 0.001$.
Regarding adenomas, 26.5% had right—side location. We did not find differences in endoscopists ADTs between locations. We found significant differences ($p < 0.0001$) regarding the histology of the adenomas, being mostly tubular in right-sided and tubulovillious in left-sided. The mean size of the largest polyp was somewhat higher in the left colon (13.9 ± 8.1 mm) with respect to the right colon (13.7 ± 12.6 mm).
The PCSCRC were located in right colon in 31.6% of the cases. 83.3% of right-sided were diagnosed at early stage. We did not find differences in mortality between both locations.
The PCICRC were located in 31.2% in right colon. 80% had good preparation in the previous colonoscopy. 20% had an incomplete resection of the polyps in a previous colonoscopy. 40% of the locations in the right colon were diagnosed at early stage. 2 patients have died, having the cancer in right location.
Conclusion: Available evidence is supporting the hypothesis that the natural history and survival of lesions in the right and left colon differ. Screening programs have greatly increased the detection of premalignant lesions. It is important to know the results and characteristics related to the locations of the lesions to implement measures that increase the effectiveness of the screening programs, improving survival, especially in right colon lesions.
Disclosure: Nothing to disclose

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P1648 MITOTIC AND APOPTOTIC ACTIVITY IN SPORADIC COLORECTAL NEOPLASIA

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Introduction: Colorectal cancer (CRC) is third most commonly diagnosed cancer worldwide. Dysregulation of mitosis and apoptosis contributes to the development of colorectal neoplasia.
Aims and Methods: The aim of the prospective study was to evaluate mitotic and apoptotic activity of epithelial cells at each stage of colorectal neoplasia.
A total of 61 persons were enrolled into the study: 18 patients with non-advanced colorectal adenoma (non-a-A), 13 patients with advanced colorectal adenoma (a-A), 13 patients with CRC and 17 controls: individuals with normal findings on colonoscopy. Biopsy samples were taken from pathology (patients) and healthy mucosa (patients and healthy controls). Samples were formalin-fixed paraffin-embedded and stained with haematoxylin-eosin. Mitotic and apoptotic activity were evaluated in lower and upper part of the crypts and in the superficial compartment. Apoptotic activity was also assessed using detection of activated caspase-3.
Results: In controls, mitotic activity was present in lower part of crypts, accompanied with low apoptotic activity. Mitotic and apoptotic activity decreased (to almost zero) in upper part of crypts. In superficial compartment, increase in apoptotic activity was observed. Transformation of healthy mucosa into non-a-A was associated with significant increase of mitotic activity in lower and upper part of the crypts and with significant increase of apoptotic activity in all three compartments; $p < 0.05$. Transformation of non-a-A into a-A did not lead to any further significant increase in apoptotic activity, but was related to significant increase in mitotic activity in upper part of crypts and superficial compartment. A significant decrease in apoptotic activity was detected in all three comparments of CRC samples compared to a-A; $p < 0.05$.
No differences in mitotic and apoptotic activity between biopsies in healthy controls and biopsy samples from healthy mucosa in patients with colorectal neoplasia were observed; $p > 0.05$.
Mitotic and apoptotic activity was not different in the left sided colonic neoplasia (distally from splenic flexure) compared to samples from right-sided colonic neoplasia; $p > 0.05$. No differences in mitotic and apoptotic activity were found in biopsies from normal tissue in patients with right-sided neoplasia when compared to normal tissue in patients with left-sided colonic neoplasia; $p > 0.05$. No differences in mitotic and apoptotic activity between females and males were observed; $p > 0.05$.
Detection of activated caspase-3 confirmed the above findings in apoptotic activity.
Conclusion: Significant dysregulation of mitosis and apoptosis during the progression of colorectal neoplasia, corresponding with histology, was confirmed. In patients with sporadic colorectal neoplasia, healthy mucosa does not display different mitotic and apoptotic activity compared to mucosa in healthy controls and therefore adequate endoscopic/surgical removal of colorectal neoplasia is sufficient.

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Disclosure: Nothing to disclose

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P1649 EXOGENOUS AND ENDOGENOUS ASSOCIATED FACTORS TO EARLY ONSET COLORECTAL CANCER

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Introduction: Early onset colorectal cancers (eoCRC), defined as arising before 50 years of age, are a growing health hazard in western and eastern countries alike. The incidence of colon and rectal cancers in young individuals is projected to increase by as much as 90% and 140%, respectively, by 2030. Although several known cancer risk factors have been investigated, there is no single compelling explanation for this epidemiological trend. While some eoCRC are associated with germline mutations in cancer predisposition genes, these appear to account for only a fraction of these cancers (~20%) and do not explain increasing incidence.
Aims and Methods: To investigate the role of exogenous risk factors (alcohol intake and smoking habits) and endogenous conditions (delays in diagnosis, gastrointestinal hereditary tumors) as associated factors of eoCRCs.
Clinical, anamnestic and pathological data were retrieved on eoCRC patients from June 2017 to April 2018. These patients were compared with a group of late onset CRC (loCRC) evaluated in the same period.
Results: We enrolled 33 eoCRCs and 48 loCRCs. According to definition, eoCRC patients were younger than loCRC, with a mean age of 40.7 ± 7.3 and 66.1 ± 9.8, respectively ($p < 0.001$). Gender was not different in the two groups with a prevalence of females (54.5% in eoCRCs and 52.1% in loCRCs). The diagnostic delay was higher in eoCRC group: only 42.4% of eoCRCs received the diagnosis in the 6th months from symptoms onset versus 100% of loCRC patients ($p < 0.001$). The syndromic familiarity (Lynch syndrome) was more frequent in eoCRC (12%) than loCRC group (0%), with a statistically significant difference ($p = 0.02$).
We also found a statistically significant difference in alcohol habit, with a percentage of no-drinker in 66.7% of eoCRCs and 41.7% of loCRCs ($p = 0.04$). Also, there was a trend through significance for no-smokers in eoCRCs.
Conclusion: CRCs should be considered earlier in the differential diagnosis in young patients. We confirmed alcohol as cofactor in the development of eoCRC and we underlined that familiar history should be collected to identify mutations carries.
Disclosure: Nothing to disclose

P1650 SLC25A22 MEDIATES EPIGENETIC REPROGRAMMING TO PROMOTE WNT/β-CATENIN SIGNALING AND CANCER STEMNESS IN *KRAS*-MUTANT COLORECTAL CANCER

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Introduction: Epigenetic dysregulation plays essential roles in the tumorigenicity of *KRAS*-mutant colorectal cancer (CRC). However, the mechanism underlying epigenetic deregulation and its functional implications remain unclear. Our preliminary data revealed that *KRAS* gain-of-function mutations in colonic and CRC cells induced epigenetic reprogramming via methylation of DNA and histones; and that *SLC25A22,* a mitochondrial glutamate transporter, plays a key role in this process.
Aims and Methods: We aim to 1) investigate the role of SLC25A22 in the epigenetic reprogramming in *KRAS*-mutant CRC; 2) elucidate the mechanisms whereby epigenetic alterations mediate an oncogenic effect; and 3) devise a therapeutic strategy to target epigenetic reprogramming in *KRAS*-mutant CRC.
Results: Using isogenic cell lines harbouring wild-type and mutant *KRAS* ($DKS8^{WT}$ vs $DLD1^{G12D}$; $1CT^{WT}$ vs $1CT^{G12V}$), we demonstrated that mutant *KRAS* drives histone and DNA hypermethylation. Stable metabolomic analyses revealed that mutant *KRAS* drives glutaminolysis via TCA cycle, leading to increased succinate/fumarate to α-ketoglutarate (αKG) ratio. An altered metabolite ratio, in turn, suppressed histone/DNA demethylases, thereby inducing hypermethylation. We thus utilized the CRISPR-Cas9 approach to knockout *SLC25A22*, a mitochondrial glutamate transporter essential for glutaminolysis, in two *KRAS*-mutant CRC cell lines (DLD1, SW1116).
SLC25A22 knockout reversed *KRAS*-mediated glutaminolysis and reduced succinate/fumarate to αKG ratio, which consequently resulted in enhanced DNA demethylation, as evidenced by the increased levels of 5-hmC. Illumina 860K Methylation BeadChip was employed to profile the methylome of *SLC25A22* knockout DLD1 cells. Pathway analysis unveiled that WNT and cadherin signaling pathways as top pathways aberrant methylated in DLD1-control cells as compared to *SLC25A22* knockout cells. Of note, *SLC25A22* knockout initiated promoter demethylation and re-expression of genes within protocadherin cluster (*PCDHαβγ*), putative tumor suppressors that were shown to negatively WNT/β-catenin signaling. Consistently, *SLC25A22* knockout or ectopic expression of *PCDHαβγ* isoforms suppressed WNT/β-catenin signaling, as evidenced by decreased nuclear localization of active β-catenin, TOPflash activity and reduced expression of WNT target genes. Moreover, histone methylation profiling identified that *SLC25A22* knockout reduced H3K4 methylation, particularly H3K4me3, a histone mark that directs active transcription. Chromatin-immunoprecipitation revealed that *SLC25A22* knockout suppressed enrichment of H3K4me3 at the promoters of *ASCL2* and *LGR5*, WNT target genes that are markers of CRC stem cells. Accordingly, *ASCL2* and *LGR5* expression were diminished in *SLC25A22* knockout CRC cells. Corroborating our mechanistic findings, *SLC25A22* knockout suppressed tumorigenicity and stemness of CRC cell lines *in vitro* and in xenograft models.
Given that cancer can promote methylation of DNA/histone by either promoting methylation or inhibiting demethylation, we hypothesized that it may be possible to reverse aberrant DNA methylation and tumorigenesis by co-targeting methyltransferases (DNMT inhibitor) and glutaminolysis (GLS inhibitor). Concomitant administration of 5-Aza and GLS inhibitors (compound 968, BPTES, or CB839) synergistically inhibited growth of *KRAS*-mutant CRC cell lines.
Conclusion: *SLC25A22*-dependent glutaminolysis drives DNA/histone hypermethylation in CRC and promotes tumorigenesis and cancer stemness. A novel epigenetic therapy co-targeting DNMTs and GLS synergistically suppressed the growth of KRAS-mutant CRC cells.
Disclosure: Nothing to disclose

P1651 TRANSCRIPTION FACTORS ATF6 AND XBP1S OF THE UNFOLDED PROTEIN RESPONSE REDUCE COLORECTAL CANCER CELL PROLIFERATION AND STEMNESS THROUGH INTERACTION WITH PERK

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Introduction: The unfolded protein response (UPR) is a cellular stress response activated upon accumulation of misfolded proteins in the lumen of the endoplasmic reticulum (ER). Activation of the UPR results in differentiation of intestinal epithelial stem cells and colon cancer stem cells via UPR kinase PERK, which results in increased chemosensitivity.
Activation of PERK and downstream phosphorylation of eIF2α attenuates protein translation. Transcriptional activity of XBP1 and ATF6 in contrast result in expansion of the ER. Previously, it was shown that knockout of XBP1 increases proliferation and tumor formation in mice. Therefore, we hypothesize that XBP1 signaling results in reduction of stemness and cellular proliferation in colon cancer cells. Since XBP1 and ATF6 have overlapping transcriptional targets, we additionally examine colorectal cancer cell proliferation upon ATF6 activation.
Aims and Methods: We generated LS174T colorectal cancer cell lines that stably carry transcripts enabling doxycycline inducible expression of the active form of XBP1 (XBP1s) or ATF6 (ATF6-373 truncated protein). In these cell lines, we measured downstream activation of UPR signaling or intestinal stem cell markers using quantitative RT-PCR or protein immunoblot. We determined proliferation using crystal violet and EdU incorporation. Global translation was measured with ^{35}S methionine incorporation.
Results: Enforced expression of transcriptionally active forms of XBP1 or ATF6 resulted in marked increase of downstream UPR target genes GRP78 and CHOP. Cellular proliferation was decreased significantly. We additionally found reduced expression of intestinal epithelial stem cell markers OLFM4 and LGR5. Interestingly, we found that XBP1s or ATF6 increased activation of PERK-eIF2α signaling, with decreased cellular translation as a result. Inhibition of eIF2α phosphorylation via constitutive expression of phosphatase GADD34 rescued XBP1 and ATF6 induced growth retardation.
Conclusion: Activation of UPR signaling in the intestinal epithelium, adenomas and colorectal cancer cells results in differentiation of stem cells. We observe that activation of transcription factors XBP1s and ATF6 inhibit proliferation and reduce translation in LS174T colon cancer cells. XBP1s and ATF6 induced proliferation inhibition exposed a novel interaction with PERK-eIF2α signaling. We identify eIF2α phosphorylation as responsible for XBP1s and ATF6 induced differentiation. Targeting PERK-eIF2α in colon cancer may thus be utilized for colorectal cancer cell differentiation and to increase chemosensitivity.
Disclosure: Nothing to disclose

P1652 KLOTHO SUPPRESSES SENESCENT MESENCHYMAL CELLS AND THE PROGRESSION OF COLORECTAL CANCER BY INHIBITING THE SENESCENCE-ASSOCIATED SECRETORY PHENOTYPE VIA THE NF-κB PATHWAY

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Introduction: The risk of colorectal cancer (CRC) is increasing with age, and cellular senescence plays an important role in tumourigenesis. We have previously showed that Klotho, an anti-senescence gene, was regulated by DNA hypermethylation and involved in the CRC cell proliferation.
Aims and Methods: This study was designed to determine the molecular mechanism of Klotho in cellular senescence and expression of senescence-associated secretory phenotype (SASP), and clarify its clinical significance and biological functions in CRC. Immunohistochemical staining was applied to identify Klotho expression in 143 CRC tissues. Senescent human mesenchymal cells were established and co-cultured with CRC cell lines. *In vitro* and *in vivo* studies were performed to determine the growth and metastatic phenotypes of colon cancer cells in response to senescent cells. Series of the senescence-associated secretory phenotype (SASP) molecules were screened after administration with recombinant Klotho. CCL-2, a candidate SASP, was validated and its functional role in CRC was studied.
Results: IHC staining showed that Klotho was down-regulated in CRC tissues and closely correlated with elderly age. High expression of Klotho was an independent prognostic factor for favorable survival in CRC patients. In addition, senescent mesenchymal cells significantly stimulated the proliferation of CRC

cells, enhanced their ability of cell migration and invasion *in vitro* and *in vivo* xenograft mouse models, while these effects could be partially blocked by the exogenous administration with Klotho. CCL-2, a SASP component, was validated to be upregulated in senescent mesenchymal cells. The pretreatment of recombinant Klotho blocked the DOX-induced senescence process, reduced the secretion of CCL-2 and restored the tumour-promoting effect of the senescent cells. Further investigations revealed that Klotho-mediated inhibition of NF-κB significantly suppressed CCL-2 expression.
Conclusion: Senescent mesenchymal cells may alter the tissue microenvironment via the secretion of SASP including CCL-2, promoting colorectal cancer growth and metastasis, which could be blocked by Klotho pretreatment. The inhibition of senescent stroma-cancer signaling pathways by Klotho has the potential to restrain colorectal cancer progression.
Disclosure: Nothing to disclose

P1653 S100P AS A NOVEL HYPOMETHYLATION TARGET IN SESSILE SERRATED ADENOMA (SSA/P)-CANCER SEQUENCE: A GENOME-WIDE DNA METHYLATION ARRAY ANALYSIS

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Introduction: A sessile serrated adenomas/polyp (SSA/P), one of the serrated polyps, is predominantly located in right-side colon. A SSA/P is recognized as a precursor lesion of colorectal cancer (CRC) characterized by BRAF mutation, CpG island methylator phenotype (CIMP), and microsatellite instability (MSI). However, the role of DNA hypomethylation during SSA/P-cancer sequence is unknown.
Aims and Methods: In this study, we aimed to investigate the biological relevance of DNA hypomethylation in SSA/P-cancer sequence. DNA hypomethylation array analysis of 7 SSA/Ps, and 2 cancer in SSA/P specimens were performed with a microarray-based integrated analysis of methylation by isoschizomers (MIAMI) method using normal colorectal epithelia as a reference. Levels of mRNA were determined by Taqman realtime PCR. The SSA/P organoid was established using biopsy specimens obtained from SSA/P with colonoscopy. The knockdown of the gene in SSA/P organoids and CRC cell lines with BRAF mutation (HT29 and WiDr) was performed using a lentiviral shRNA vector and siRNA respectively. The cell viability of SSA/P organoids and CRC cell lines were determined by ATP assay and BrdU colorimetric assay respectively. The DNA hypomethylation at CpG sites of the gene was quantitated by MassARRAY analysis. The protein expression was evaluated by immunohistochemistry and Western blotting.
Results: The mean number of hypomethylated genes in SSA/P and cancer in SSA/P were 41.6 ± 27.5 and 214 ± 19.8, respectively, showing astepwise increment of hypomethylation during the process of formation of SSA/P and subsequent cancer. The novel 4genes (S100P, S100α2, PKP3 and MUC2) were identified as most commonly hypomethylated genes in SSA/P. Of these, mRNA levels of S100P, S100α2, and MUC2 were significantly elevated in SSA/P than in normal epithelia. Particularly, the mRNA and protein expression levels of S100P were even higher than normal epithelia. The knockdown of the S100P gene in SSA/P organoids inhibited cell growth by 65% ($P < 0.01$). Similarly, the knockdown of S100P gene in HT29 and WiDr cells inhibited cell growth by 22 and 43% respectively ($P < 0.05$ respectively). The significant hypomethylation was detected at specific CpG sites in the intron 1, exon 1 and 5'-flanking promoter region of the S100P gene. The hypomethylation at the CpG sites in the intron 1 wasthe strongest among these regions.
Conclusion: Our results suggest that DNA hypomethylation including S100P, S100α2, and MUC2 hypomethylation is closely associated with SSA/P-cancer sequence. S100P, which is overexpressed probably due to hypomethylation at the specific CpG sites in the intron 1, exon 1 and 5'-flanking promoter region, plays an important role in cell proliferation of SSA/P. Thus, S100P may be a novel therapeutic target for colorectal carcinogenesis through SSA/P-cancer sequence.
Disclosure: Nothing to disclose

P1654 THE GUT MICROBIOTA INFLUENCES INTESTINAL EPITHELIAL PROLIFERATIVE POTENTIAL

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Introduction: The intestinal epithelium is comprised of a single layer of cells which serves a number of critical functions including the formation of a physical barrier to environmental pathogens and chemical substances, and the absorption of essential nutrients, electrolytes and water. It is also the site of the gut microbiota, a complex and diverse community of bacteria, viruses and fungi, which exists in a mutually beneficial relationship with the human host. The epithelial barrier is maintained through tightly regulated processes of stem cell renewal, epithelial maturation, cell migration and cell death. Failure to finely coordinate these processes can lead to disease states such as cancer.
Aims and Methods: In this study, we aimed to investigate and characterise the role of the intestinal microbiota on epithelial cell proliferation. We determined the rates of epithelial proliferation in the intestines of Specific-Pathogen-Free (SPF) mice and Germ-Free (GF) mice. We utilised a previously described method which integrates cell tracking using the thymidine analogue Bromodeoxyuridine (BrdU) in crypt-villus units, with a tailored mathematical model, to determine the spatiotemporal dynamics of epithelial cell behaviour in SPF and GF conditions.
Results: The rate of epithelial cell production in GF conditions was significantly slower in the colon, ileum and jejunum in comparison to SPF conditions. In the duodenum, there were no significant differences in proliferation rates in GF and SPF conditions. Cell production rates progressively decreased towards the distal part of the intestine, which inversely correlate with the concentration of organisms constituting the intestinal microbiota.
Conclusion: These findings indicate that the gut microbiota plays an important role in determining intestinal epithelial cell proliferation rates. This relationship may have important implications in disease states such as cancer and inflammatory bowel disease, where differences in microbial signatures are known to exist. In turn, it may be possible in the future to harness this knowledge to alter disease progression by modifying the host microbiota.
Disclosure: Nothing to disclose

P1655 MOLECULAR BIOLOGY ANALYSES USING NEXT-GENERATION SEQUENCING IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH INTESTINAL CANCERS

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Introduction: Molecular analysis of intestinal cancers is determined routinely in clinical practice. Data in the subgroup of tumors occurring in IBD population remain scarce. Two recent studies (1,2) suggest that colorectal tumors developed in IBD patients display different molecular profile than the sporadic ones and may vary considering the subtype of IBD.
Aims and Methods: We aimed to characterize the spectrum of genomic alterations in SBA and CRC in patients with IBD
We included retrospectively all the patients treated for both SBA and CRC in a French tertiary IBD unit from 2001 to 2017. Samples of the primitive tumor were extracted from biopsies made by colonoscopy or from a surgical specimen and analyzed on the same molecular biology platform. Samples were analyzed using Next-Generation Sequencing (NGS) with the Truesight Tumor 26 preparation Kit (Illumina) after DNA quality control testing. IDH1 status was determined using High Resolution Melting (HRM) analysis on the LightCycler 480 System (Roche).
Results: Among a cohort of 5716 IBD files (Crohn's Disease: CD, Ulcerative Colitis: UC), 51 (0.9%) patients were diagnosed with SBA or CRC during the study period and were all included. In 7 cases (14%), samples analysis didn't provide interpretable data (DNA deterioration n = 6; insufficient histological specimen n = 1). In 13 cases (25.5%) specimens are undergoing complementary quality control. Among the 31 remaining patients, 11 (21.5%) have reliable DNA support but are not fully interpreted yet. In total, 20 patients (39%) were analyzed (male 55%; CD 50%, colorectal cancer 90%, median age at cancer diagnosis: 42.7 years, median time between IBD and cancer diagnosis: 16.1 years). In the 10 CD patients, tumor was located to the colon in 6 cases, the rectum in 2 cases and the small bowel in 2 cases. In the 10 UC patients, tumor was colonic in 5 cases and rectal in the 5 other cases. At cancer diagnosis, IBD was active in 53% of the patients (symptoms and/or endoscopic lesions not related to tumor onset) and 30% were exposed to an immunosuppressive agent (azathioprine mainly) or anti TNF therapy (infliximab mainly). In 13 cases, tumor was initially localized (colonic n = 9; rectal n = 4). After a median follow-up of 36,3 months a remission was maintained in 7 cases (54%). Median overall survival of these patients with TNM I to III status was 27 months. In 13 cases, (relapsers n = 6; metastatic at diagnosis n = 7; colorectal n = 11) patients presented with metastasis. In those patients, all received double or triplet chemotherapy (first-line only: 31%). The drugs used were: 5FU (100%), Oxaliplatin (85%), Irinotecan (54%), Bevacizumab (54%), anti-EGF-R agents (54%). The median overall survival of these metastatic patients was of 21 months.
Of the 20 NGS analyses, 17 samples presented a known functional P53 mutation (85%). An APC mutation was found in 1 patient (5%). NRAS exons 2 and exons 4 were mutated in 4 (20%) and 1 (5%) cases respectively. Two PIK3CA (10%) and SMAD4 (10%) (Both in CD patients) mutations were found. There was no KRAS, GNAS, BRAF, HER2 and IDH1 mutation. No significant difference in genomic alterations was found between tumors developed on CD and those on UC.
Conclusion: In this preliminary descriptive study, the prognosis of intestinal IBD cancer patients seems poorer than sporadic ones. We observed a high P53 mutation and a low APC and RAS mutations rates, which seem to be different from sporadic colorectal cancers. Conversely to some data in the literature, no IDH1

alteration was found. Further prospective data are needed to confirm those results.
Disclosure: Nothing to disclose

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P1656 SCNN1B FUNCTIONS AS A TUMOR SUPPRESSOR IN COLORECTAL CANCER BY INHIBITING THE MEK-ERK PATHWAY

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Introduction: Promoter hypermethylation plays a vital role in cancer through transcriptional silencing of tumour suppressive genes. Integrated epigenomic and transcriptomic analyses of the Cancer Genomic Atlas (TCGA) colorectal cancer (CRC) cohort showed that SCNN1B as an outlier gene aberrantly silenced in CRC. In this study, we investigated the function, molecular mechanism and clinical significance of SCNN1B in CRC.
Aims and Methods: In this study, we aim to 1) evaluate the clinical significance of SCNN1B in CRC; 2) investigate the biological function of SCNN1B in CRC; and 3) to elucidate the molecular pathways involved in tumor suppressive effect of SCNN1B. Clinical significance was validated by methylation-specific PCR (MSP), bisulfite sequencing (BGS) and real-time PCR analysis. In vitro functional assays were carried out by cell viability, colony formation, apoptosis, cell cycle, cell invasion and migration assays. Pathway analysis was performed by Gene Set Enrichment Analysis (GSEA), and validated by Western blot and luciferase reporter assay.
Results: Using volcano plots analyses of RNAseq and 450K methylation array dataset, we identified that SCNN1B is an outlier gene in TCGA CRC cohort which is silenced at mRNA level, but hypermethylated at its promoter CpG sites. RT-PCR showed that SCNN1B mRNA was silenced in all ten CRC cell lines tested compared to normal colonic tissues. MSP and BGS analysis confirmed SCNN1B promoter methylation in all ten CRC cell lines. SCNN1B expression was restored by demethylation treatment, suggesting that promoter methylation mediates its transcriptional silence. In a Hong Kong CRC cohort, we validated the silencing of SCNN1B mRNA and protein expression, by real-time PCR and immunohistochemistry (IHC), respectively, concomitant with its promoter methylation. Survival analysis of TCGA dataset demonstrated that mRNA expression of SCNN1B is independently associated with good outcome in CRC ($P < 0.001$); whereas its promoter methylation predicts poor survival ($P = 0.006$), indicating that SCNN1B might be a functional tumor suppressor in CRC. Ectopic expression of SCNN1B in two CRC cell lines inhibited cell proliferation and colony formation. SCNN1B exerted its effect by inducing apoptosis and cell cycle arrest. Consistent with this, Western blot analysis revealed that activation of caspase-7 and PARP, up-regulation of cell cycle inhibitors p21, p27 and p53, together with the down-regulation of cyclin D1. Moreover, SCNN1B suppressed cell migration, as determined by wound healing assay. To probe for pathways that can be regulated by SCNN1B, GSEA analysis was performed on TCGA CRC cohort. GSEA revealed a significant association of SCNN1B with down-regulation of KRAS oncogenic signature. Consistent with this observation, Western blot showed that SCNN1B overexpression decreased the expression of p-MEK and p-ERK, key downstream factors of oncogenic KRAS. Moreover, ectopic SCNN1B expression inhibited SRE luciferase activity, indicating suppression of RAS-MEK-ERK oncogenic signalling.
Conclusion: SCNN1B is a tumor suppressor silenced by promoter methylation in CRC. It inhibits colorectal tumorigenesis via inhibition of RAS-MEK-ERK signalling. SCNN1B mRNA expression and promoter methylation may serve as an independent prognostic biomarker for CRC patients.
Disclosure: Nothing to disclose

P1657 DIAGNOSTIC AND PROGNOSTIC ROLE OF CIRCULATING CELL FREE DNA (CF DNA) IN DIFFERENT STAGES OF COLORECTAL CANCER

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Introduction: Cell-free DNA (cfDNA) represents DNA originating from dying cells and from active release from viable cells. CfDNA reflect the genomic mutation profile of the tumor. The clinical utility of blood level of (cfDNA) in patients with metastatic colorectal cancer (mCRC) hasn't been much described before.
Aims and Methods: To assess the level of (cf DNA) as a serum biomarkers in diagnosis and progression of colorectal cancer (surgically resected and non-resected) at different tumor stages. A cross sectional study was conducted on 90 persons who fulfilling the designed inclusion criteria and classified into four groups, Group I include 30 patients with colorectal cancer (pre-operative), Group II : 30 patients with colorectal cancer (post-operative), Group III : 15 patients with colorectal polyps (low grade dysplasia), Group IV : 15 healthy volunteers as control group, All participant after detailed history, clinical examination, imaging study and endoscopic assessment were subjected to routine laboratory investigation, carcinoembryonic antigen (CEA) and serum level of circulating cfDNA.
Results: The mean DNA concentration was 2.46 μg/ml, for CRC(pre-operative), 0.519 μg/ml for CRC (post-operative), 1.684 μg/ml for colorectal polyps (low-grade dysplasia) and 1.068 μg/ml for healthy controls. DNA concentration was significantly higher in CRC (pre-operative) patients compared with healthy controls ($P = 0.05$). The mean DNA concentration was significantly higher in CRC (pre-operative) patients compared with CRC (post-operative) patients ($P = 0.01$) But the mean DNA concentration was non-significantly higher in CRC (pre-operative) patients compared with colorectal polyps ($P = 0.3$). The sensitivity, specificity, positive and negative predictive values of DNA concentration in distinguishing CRC patients from healthy controls were 36.7% and 100%, 100% and 50.5% respectively.
Conclusion: Cf-DNA is a useful non-invasive tumor biomarkers and can improve diagnostic and prognostic value for CRC disease at different tumor stages, and the results suggest that the combination of cfDNA with CEA could improve the diagnostic performance for benign tumor and CRC.
Disclosure: Nothing to disclose

P1658 METACHRONOUS COLORECTAL CANCER IN A POPULATION-BASED SECREENING PROGRAMME

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Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide. Most CRC develop via the adenoma-carcinoma sequence. Screening for colorectal cancer programmes with biennial fecal occult blood test has shown to increase early diagnosis and thereby decrease the incidence and mortality. With the screening programs the endoscopic resections as a potential curative treatment has increase. Nevertheless, some lesions are potentially missed or had potential incomplete resection.
Aims and Methods: The aim of our study is to determine the incidence of the metachronous CRC and their surveillance and characteristics in a population based screening programme with a high participation rate. We collected data retrospectively from a population-based screening programme registry with 54,746 colonoscopies and 1,835 CCR diagnosed, from January 2009 to December 2014. Data of clinical characteristics of patients, screening history, endoscopic procedure and histology results were collected.
Results: The rate of metachronous cancers ($n = 18$) over those detected in the screening programme was 0.98%. The mean age was 61.76 ± 6.49 years at diagnosis, being 77.8% females. Relevant medical history: dyslipidemia 27.8%, hypertension 38.9%, obesity 28.6%, diabetes mellitus 5.6%, tabaco smokers 11.1%, alcohol risk intake 16.7%, Charlson Comorbidity Index Score ≥ 2 76.5% and most deprived index 56.3%. In 94.4% of patients, their first cancer was diagnosed at the first participation in the programme. The location of first cancer was: 38.9% rectum, 22.2% rectosigmoid junction, 22.2% sigmoid colon, 11.1% descending colon and 5.6% transverse colon. 38.9% were diagnosed at an advanced stage. In the colonoscopy of the first cancer 76.9% of patients had polyps. 50% of the patients with polyps identified in the first colonoscopy had ≥ 3 polyps and size of the biggest polyp had a mean of 22.43 ± 11.6mm. 2 patients also had synchronous cancer at the first diagnosis. Different pre-operative systemic inflammation ratios were calculated, identifying in high-risk category: 13.3% for neutropil-lymphocyte ratio, 33.3% for lymphocyte-monocyte ratio, 40% for platelet-lymphocyte ratio and 60% for Systemic immnune-inflammation index. In 10 cases (55.6%) the second cancer appeared "de novo", in 7 cases (38.9%) after an incomplete resection and in 1 case (5.6%) with a previous polyp. The mean adenoma detection rate of the endoscopist at the first colonoscopy was $34.4 \pm 8.9\%$, presenting a 35.7% of them a rate higher than 35%. The location of the second cancer in 38.9% was in right side of the colon while in the first cancer only 5.6% had right location. The median time between first and second cancer was 21.49 months (IQR: 13.46–34.37). 44.4% of patients died and survival mean was 6.97 years (IQR: 5.64–8.29). 1 year survival was 94.1%, and 5 yr-survival 82.4%. We calculated the survival for interval cancer and screen-detected cancer at the programme. Interval cancer 1-yr survival 91.2%, 5-yr survival 76.3%; screen-detected 1-yr survival 97.8% and 5-yr survival 90.1%.
Conclusion: The incidence rate of metachronous cancers at the population-based screening programme is not very high; however, it should be noted that a significant percentage of them appear after complete resection or lack of resection of a potentially cancerous polyp in the screening colonoscopy. We also highlight how second cancers have a higher prevalence in the right colon. This suggests that in the screening programs the registration of quality indicators and the application of measures to control them are fundamental.
Disclosure: Nothing to disclose

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P1659 OVEREXPRESSION OF AT-RICH INTERACTIVE DOMAIN 3A CORRELATED WITH FAVORABLE PROGNOSIS IN PATIENTS WITH RESIDUAL RECTAL CANCER AFTER PREOPERATIVE CHEMORADIOTHERAPY

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Introduction: This study aimed to explore the clinical and prognostic impact of AT-rich interactive domain 3A (ARID3A) expression in patients with residual rectal cancer who underwent neoadjuvant chemoradiotherapy (NACRT).

Aims and Methods: Between January 2006 and December 2011, the surgical specimens of 146 patients with residual rectal cancer who underwent NACRT were analyzed. To assess ARID3A expression, immunohistochemistry was performed on whole tissue sections. *KRAS* exon 2 (codons 12 and 13) and *BRAF* V600E mutation status and microsatellite instability (MSI) were determined using polymerase chain reactions.

Results: Of the 134 eligible patients, overexpression of ARID3A was found in 64.5% ($n=91$) and inversely correlated with perineural invasion ($P=0.031$). However, overexpression of ARID3A had no correlations with *KRAS* and *BRAF* mutation status, or with MSI status (all $P>0.05$). In univariate analysis, over-expression of ARID3A was significantly associated with favorable cancer-specific survival (CSS) ($P=0.006$) and disease-free survival (DFS) ($P=0.039$). Multivariate analysis revealed that overexpression of ARID3A was independently associated with favorable CSS ($P=0.030$, hazard ratio [HR] = 2.640, 95% confidence interval [CI] = 1.098–6.345) but not DFS ($P=0.082$, HR = 1.676, 95% CI = 0.937–2.996).

Conclusion: Our study showed that high nuclear expression of ARID3A can predict favorable outcomes in patients with residual rectal cancer after NACRT.

Disclosure: Nothing to disclose

P1660 OPTICAL TECHNOLOGIES FOR ENDOSCOPIC REAL-TIME HISTOLOGICAL ASSESSMENT OF COLORECTAL POLYPS – A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Accurate, real-time, endoscopic risk stratification of colorectal polyps would improve decision-making and optimise efficiency of endoscopy units. Several technologies exist to either manipulate or augment endoscopic optical outputs to enhance diagnostic accuracy. However, it is unclear how these technologies have improved over time, nor if they are sufficient for a safe 'resect and discard' or 'no resection' strategy (1, 2).

Aims and Methods: This meta-analysis aims to compare such technologies in the real-time histological prediction of colorectal polyps, documenting the current state and chronological progression of diagnostic accuracy. A systematic search strategy was applied to the databases MEDLINE, Embase and Cochrane Library in January 2018. Inclusion criteria were prospective deployment of a single endoscopic optical technology for *in-vivo,* real-time histological prediction of colorectal polyps; presenting the diagnostic accuracy in differentiating adenomas from hyperplastic or normal tissue after pathological assessment. Exclusion criteria were polyposis syndromes, inflammatory bowel disease, if the diagnosis was made *post-hoc* from images or if data were not primary. When three or more studies presented a similar technology, Bayesian bivariate meta-analysis using a binomial normal model was performed with a defined as 0.05 and 95% confidence intervals (CI) presented.

Results: Of the 3,984 studies identified, 92 were suitable for inclusion. Four types of optical technology were used on 31,337 colorectal polyps across 122 patient cohorts. Digital chromoendoscopy (n = 21,926) diagnosed adenomas with sensitivity of 0.922 (0.904–0.938) and specificity of 0.843 (0.819–0.866), with an area under the curve (AUC) of 0.86 (0.84–0.93). There was no difference between the constituent technologies of narrow-band imaging, Fuji Intelligent Chromo Endoscopy and iSCAN; or when only diminutive polyps (less than 5mm) were tested. Dye chromoendoscopy (n = 7 731) had sensitivity of 0.931 (0.904–0.952), specificity of 0.874 (0.838–0.906) and AUC 0.90 (0.81–0.96). This decreased with diminutive polyps AUC 0.74 (0.56–0.94), however this was not statistically significant. Spectral analysis of tissue fluorescence (n = 893) suffered from high false positives, with sensitivity of 0.915 (0.822–0.971), specificity of 0.625 (0.360–0.849) and AUC of 0.92 (0.72–0.97). Cellular imaging with endomicroscopy (n = 787) had sensitivity of 0.959 (0.915–0.987) and specificity of 0.939 (0.865–0.985). Subgroup analysis of high-confidence predictions, use of trained endoscopists and use of HD scopes did not significantly improve the accuracy of any technology. No single technology can currently demonstrate an estimated negative predictive value (NPV) for adenoma above 90%. Chronological aggregate meta-analysis was applied to all groups and shows a falling NPV over time. This holds when applied to trained endoscopists making high confidence predictions. Significant publication bias was evident across all technologies, appearing to over-estimate diagnostic value.

Conclusion: This is the most comprehensive meta-analysis assessing the ability of endoscopic optical technologies in real-time diagnosis of colorectal adenomas. Using a novel approach, it demonstrates that existing technologies are increasingly unlikely to meet the requirements for a safe 'resect and discard' strategy and that step-change innovation is required to disrupt clinical practice. It is likely that optical approaches may never be sufficiently accurate and that molecular data should be incorporated using techniques such as real-time mass spectrometry.

Disclosure: Nothing to disclose

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P1661 AUTOMATED EXTRACTION OF ENDOSCOPIC ADENOMA DETECTION RATES FROM ENDOSCOPIC-PATHOLOGICAL DATA IS AS SENSITIVE AND SPECIFIC AS MANUAL EXTRACTION

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Introduction: Medical data is increasingly moving into electronic formats. Endoscopic data in the UK is almost exclusively electronic. Pathology reporting of specimens taken at endoscopy is also electronic.

Although the data is digitalized much of it is captured in natural language, semi-structured formats. Furthermore pathology datasets are often stored separately to endoscopic datasets so that the merging a pathology report to a specific patients endoscopy date can be difficult. As a result, the data for one of the best validated indicators of endoscopic quality, the adenoma detection rate (ADR), is often done manually, and often inaccurately extrapolated from the endoscopy report only.

Automated extraction from text has become simplified using natural language tools. EndoMineR[1] is an open source software package written in R and is specifically designed to automate the process of extracting data from endoscopic and pathology datasets. Furthermore the package merges endoscopic and pathologic datasets by patient and (fuzzy) date and allows downstream analyses that depend on the merge between both datasets, such as the adenoma detection rate.

Aims and Methods: We aimed to determine the sensitivity and specificity of adenoma detection rates when using an automated process (EndoMineR) when compared to manual extraction.

For the manual extraction, the endoscopy reporting database was used to extract reports of all colonoscopic examinations carried out between July 1st 2017 and January 1st 2018 at St Thomas' Hospital. If the report mentioned a polypectomy having been performed, the pathology report for that endoscopy was accessed via the electronic patient record to determine whether it was an adenoma. The per endoscopist ADR was the calculated.

For the automated extraction, all pathology reports between the dates above were downloaded for all patients who underwent endoscopic examinations between the two dates. EndoMineR managed the merging of pathology and endoscopic reports for each patient at each time point. EndoMineR also extracted all adenomas, including the exclusion of reports mentioning the absence of adenomas, and calculated the per endocopist ADR.

Results: Between July 31st 2017 and Jan 1st 2018 2588 colonoscopies were performed. Endoscopic reports were available for all the endoscopies. Of the 1388 endoscopies where tissue was sent to histopathology, all the pathology reports were available. Manual extraction detected 499 endoscopies where an adenoma was detected and confirmed with histopathology. EndoMineR detected 501. Further examination of the dataset revealed that manual extraction had missed two cases such that the sensitivity and specificity of EndoMineR for this dataset was 100% and 100%. Manual extraction took 4.5 hours. The automated extraction took 5.3 seconds.

Conclusion: Automated adenoma detection rates can be calculated from semi-structured text reports accurately using merged endoscopic-pathology records. This technique should also be applicable to the detection of other pathologies detected at endoscopy and therefore has the potential to allow further metric development to assess endoscopic quality.

Disclosure: Nothing to disclose

Reference

1. https://ropensci.github.io/EndoMineR/.

P1662 DELAYING AND DRYING EFFECTS ON THE RESULTS OF GUIAIC FAECAL OCCULT BLOOD TESTING

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Introduction: In the UK guaiac-based faecal occult blood testing (gFOBt) is the primary means of national screening for colorectal cancer (CRC). However, variations in positivity rates not easily explained by background disease levels are seen across the country.
In particular, kits sent to the Eastern England Hub are 50% more likely to be tested positive than those sent to other hubs which has significant consequential affects for example on colonoscopy services.
Aims and Methods: We aimed to determine if delays in kit processing could be impacting positivity rates through the effects of sample drying.
In the Eastern Hub of the UK Bowel Cancer Screening Programme ~2500 gFOBt kits are processed daily.
1) For one month during winter 2017 received kits were randomly assigned to usual practice (test on day of receipt) or delay before testing of 2–3days. For 90% power (1 sided p = 0.05) 1,628 kits were required in each group.
2) For a further month received kits were randomly assigned to usual practice (test on day of receipt) or 'drying' with kits left for 24hrs spread out in a warm room (average temp 21°C).
Results: 1) The study consisted of n = 1783 in the no delay group and n = 1741 in the delay group.
Kit positivity of the control group was 18.4%, decreasing to 17.4% in the 2 day delayed group (n = 1192) and 16.7% in the 3 day delayed group (n = 221).
Window positivity was then investigated and showed a significant decrease in the positivity of windows 5 & 6 (the 3rd stool sample) when testing of the kit was delayed; particularly in window 6 where the proportion of positives decreased from 10.0% to 7.4%. Little effect was seen in the first 2 samples (windows 1–4).
2) In the second study n = 1793 in the control group and n = 1810 in the drying group.
Overall kit positivity was shown to decrease from 21.1% to 17.5%.
Window positivity showed a decrease in the positivity of windows 5 & 6 as with the 1st trial, but this time a larger decrease was experienced in those kits left in the warmer laboratory (10.5% to 8.4% and 11.4% to 8.0% in windows 5 & 6 respectively).
Conclusion: Positivity rates in kits delayed and dried were significantly lower than those processed quickly and whilst still moist. This was most notable for the 3rd sample from patients (i.e. the most recently sampled).
It is likely that variation in the timing of receipt and processing of samples will lead to variations in positivity rates found.
Further research is required to determine the positive predictive value of different delaying strategies for the detection of colorectal cancer in order to determine optimal operational protocols.

	Trial 1		*Trial 2*	
	0 DAYS DELAY (n = 1783)	ANY DELAY (n = 1741)	NO DRYING (n = 1793)	DRYING (n = 1810)
Total positive kits	18.4%	17.5%	21.1%	17.5%
Sample 1	6.7%	6.5%	6.8%	6.8%
Sample 2	7.1%	7.9%	8.4%	8.5%
Sample 3	11.6%	10.3%	14.2%	10.7%

[Figure 1. Positivity by stool sample]
Disclosure: Nothing to disclose

P1663 COMBINATION OF FAECAL OCCULT BLOOD TEST AND FAECAL CALPROTECTIN IS NOT AN EFFECTIVE STRATEGY TO AVOID NON PATHOLOGICAL COLONOSCOPIES IN A COLORECTAL CANCER SCREENING PROGRAM

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Introduction: It has been demonstrated that colorectal cancer (CRC) screening program with faecal occult blood test (FOBT) reduces incidence and mortality. However, around 40% of colonoscopies performed in the setting of CRC screening program are normal or detect only benign pathology. Strategies to avoid non-pathological colonoscopies are highly necessary.
Faecal calprotectin (FC) test is an accepted biomarker for inflammatory bowel disease activity, but data about its value for CRC and adenoma detection are lacking.
Aims and Methods: We aimed to evaluate the accuracy of the combination of FOBT and FC compared with FOBT alone in a CRC screening program setting (with a previous positive FOBT) for reducing the number of colonoscopies with benign or no pathological findings.
Patients with previous positive FOBT who completed colonic investigations and returned stool samples the same of the colonoscopy were prospectively recruited.
FOBT was performed by FOB Turbilatex ® (Certest Biotec S.L, Zaragoza, Spain), with a cut-off of 29 μg/gr. FC was performed by Calprotectin Turbilatex® (Certest Biotec S.L, Zaragoza, Spain), with a cut-off of 50 μg/gr.
We considered as relevant pathology CRC and advanced adenoma (>3 adenomas, >1cm, high grade dyspasia, villious component).
Positive and negative predictive values, sensitivity, specificity and area under ROC curve (AURC) of FOBT, FC and the combination of both tests were calculated.
Results: 173 patients were prospectively recruited and included in the final analysis (109/173 63% male). 58 (33.5%) had relevant colonic pathology. 6 (3.5%) had CRC.
Diagnostic accuracy of FOBT, FC and combination of both test are summarized in table 1.
PPV: positive predictive value NPV: negative predictive value

Test	PPV	NPV	Sensitivity	Specificity
FOBT	47.5%	85.1%	81.0%	54.8%
FCP	32.3%	64.8%	56.9%	40.0%
Combination	38.4%	85.8%	91.4%	26.1%

[Table 1]
AUROC for CRC and advanced adenoma were 0.48 (95% CI:0.39–0.58) for FC; 0.76 (95% CI: 0.68–0.83) for FOBT and 0.71 (95% CI:0.62–0.80) for the combination of both tests, respectively. Neither FC nor the combination of both tests showed a better diagnostic accuracy that FOBT alone.
Conclusion: The combination of FOBT and FC in a CRC screening program setting does not improve the diagnostic accuracy for detection of advanced adenoma and CRC compared with FOBT alone
Disclosure: Nothing to disclose

P1664 INCREASING THE CUT-OFF VALUES OF FIT IN POPULATION BASED COLORECTAL CANCER SCREENING IMPROVES FALSE POSITIVE RATES AND HEALTH RESOURCE UTILIZATION IN A NATIONAL PUBLIC HEALTH SERVICE

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Introduction: Fecal immunochemical test (FIT) is commonly used in colorectal cancer (CRC) screening programs. These programs are planned based on assumptions of participation and positivity rates, population characteristics and country colonoscopy resources. We planned our regional CRC screening program based on data obtained from the COLONPREV study (Quintero et al. NEJM 2010) conducted in our community.
Aims and Methods: To analyse the results obtained 3 years after initiation of the program in order to accommodate and adjust current outcomes to available endoscopic resources of the current strategy. We have collected data from 128,412 average-risk individuals in Aragón (Spain), 60–69 years old, who were invited to a first round of a population-based CRC screening program with FIT. Fecal samples were collected, and levels ≥ 20 μg Hb/g feces (FOB-Gold® test) were considered positive. Subjects with a positive FIT were scheduled for colonoscopy within 4 weeks.
Results: In total, 64,989 (50.6%) individuals participated in the study; 9,329 (14.4%) had a positive test result and 97.0% underwent a valid colonoscopy. Colorectal cancer and advanced adenomas were detected in 5.7% and 29.7% of individuals respectively. The risk of cancer increased with increased levels of Hb in feces for both men and women, specially with the highest levels: Quartil (Q)1 = reference; Q2: 0.99; 95%CI (0.62–1.60); Q3: 1.82 (1.20–2.78); Q4: 6.54 (4.53–9.44). Attendance and positive test results were greater than those originally planned and overcame by far the planned regional colonoscopy resources (Table).

	Attendance	FIT + PPV	Expected number of colonoscopies per round	Detection of CRC	PPV Cancer + advanced adenoma
Estimated	38.2%	9.9%	11763	6%	45.6%
Current	50.6%	14.4%	17117	5.7%	43.1%

[PPV: positive predictive value]
Increasing the cutoff concentration of Hb in feces from 20 to 85.5 μg Hb/g feces would adapt current outcomes to available endoscopic resources by reducing the proportion of subjects who underwent colonoscopy evaluation by 42.4% (6.846 procedures). This would result in a reduction of false positive results for cancer

(from 94.3% to 52.8%) cancer + advanced adenoma (from 64.6% to 32.8%) with a 0.9% of cancer or a 10.6% cancer + advanced adenoma being missed, and an increase in PPV for cancer from 5.7% to 8.4% and for cancer+advanced adenoma from 35.4% to 43.1%
Conclusion: 1. Detection of cancer and advanced adenomas by FIT increase significantly with fecal Hb cutoff concentration for both men and women. 2. Participation and positivity FIT rates overcome the initial design of endoscopy needs. **3**. Increasing the cutoff concentration reduces the numbers of patients who undergo colonoscopy evaluation, adjust available endoscopic resources and improves results on positive predictive values at the expense of missing a small percentage of colorectal cancer and advanced adenomas.
Disclosure: Nothing to disclose

P1665 LATE DIAGNOSIS OF COLORECTAL CANCER IN MOROCCO : WHAT REASONS BEHIND?

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Introduction: Because of its frequency and seriousness, colorectal cancer is a major challenge for public health. In our country it is the first digestive cancer according to the two major regional registers. Early detection allows better survival and certainly reflects the strength of the health system. Our work aims to analyze the reasons for late diagnosis of colorectal adenocarcinoma to provide solutions for improving early diagnosis.
Aims and Methods: We analyzed the preliminary results of a multicenter prospective cohort including 220 patients with colorectal adenocarcinoma between February 2016 and April 2017 in 5 hospital departments. A period exceeding 30 days between the appearance of first symptoms and the date of diagnosis is considered as delay of diagnosis. Factors related to this late diagnosis were analysed.
The descriptive and analytic study of the data was carried out with SPSS software version 16.0.
Results: The mean age of our patients was 56.72 years [22 -86] with a sex-ratio F / H of 1.12.
In 25% of cases, patients were under age of 45 (n = 55). The initial clinical symptoms were dominated by transit troubles (42.30%), abdominal pain in 36.54% of cases and lower bleeding in 21.16% of cases. Fifty-six percent of patients were diagnosed at the locally advanced or metastatic stage. The average time between onset of symptoms and diagnosis was 7 months on average with 79% of the time exceeding 30 days (n = 83). In 31% of cases (n = 68), an underestimation of the severity of symptoms was reported by patients as the cause of the consultation delay. In 36% of patients (n = 79) the symptoms were attributed to hemorrhoidal pathology and in 14% of cases (n = 30) the first visit indicated symptomatic treatment without any endoscopy investigation. Analysis of certain factors that explain the delay in diagnosisas age under 45, sex, location of tumor, lower bleeding, occlusion and advanced stage, has shown that only the absence of lower bleeding was correlated with a diagnosis delay with $p < 0.001$.
Conclusion: The late diagnosis of colorectal cancer is a real public health problem in our country with an average delay of 7 months. Only the presence of lower bleeding seems to alarm the patients. The reinforcement of public awareness campaigns could certainly shorten this diagnostic delay and improve the prognosis.
Disclosure: We would like to thank Hala AZZAM and his team for the workshops organized in Morocco on the capacity building that allowed this project to be launched We would also like to thank Dr. Karima EL RHAZI Dr. Anna R. GIULIANO and Dr. Peter A. KANETSKY for coordinating this project and follow-up workshops and Training. Funding of this project is supported by Moffitt Cancer Center under the NIH International Fogarty Center award number 5D43TW009804, PIAnnaGiuliano

P1666 THE EFFECT OF METFORMIN ON TUMOR RESPONSE OF NEO-ADJUVANT CCRT OF RECTAL CANCER

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Introduction: Metformin might have the potential effect of reducing cancer risk and could improve response to radiotherapy in several malignancies.
Aims and Methods: We aimed to investigate whether metformin could have the beneficial effect in radiotherapy-induced tumor response in rectal cancer with diabetes. From January 2000 to November 2017, 91 patients with rectal cancer taking diabetes medication who were treated with neoadjuvant chemoradiotherapy followed by radical surgery were reviewed. Patients were divided into two groups: diabetics taking metformin (n = 56) and diabetics not taking metformin (n = 35). Tumor response and survival were compared between groups.
Results: The rates of T downstaging, N downstaging and tumor regression grades (TRG) 1–2 were significantly higher in diabetics taking metformin ($p = 0.018$, $p < 0.001$ and $p = 0.01$, respectively).
There were no significant differences between groups in terms of pathologic complete response, however, size of primary tumor and nodes decreased significantly in diabetics taking metformin ($p < 0.001$ and $p < 0.001$). The rates of T downstaging, N downstaging and tumor regression grades (TRG) 1–2 were significantly higher in diabetics taking metformin ($p = 0.018$, $p < 0.001$ and $p = 0.01$, respectively). There were no significant differences between groups in terms of pathologic complete response, however, size of primary tumor and nodes decreased significantly in diabetics taking metformin ($p < 0.001$ and $p < 0.001$).
Conclusion: Metformin is associated with higher tumor response rates and downsizing of tumor to radiotherapy in rectal cancer, especially in patients with diabetes
Disclosure: Nothing to disclose

Reference

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P1667 LONG-TERM RESULT OF "WATCH AND WAIT" WITHOUT RADICAL SURGERY FOR COMPLETE CLINICAL RESPONSE OF RECTAL CANCER AFTER NEOADJUVANT CONCURRENT CHEMORADIATION THERAPY IN A SINGLE INSTITUTION IN TAIWAN

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Introduction: Colorectal cancer is the most common malignancy in Taiwan, and rectal cancer was about 36.9% of these patients. Neoadjuvant concurrent chemoradiation therapy (CCRT) before radical surgery is the choice for advanced rectal cancer. Some lucky cases got complete clinical response after CCRT. Therefore, "watch and wait" without radical surgery could be the choice for the selected patient. We hereby presented the long-term result of "watch and wait" without radical surgery for complete clinical response of rectal cancer after CCRT in Tri-Service General Hospital in Taiwan.
Aims and Methods: This was a retrospective study in a single institution in Taiwan. The patients of advanced rectal cancer with complete clinical response after CCRT were included from Jan, 2007 to Oct, 2017.
Results: There were 40 patients diagnosed with rectal cancer following the "watch and wait" without radical surgery policy. Three residual tumors were found among 13 cases (13/40, 32.5%), who got transanal wide excision for obvious mucosal lesions, 3 months to 1 year later after CCRT. No local recurrence was noted after local excision. Among the 27 cases without local excision, 2 patients (2/40, 5%) had local recurrence and 1 (1/40, 2.5%) got distal metastases within one year after CCRT. Salvage radical surgery was successful for these patients and no associated morbidity or mortality.
Conclusion: According to our study, the long-term result revealed no mortality or morbidity in the selected patients of rectal cancer with complete clinical response after CCRT.
Therefore,"watch and wait" without radical surgery could be the choice for the selected case of rectal cancer with complete clinical response after CCRT.
Disclosure: Nothing to disclose

P1668 ACID-RESPONSIVE DRUG-COMPLEXED POLYPEPTIDE NANOPARTICLE EFFECTIVELY AND SAFELY TREATS COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is one of the most common malignant tumors worldwide, and in which chemotherapy plays an irreplaceable role. However, the efficacy is seriously unsatisfactory for the poor distribution specificity, short circular half-life and dosage-dependent side effects of traditional drugs. For this situation, a facilely prepared pH-responsive nanoparticle was prepared based on polypeptide to deliver antitumor drugs more efficiently and safely.
Aims and Methods: Epirubicin (EPI) as a model drug was loaded into nanoparticle (NP/EPI) via the electrostatic interaction between poly (ethylene glycol)-*block*-poly (L-glutamic acid) (mPEG-*b*-PGA) and EPI, and the subsequent

hydrophobic interaction among PGA/EPI complexes. The characterizations of NP/EPI were ensured by transmission electron microscopy (TEM) and Dynamic laser scattering (DLS). In vitro release experiment and nanoparticle stability assessment were employed to detect the pH-responsibility of NP/EPI. Subcutaneous C26-xenografted CRC murine model was established to evaluate the antitumor efficacy and security of NP/EPI with 4 times drug administration at EPI equivalent dose of 8.0 mg/kg. The tumor volumes and body weights of mice were measured every other day. Furthermore, the microscopic examinations were carried out by H&E staining and *in situ* apoptosis assay of isolated tumors.
Results: The loading nanoparticle appeared spherical with a medium hydrodynamic diameter of 93.71 ± 8.37 nm. The NP/EPI had faster release efficiency and higher cumulative release rate in intratumoral microenvironment of pH 6.8 than that in physiological condition (*i.e.*, pH 7.4), and in intracellular acidic microenvironment of pH 5.3 the difference was more significant. Similarly, the particles exhibited nearly constant diameters in solution of pH 7.4, which increased gradually with the decline of pH value, and further confirmed the pH-responsibility of NP/EPI. In vivo, the two drug formulations both inhibited the growth of CRC while the NP/EPI showed a significantly enhanced efficacy than that of EPI. Microscopic examinations displayed that nanoparticle could improve tumor tissue necrosis and cell apoptosis caused by EPI effectively. In the aspect of safety, the body weight of mouse in NP/EPI group was 22.08 ± 1.76 g, which was significantly higher than that in EPI group (*i.e.*, 18.02 ± 1.84 g). More meaningfully, only 30% mice survived with EPI administration while that with NP/EPI reached 70%.
Conclusion: With perfect pH-responsibility, drug-loaded nanoparticle based on mPEG-b-PGA could significantly enhance efficacy and reduce side effects of traditional drugs, and holds great potential for the CRC chemotherapy in clinic.
Disclosure: Nothing to disclose

P1669 DOES BRIDGE-TO-SURGERY STENT PLACEMENT PROVIDE BETTER ONCOLOGICAL OUTCOMES FOR OBSTRUCTIVE COLORECTAL TUMORS?

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Introduction: Endoscopic self-expanding metal stent (SEMS) placement as a bridge to surgery is an option for obstructive colorectal tumors. SEMS could be used for definitive palliative treatment for unresectable or inoperable patients. Also SEMS are used as a bridge to elective curative resections. Although it is thought that emergency colorectal resections may cause worse oncological outcomes, the debate is still ongoing regarding to SEMS superiority and oncological safety. In this study, it is aimed to determine the benefits of SEMS placement in obstructive colorectal tumors.
Aims and Methods: Between 2012–2018, 136 patients admitted to University Hospital Emergency Clinic with acute obstructive colorectal tumors. Ninety-four of them were included in the study. Palliative SEMS placements for multi organ and/or peritoneal metastatic patients, patients whom undergone emergency surgery regarding to SEMS complications, palliative decompressive ostomy patients, patients with benign obstructive causes, patients with complications of previous surgery, were excluded.
Patients undergone surgical procedures immediately, were defined as Group 1 and patients who undergone elective surgery after SEMS placement were defined as Group 2.
The demographic data, signs in emergency service, operation techniques, ostomy entity, pathological results and oncological follow-up were reviewed retrospectively. Statistical analysis of groups with Chi-square test, Fisher Exact t test, student's t test, log rank and Kaplan-meier tests were done on SPSS Version 23.
Results: The demographic data, pathological results, clinical findings, and surgical outcomes were summarized in Table 1. The tumor localization of the Group 1 and 2 were, 53% and 10% right sided tumors, 8% and 29% descending colon, 33% and 43% sigmoid colon tumors, 6% and 38% for rectal tumors, respectively. There was no difference between groups as to distant organ metastasis (p:0.77).
End ostomy (without anastomosis) was created for 36 patients (49%) in Group 1. Only 36% of these ostomies were reversed.
Overall survival rates were significantly higher in Group 2 but there was no difference between groups according to disease free survival rates (p:0.041 and 0.1 respectively).
Conclusion: SEMS placement as a bridge to surgery provided better results in reference to permanent ostomy and overall survival.

	Group 1 (n:73)	Group 2 (n:21)	p
Female	39.7% (n:29)	42.9% (n:9)	0.79
Male	60.3% (n:44)	57.1% (n:12)	0.79
Age	67.68 ± 14.24	57.71 ± 11.68	0.004
Ileus day (mean ± SD)	4 ± 3.2	3.05 ± 2.2	0.31
Specimen lenght (cm)	30.7 ± 24.16	24.62 ± 9.27	0.26
Tumor size (mm)	27.29 ± 24.25	59.29 ± 20.69	0.73
Harvested lymph node	20.03 ± 10.35	24.38 ± 16.11	0.14
Metastatic lymph node	3.29 ± 5.1	2.38 ± 3.29	0.65
T stage (median)	3.00	3.00	0.006
N stage (median)	1.00	1.00	0.98
Hospital stay (mean ± SD)	10.40 ± 10.25	11.10 ± 10.49	0.88
End ostomy	49% (n:36)	16% (n:3)	0.001
Laparoscopic approach	4% (n:3)	33% (n:7)	0.001
Complications	15% (n:11)	23.8 8n:5)	0.35
Overall survival (mean ± SD)	34.83 ± 3.2 months	49.61 ± 4.4 months	0.041
Disease free survival (mean ± SD	33.23 ± 2.8 months	49.71 ± 4.4 months	0.10

[Table 1]
Disclosure: Nothing to disclose

P1670 ENDOSCOPIC FULL-THICKNESS RESECTION OF NEUROENDOCRINE TUMORS IN THE RECTUM – A SUBGROUP ANALYSIS OF THE GERMAN FTRD-REGISTRY

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Introduction: Subepithelial tumors (SET) in the colorectum are rare and usually detected incidentally during colonoscopy. The incidence of SET in the colorectum was reported to be about 0.3% and up to 27% are described to be malignant or to have malignant potential. Neuroendocrine tumors (NET) and gastrointestinal stromal tumors (GIST) are the most common SET with malignant potential. Endoscopic ultrasound (EUS) allows further characterization of SET, but is associated with limited diagnostic accuracy. In consequence, histological examination should be performed but obtaining a diagnostically conclusive sample might be difficult as SET are originating from deeper layers than the mucosa. Management of colorectal SET depends on dignity, tumor size and presence of symptoms. Further surveillance, endoscopic resection (ER) or surgical resection (SR) are potential options. ER of SET using the standard techniques such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is difficult and associated with an increased risk of bleeding or perforation. Clip-assisted endoscopic full-thickness resection (EFTR) has shown to be feasible, effective and safe for smaller colorectal SET (1).
Aims and Methods: The FTRD-System (Full-Thickness-Resection Device) is available for clip-assisted EFTR in the lower gastrointestinal tract since 2014 in Europe. In September 2015 an online FTRD-registry has been created as part of a post-market clinical follow up (PMCF). FTRD-procedures of 31 German centers were entered into the database. This retrospective analysis further evaluates EFTR of rectal NET. The aim of this analysis is to show that EFTR with the FTRD-System is feasible, effective and safe for rectal NET and allows definite histological diagnosis and therapy (complete resection, R0).
Results: 501 procedures were entered from September 2015 to May 2017. 20 German centers contributed 35 cases of SET (7%). 10 cases were excluded (4 leiomyomas, 2 lipomas, GIST, MALT, inflammatory fibroid polyp, granular cell tumor) and 25 NET (24 rectum, 1 sigmoid) were included for this analysis. The median age of the patients (11 male, 14 female) was 57 years (range 28–81 years). The median size of the lesion was 8.3 × 7.5 mm (from 3 × 3 mm to 25 × 10 mm), mainly located in the middle rectum. EUS was performed in 9/25 patients (36%) and could not provide a definite diagnosis. Biopsies were taken before EFTR in 19/25 patients (76%) and all biopsies showed well differentiated (G1) NET. However, in all cases resection status was unclear or incomplete (Rx in 7 patients, R1 in 5 patients, missing statement in 7 patients). 5 NET (20%) were recurrent NET and had been treated previously (multiple forceps biopsies or snare resection). Mean procedure time of EFTR was 23 minutes (range 7–60 min). EFTR with the FTRD was macroscopical and histological complete (R0) in all cases. However in 7 cases (28%) a NET could no longer be proven. A full-thickness-resection specimen could be obtained in all cases. In 3 cases (12%) minor peri-interventional bleeding occurred and was managed endoscopically. Follow-up was available for 20/25 patients (80%) with a median of 17 weeks after EFTR (range 1–48 weeks). The OTSC was dislocated in 14/20 (70%) and in situ in 6/20 (30%) cases (no removal). No signs of a residual or recurrent tumor were observed.
Conclusion: EFTR with the FTRD for rectal NET is feasible, safe and effective and allows a definite diagnosis and therapy at once.
Disclosure: Nothing to disclose

Reference

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P1671 RED BLOOD CELL DISTRIBUTION WIDTH INDEPENDENTLY PREDICTS SURVIVAL IN R0 RESECTED COLORECTAL CANCER

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Introduction: Red blood cell distribution width (RDW) is related with inflammatory response and nutritional status in cancer patients, which could have a prognostic value in colorectal tumors. Nevertheless, studies in western countries are scarce
Aims and Methods: We aimed to study the possible prognostic value of RDW, determined at the moment of diagnosis, in long-term survival after a R0 colorectal resection.
Patients with haematological diseases and blood transfusion before diagnosis were excluded. We retrospectively studied 205 colorectal carcinomas, consecutively treated with R0 resection and with a minimum 5-year clinical controlled follow-up. The cut-off point of RDW was determined using ROC curves, considering "high" a RDW $\geq$ 17%: Cancer specific survival curves were analysed between both groups with a pretreatment RDW value $\geq$ and $<$17% (Kaplan Meier- log rank test), calculating hazard ratio (HR) and 95% confidence interval (CI95%). A multivariate analysis of cancer-specific survival rate (Cox model, stepwise) was performed, including in the model: RDW $\geq$ 17%, gender, age $>$ 70 years, (ROC curves), rectal or colonic localization, differentiation grade (1–3), pTNM stage (I-IV) (AJCC 7^{a}Ed.) and neoadjuvant and adjuvant treatment administration (yes/no).
Results: Median clinical follow-up was 40 months for deceased cases and 88 months for survivors. Tumor specific mortality was 23.9%. We registered 40/205 (19.5%) cases with RDW $\geq$17%. Survival curves were significantly worse in patients with pre-treatment RDW $\geq$ 17%: [p = 0.003; HR = 2.35; CI95% = (1.32–4.21)]. The multivariate analysis confirmed a lower survival in the RDW $\geq$ 17% group: [p = 0.009; HR = 3.07; CI95% = (1.33–7.08)].
Conclusion: 1.- In our series of R0 resected colorectal cancer, cases with "high" pre-treatment RDW values ($\geq$ 17%) show a significant worse cancer-specific survival curve,
2.- This unfavourable prognosis of an elevated RDW is independent of the rest of analysed parameters.
3.- If these data were confirmed, RDW could be a simple, low-cost and very easy to obtain parameter, useful to orientate the initial prognosis in the resected colorectal carcinoma.
Disclosure: Nothing to disclose

P1672 SURVEILLANCE PROTOCOL FOR ABDOMINAL DESMOID TUMOURS IN FAMILIAL ADENOMATOUS POLYPOSIS (FAP): EXPERIENCE OF A REGIONAL REFERRAL CENTRE

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Introduction: Desmoid Tumours (DTs) are benign proliferations of stromal cells, rare in the general population and common in patients with Familial Adenomatous Polyposis (FAP) who have undergone prophylactic colectomy. In 10% of the cases DTs show a locally aggressive and rapid growth and are a main cause of death after prophylactic colectomy in FAP patients. Nevertheless International Guidelines have not defined a surveillance protocol yet.
Aims and Methods: Aims of the present study were: to define a surveillance protocol and to evaluate the best diagnostic tool between MRI and CT; to identify DTs with aggressive behavior.
From January 2010 to March 2018, patients who referred to the "Regional Referral Centre for FAP of Lazio Region" with a proven diagnosis of FAP were enrolled in the study. All patients underwent contrast-enhanced (CE) abdominal CT and MRI at least 1 year after prophylactic colectomy. Patients with DTs and without intestinal obstruction and ureteral compression received follow up examination after 6–12 month or alternatively after 2–3 month. Patients without DTs underwent follow up examination after 3 years. DTs growth assessment was performed by using RECIST criteria 1.1. The "average monthly growth rate" was also evaluated.
Results: One hundred patients (55F/45F) were enrolled in the study. DTs were detected in 13/100 (13%) cases (5F/8M): 2 abdominal wall DTs (AWD), 10 intrabdominal DTs (IAD), one patient presented lesions in both localizations. The average age at diagnosis was 32,5 years (range 19–53), the average time of onset after colectomy was 43,9 months (range 13–228). In 5/13 cases (38.5%) the IAD showed an aggressive behavior (asymptomatic intestinal obstruction and ureteral compression seen at imaging in 3 cases and symptomatic intestinal perforation in two cases). The "average monthly growth rate" was 0.58 cm (range 0.47–0.75 cm) for an average follow up of 11 months (range 4–20 months). The highest value was detected in the unique symptomatic case. CT was better than MRI for imaging IAD in 13 vs 9 cases.
In 18/100 patients (8F/10M), MRI and CT showed dubious alteration for DTs, describing an aspect of diffuse or localized mesenteric thickening. The average follow-up time for these patients was 15.1 years (range 1–35) and none of these patients presented any clinical symptom during clinical and radiological surveillance.
Conclusion: The proposed surveillance protocol allowed to detected early asymptomatic intestinal obstruction and ureteral compression in 3 cases improving clinical management. CT had a better diagnostic output than MRI and could play an important role for the first diagnosis of DTs. The evaluation of the "average monthly growth rate" could allow the identification of IAD with aggressive behavior, improving, thus, clinical management. The presence of a "mesentery thickening" at MRI or CT, does not appear predictive of desmoid development or disease aggressiveness. Therefore, these patients can be surveilled as negative ones.
Disclosure: Nothing to disclose

P1673 HIGH EXPRESSION OF LONG NON-CODING RNA LINK-A ASSOCIATES WITH POOR SURVIVAL IN PATIENTS WITH COLORECTAL CANCER

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Introduction: Long non-coding RNAs (lncRNAs) have been proved to be involved in the development of many diseases, including cancers. Long intergenic non-coding RNA for kinase activation (LINK-A), a newly discovered lncRNA, has been reported to enhance the occurrence and progression of breast cancer. LINK-A promotes breast cancer tumorigenesis via activating AKT or normoxic HIF-1α signaling pathway. AKT and HIF-1α pathway activation has been demonstrated to promote tumor formation, progression, and metastasis of colorectal cancer (CRC). However, whether LINK-A is related in the tumorigenesis of CRC is remained unknown.
Aims and Methods: To evaluate the expression of LINK-A in colon adenocarcinoma and establish the correlation between LINK-A and CRC prognosis. The expression of LINK-A was evaluated by qRT-PCR on cDNA tissue microarray, which contained 15 pairs of human colon adenocarcinoma and paracancerous tissues and another 65 colon adenocarcinoma tissues. The total 80 patients were devided into low and high expression groups according to the LINK-A levels. Then relationships between LINK-A expression and clinicopathological characteristics of colon adenocarcinoma were analysed between that two groups. Kaplan-Meier survival analysis was used to assess the LINK-A function on the survival of colon adenocarcinoma. Multivariable Cox regression analysis was also used to explore the risk factors for prognosis of colon adenocarcinoma between the high and low LINK-A expression groups.
Results: The expression level of LINK-A in colon adenocarcinoma was higher than those in paracancerous tissues (P = 0.047). Furthermore, overexpression of LINK-A was proved to be associated with advanced TNM stage (P = 0.013), positive lymph nodes (P = 0.024), low 5-year survival rate (P = 0.024) and even 10-year survival rate (P = 0.007). Besides LINK-A, advanced age (P = 0.036), high TNM stage (P = 0.023), deep infiltration degree (P = 0.032) and positive lymph nodes (p = 0.013) were also found to be positively related to poor overall 5-year survival by Kaplan-Meier survival analysis. Then, multivariable Cox regression analysis revealed that LINK-A was an independent risk factor for prognosis of colon adenocarcinoma (P = 0.047).
Conclusion: High expression of LINK-A associates with poor survival in patients with colorectal cancer. And LINK-A may serve as a candidate prognostic biomarker for colon cancer.
Disclosure: Nothing to disclose

P1674 RISK OF METACHRONOUS ADVANCED NEOPLASIA IN PATIENTS WITH MULTIPLE DIMINUTIVE ADENOMAS

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Introduction: Individuals with advanced adenomas or three or more adenomas have a higher risk for metachronous advanced neoplasia (AN) and are recommended to undergo surveillance colonoscopy at shorter intervals. Recently, improvements of colonoscopy technology have resuled in higher detection rates for diminutive polyps. In more recent screening studies, adenoma detection rates of 40% or more have been reported. Therefore, it is questionable whether patients with multiple (three or more) non-advanced diminutive adenomas should be considered as high-risk.
Aims and Methods: We analyzed 5,482 patients diagnosed with 1 or more adenomas during their first colonoscopy screening and who underwent a follow-up colonoscopy. Patients were categorized into four groups based on adenoma characteristics at baseline: Group 1, 1–2 non-advanced adenomas; Group 2, $\geq$3 non-advanced, diminutive (1 to 5 mm) adenomas; Group 3, $\geq$3 non-advanced, small (6 to 9 mm) adenomas; and Group 4, advanced adenomas.
Results: During a median follow-up of 38 months, the incidence of metachronous AN at surveillance colonoscopy was 5.6%. The incidence of AN was 3.9% in

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Table 1: Risk for metachronous advanced neoplasia based on baseline adenoma characteristics (different reference groups)

	Total number	Number of cases	Incident rate	aHR (95% cI)	P value	aHR (95% cI)	P value	aHR (95% cI)	P value
Group 1	4302	168	3.9	1.00 (reference)		0.19 (0.13–0.28)	<0.001	0.59 (0.34–1.01)	0.059
Group 2	472	28	5.9	1.71 (0.99–2.94)	0.059	0.32 (0.18–0.59)	<0.001	1.00 (reference)	
Group 3	378	40	10.6	2.76 (1.72–4.44)	<0.001	0.52 (0.31–0.89)	0.008	1.62 (0.84–3.12)	0.309
Group 4	330	73	22.1	5.23 (3.57–7.68)	<0.001	1.00 (reference)		3.07 (1.69–5.56)	<0.001

group 1, 5.9% in group2, 10.6% in group 3, and 22.1% in group 4. The adjusted hazard ratios (HRs) [95% confidence intervals (CIs)] for metachronous AN between group 2, group 3, and group 4, and low risk group 1 were 1.71 (0.99–2.94), 2.76 (1.72–4.44), and 5.23 (3.57–7.68), respectively. Compared with group 4, the adjusted HRs (95% CIs) for group 1, group 2, and group 3 were 0.19 (0.13–0.28), 0.32 (0.18–0.59), and 0.52 (0.31–0.89), respectively.

Conclusion: Risks for advanced neoplasia among individuals with high-risk features vary based on baseline adenoma characteristics. We found that patients with 3 or more non-advanced diminutive adenomas had a borderline increased risk of metachronous AN compared with patients with low-risk adenomas. The surveillance interval for patients with multiple diminutive adenomas may be lengthened from the recommended interval for patients at high risk.

Disclosure: Nothing to disclose

P1675 ONCOLOGICAL RECURRENCE OUTCOMES AFTER STENTING AS BRIDGE TO SURGERY COMPARED TO EMERGENCY SURGERY FOR LEFT-SIDED MALIGNANT COLONIC OBSTRUCTION: RETROSPECTIVE BICENTRIC STUDY

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Introduction: Symptomatic left-sided malignant colonic obstruction is a medical and surgical emergency that requires an urgent intervention, which has been classically emergency surgery (ES), which still represents a high morbidity (30–60%) and mortality (10–30%).[1,2]

Stents bridge to surgery (SBTS) restore intestinal transit and allows to transform emergency surgery into elective surgery.

SBTS is widely accepted in palliation, but disagreement exists about its role in patients whose disease is potencially curable due to the possible risk of tumour spread.

At present, there are no consistent studies able to demonstrate that one strategy is superior to the other in terms of oncological benefit.[3]

Aims and Methods: Our aim is to evaluate the oncological outcome in terms of recurrence and recurrence-free survival of stented patients who went on to elective surgery compared to those who had ES. We retrospectively selected patients with clinically and radiologically left-sided malignant colonic obstruction between January 2006 to May 2012 in two Specialty Hospitals in the south of Spain.

Exclusion criteria were age under 18, tumour located in right or transverse colon, or in medium/inferior rectum; metastasic disease (stage IV of the American Journal Committee on Cancer (AJCC)) independently of the location or resecability of the metastases and perforation at the moment of the diagnosis.

Firstly, we analyzed demographic data, recurrence rate (RR) and recurrence-free survival (RFS) between both hospitals, without finding statistically significant differences and achieving an homogeneous sample for the analysis. Then we analyzed RT and RFS comparing SBTS vs ES groups. Multivariate analysis was made to find relative factors to oncological recurrence.

Results: We found a higher RR near statistical significance in the ES group compared to the SBTS group (34.8% vs 19.7; P = 0.072). The median follow-up time until recurrence was higher in the SBTS group, 58 vs 24 months (p = 0.053). We did not find differences between groups in recurrence location when distinguishing between local or distant recurrence (p = 0.999). Results are shown in table 1.

	SBTS (n = 71)	ES(n = 66)	P
Recurrence rate	14(19.7)	23(34.8)	0.072
Recurrence-free follow-up time (m)	58(14–85)	24(8.75–68)	0.050
Local Recurrence	8(57.1)	13(56.5)	0.999

[Table 1. Recurrence results. Values are presented as median (p25-p75) or n (%)]

Three-year and five-year RFS survival were lower for the ES group (67.5% and 60%), compared to the SBTS group (79.3% and 75.6%), but the Kaplan-Meier curve showed no difference in the RFS between two groups (log-Rank test, P = 0.220)

Stratifying according the AJCC stage, there are not statistically significant differences between groups for stage I(P = 0.317) or II(P = 0.884), but there is a lower RFS for stage III in ES group, where 3-years RFS suppose the 42.5% compared to 74.5% in the SBTS group; and 30% vs 69.7% according 5-year RFS (log-Rank test, P = 0.004; Fig. 2)

Performing a multivariate analysis, we find as hypothetical predincting variables of recurrence the type of emergency procedure and the AJCC stage, so that the patients who had ES have 2.12 [IC95%:(1.09;4.13); P = 0.027] more risk of recurrence than those who were treated with SBTS; and those with AJCC stage III have 2,97[IC95%:(1,53;5,78); p = 0,001) more probability of recurrence than those with a lower stage.

Conclusion: This study shows a clear trend to lower RR in patients who undergo SBTS compared to those who have ES for left-sided malignant obstruction and reaches statistically significant for recurrence-free follow-up time.

Patients who went to ES or was AJCC stage III had more probability of oncological recurrence.

Disclosure: Nothing to disclose

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P1676 EARLY- ONSET ENDOMETRIAL CANCER PATIENTS WITH OR WITHOUT FAMILY HISTORY ARE AT HIGH RISK FOR LYNCH SYNDROME

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Introduction: Women with Lynch syndrome (LS) have up to 71% lifetime risk of developing endometrial cancer (EC). Several studies evaluated the prevalence of Lynch Syndrome (LS) in young onset EC patients and the results were extremely variable (5%-22,8%). Molecular screening with Immunohistochemistry (IHC) for Mismatch Repair (MMR) proteins and/or Microsatellite Instability (MSI) analysis on cancer tissue have to be shown cost effective. Nonetheless, the approach of a universal vs a selective screening on tumor tissue is still debated. A pre-selection with family history criteria could improve the cost effectiveness of molecular screening.

Aims and Methods: The aim of our study was to evaluate the prevalence of LS in early-onset EC without family history compared with those with family history. Early-onset EC patients (≤ 50 years) were prospectively recruited in the study. Family history of Lynch-associated cancer (LAC) was recorded. IHC for MMR and MSI analysis were performed. Germ-line mutation analysis (GMA) was carried out in all MMR deficient tumors or when neoplastic tissue was not available. Results were compared with a published series of early -onset Colorectal cancer (CRC) undergone to molecular screening for LS and cathegorized according with family history of LAC.

Results: Twenty-two early- onset EC cases with a median age at diagnosis of 43 years were analysed. Patients were categorized in three groups according with family history of LAC: group A, Amsterdam II criteria fulfilled, 10 patients; group B, family history of LAC, Amsterdam Criteria not fulfilled, 3 patients; group C, no family history of LAC, 9 patients.

IHC and MSI were performed in 12 patients and showed MMR deficiency in 3/6 patients (50%) of group A, and 2/5 (40%) of group C. GMA was carried out in the 5 pts with somatic MMR deficiency and in the remaining 10 cases. It showed a deleterious mutation in 7/10 patients (70%) of group A, 1/3 (33.3%) of group B and 1/9 of group C (11.1%). 4/7 (57.1%) patients of group A with a deleterious mutation of MMR genes had a previous colorectal cancer.

The comparison between early onset CRC and early-onset EC showed significative differences for LS identification in group C only (0% vs 11.1%, p = 0.05).

Conclusion: Early-onset EC with or without family history of LAC are at high risk to develop LS. In our series we identified 40.9% LS cases. However, despite what reported for early onset CRC family history could not be used as a pre-screening tool to evaluate whether or not patients should undergo tissue molecular screening.
Disclosure: Nothing to disclose

P1677 STENT OR DECOMPRESSING COLOSTOMY AS BRIDGE-TO-SURGERY VERSUS ACUTE RESECTION IN OBSTRUCTING LEFT-SIDED COLON CANCER: A NATIONWIDE ANALYSIS OF 2587 PATIENTS

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Introduction: Resection of obstructing left-sided colon cancer in the acute setting is associated with an increased risk of postoperative morbidity and mortality, especially in the elderly, frail patient (1–4). Bridge-to-surgery management with stent placement or decompressing colostomy may improve postoperative outcomes (5–6).
Aims and Methods: In this nationwide retrospective cohort study, our aim was to describe national practice and compare mortality and morbidity rates between acute resection and stent or stoma as bridge-to-surgery. All patients with curable obstructing left-sided colon cancer treated between 2009–2016 were included from the Dutch Surgical Colorectal Audit. Additional data including 90-day mortality and morbidity as primary outcomes were retrospectively collected.
Results: In total, 2587 patients were included of whom 2013 underwent acute resection and 574 bridge-to-surgery by stent (n = 229) and stoma (n = 345). Acute resection showed a 90-day mortality rate of 7.6% versus 1.4% with stoma ($p < 0.001$) and 5.2% with stent ($p = 0.2$). Complication rate was 38.4% in the acute resection group versus 31.9% in the stoma group ($p = 0.02$) and 39.7% in the stent group ($p = 0.7$). In patients ≥ 70 years, acute resection showed a mortality rate of 11.7% versus 3.2% with stoma ($p = 0.001$) and 8.3% with stent ($p = 0.2$). In patients with an ASA score of ≥ 3, mortality was 15.5% with acute resection versus 6.4% with stoma ($p = 0.03$) and 12.3% with stent ($p = 0.5$). The acute resection group showed a significantly lower primary anastomosis rate of 39.5% compared to the stoma group (84.9%, $p < 0.001$) and the stent group (74.1%, $p < 0.001$).
Conclusion: In this nonrandomized population, colostomy as bridge-to-surgery significantly reduced postoperative mortality and morbidity. Both decompressing colostomy and stent placement were associated with an increased primary anastomosis rate.
Disclosure: J.V. Veld: research grant Koningin Wilhelmina Fonds (KWF) Kankerbestrijding (funding for cancer research)

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P1678 COLD SNARE PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION (CSP-EMR) OF LARGE SESSILE COLONIC POLYPS ≥20 MM IS FEASIBLE, SAFE AND EFFECTIVE

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Introduction: Endoscopic Mucosal Resection (EMR) is the standard of care for resection of large (≥20 mm) non-malignant sessile colonic polyps. Serious adverse events are mostly due to electrocautery. This could potentially be avoided by cold snare EMR. Traditionally it was thought impossible to resect large polyps with cold snare. We hypothesized that aggressive wide field cold snare piecemeal EMR (CSP-EMR) could be as effective as conventional EMR, but with fewer adverse events.
Aims and Methods: The study aimed to evaluate safety and efficacy of CSP-EMR of sessile colonic polyps sized ≥20mm. All cases of CSP-EMR performed by a single endoscopist at two academic hospitals for sessile polyps ≥20 mm, from Jan 2016 – Dec 2017, were identified retrospectively. During this period, all lesions that were not suspicious for submucosal invasion, and were not very large Paris 0-Is lesions where cold snare resection would be technically very difficult, were performed by CSP-EMR. Efficacy was defined as the absence of residual or recurrent polyp tissue during the first surveillance colonoscopy. At surveillance, EMR scars were rigorously inspected using Olympus 190 series colonoscopes with high definition white light, then NBI, and then multiple cold biopsies of the centre and margins of the scar for histology. Adverse events including clinically significant intra-procedural or post-procedural bleeding, perforation, post-procedural pain requiring hospital admission, post-polypectomy syndrome, histological outcomes and surveillance colonoscopy findings were assessed by reviewing electronic medical records.
Results: 148 polyps sized ≥20mm were successfully excised by CSP-EMR in 133 patients (median age 67 yrs, IQR 56–74 yrs; men 31.1%). Mean polyp size was 25.3 mm (median 20mm, IQR 20–30 mm; range: 20–60 mm) and 137 (92.5%) polyps were Paris class 0-IIa. 85% of polyps were lifted with submucosal injection of Gelofusine with Methylene-Blue and Adrenaline (1:100,000) before resection. Histology was 90 (60.8%) sessile serrated adenomas, 42 (28.4%) tubular adenomas and 13 (8.8%) tubulovillous adenomas. Cytological dysplasia was absent in 89 (60.1%) polyps, low-grade in 57 (38.5%) and high-grade in 2 (1.3%). 110 of 133 patients had surveillance colonoscopy for 124 polyps over a median follow-up of 5 months (range: 2–16 months). EMR scar biopsies were taken in 113 of 124 polyps (94.2%). Residual or recurrent polyp was noted in 4 cases (3.2%). Clinically significant intra-procedural bleeding occurred in 2 patients (1.5%) and was successfully treated with clips. 4 patients (3%) experienced clinically significant post-procedural bleeding that settled spontaneously. 1 patient (0.7%) required overnight stay for post-EMR abdominal pain that settled spontaneously. None experienced post-polypectomy syndrome, deep mural injury or perforation.
Conclusion: CSP-EMR of sessile colonic polyps ≥20mm is technically feasible and potentially more effective than conventional EMR, but with a superior adverse event profile. We hypothesise that the enhanced safety of cold snare resection allowed for an aggressive and wide field resection that reduces recurrence rates. However, due to the likelihood of selection bias in terms of the polyps selected for CSP-EMR in this series, randomised controlled trials or large multicentre prospective observational studies are required to more rigorously demonstrate the non-inferiority and improved safety profile of CSP-EMR compared to conventional EMR, and to further determine which polyp morphologies are best suited to CSP-EMR.
Disclosure: Nothing to disclose

P1679 BUTYRATE AS A RADIOSENSITIZER IN COLORECTAL CANCER PATIENTS-DERIVED ORGANOIDS MODEL

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Introduction: Enhancing the radio-responsiveness for locally advanced rectal cancer is important to local control and related long term prognosis. Despite the effectiveness of radiotherapy in treating cancer, harmful damage caused by radiation to the surrounding normal cells is often unavoidable. Therefore, it is necessary to treating tumor and minimizing side effects. Radiosensitizer can make cancer cells more sensitive to radiation using a low and safe radiation dose. Butyrate, one of the short chain fatty acid (SCFA), is used as energy source for histone acetyltransferase (HAT) activity in normal colonocyte. Due to the Warburg effect, cancer cells rely on glucose as their primary energy source, so butyrate is accumulated and function as a histone deacetylase (HDAC) inhibitor. There are reports that HDAC inhibitor enhance radiosensitivity, we assumed butyrate as a potential strategy for enhancing the radio-responsiveness for colorectal cancer patients.
For the test of the response to radiotherapy, the animal models have been used only due to the poor survival rate of patient-derived cell culture. However, the recently developed ex-vivo culture techniques for single crypt or a stem cell derived organoid with essential features of the in vivo tissue architecture has been demonstrated as useful and physiologically relevant tools to study the treatment response.
Aims and Methods: This study was aimed to prove the effect of SCFAs as radiosensitizer using the 3D-cultured organoids derived from colorectal cancer patients.
To culture organoids, normal mucosa fragments were cut into 3–5mm. Crypts were isolated by EDTA chelation and resuspended in matrigel and grown in culture media including EGF, Noggin, R-spondin, A83-01 and WNT. Tumor tissues were cut into pieces and incubated with Collagenase II, Dispase II and Y27632 at 37°C while shaking. Cells were incubated with culture media without Wnt and R-spondin for selecting only cancer cells. Organoids were treated with

1mM SCFAs and irradiated with 5Gy after 6hr. The evaluation of irradiated organoids was performed by measuring MTT assay, organoid size, and organoid-regenerating capacity.
Results: We screened SCFA for their anti-cancer effect on colorectal cancer organoid. Of the three SCFA, the butyrate only suppressed organoids proliferation and propionate and acetate had no effect. In the response of radiation, the butyrate significantly enhanced radiation-induced cell death in cancer organoids and it was more effective than treatment radiation or butyrate only. And also cancer organoid-regenerating capacity were decreased by radiation and butyrate treatment. Combination of radiation and butyrate reduced Ki-67 (proliferation marker) positive cells and decreased numbers of S phase cells in cancer organoids through expression of cell cycle regulator such as Cdkn1a, Cdkn1c and Gadd45b. Importantly, butyrate do not increase radiation-induced cell death and improve organoid-regenerating capacity after treatment with radiation on normal organoids. It suggest that butyrate have some tumor selectivity as radiosensitizer.
Conclusion: In this study, the butyrate increased radiosensitivity of colorectal cancer, whereas protected normal mucosa from radiation in patient derived organoids models. Considering their clinical application such as safety, they could be possible strategy for increasing radiotherapy efficiency without additional toxicity.
Disclosure: Nothing to disclose

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P1680 THE CHEMOPREVENTIVE EFFECT OF COMBINATION TREATMENT OF ASPIRIN AND METFORMIN FOR COLORECTAL CARCINOGENESIS

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Introduction: The prevalence and mortality of colorectal cancer (CRC) are increasing worldwide. New strategies for prevention, such as chemoprevention, are needed to lower the burden of this disease. The most precise chemoprevention agent for CRC is NSAIDs, especially aspirin. However, the chemoprevention effect of aspirin is not so strong and has some adverse effect, such as gastrointestinal bleeding. We previously analyzed the chemopreventive effect of low dose metformin in rodent model and conducted clinical trial for adenoma prevention, and revealed good response for colorectal carcinogenesis both in rodent model and human. Furthermore, we reported there is no severe adverse events to use of low-dose metformin. However, the chemopreventive effect of metformin is also not strong. For the antihypertensive and antidiabetic treatment, we often use multiple low-dose agents with different mechanism of action for good response and avoid adverse effects. Then we analyzed the chemopreventive effect of combination treatment of aspirin and metformin for colorectal carcinogenesis.
Aims and Methods: We obtain normal colorectal tissue, adenoma and cancer from CRC patients by colonoscopy and cultured organoid in the matrigel. Then we treated both or with or without aspirin and metformin and analyzed the chemoprevention effects.
Results: Combination treatment of aspirin and metformin significantly suppressed cell proliferation in both in normal tissue, adenoma and cancer compared with single treatment of aspirin or metformin. Combination treatment significantly activated AMPK and suppressed mTOR pathway. The chemopreventive effect of combination treatment of aspirin and metformin for colorectal carcinogenesis is stronger than that of single use of aspirin or metformin.
Conclusion: The combination treatment of aspirin and metformin is one of the option for the CRC chemoprevention.
Disclosure: Nothing to disclose

P1681 COMPREHENSIVE TREATMENT DECISION SUPPORT OF GASTROINTESTINAL CANCERS BY AN ARTIFICIAL INTELLIGENCE-SUPPORTED SOFTWARE (MH GUIDE)

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Introduction: Comprehensive characterization of the cancer genome provided important insights for development of new therapies. Current NGS-based personalized medicine requires the combination of the patients' molecular information with suitable databases and identifying appropriate publications to create a report. Here we report on 454 cancer patients with gastrointestinal (GI) tumors analyzed with MH Guide and highlight the importance of assessing the safety of suggested treatments.
Aims and Methods: We constructed an integrated database – the so-called Dataome®. Based on that, we have developed and registered an in-vitro diagnostic medical device MH Guide in Europe for clinical treatment decision support (TDS).
Results: In the 454 cases, MH Guide identified potential drug responses based on effective (4.5k), ineffective (0.7k) and toxic (1.6k) biomarker information in GI cancer cases. On average, about 16 distinct biomarker information were identified for each patient. MH Guide classifies biomarkers in germline and somatic lineage and categorizes them into three different levels of established clinical validity:
1) clinically endorsed (approved by FDA) (0.5k),
2) clinically observed (predictive effect observed in clinical trials) (3.1k), or
3) translational (supported by pre-clinical or computational evidence) (3.9k).
Furthermore, we evaluated different aspects e.g., recommended drugs, drug approval states, biomarker approval states, and clinical trial matching for off-label drugs.
Conclusion: To benefit from the comprehensive characterization of the cancer genome in the routine medical practice, technologies are required that efficiently interpret clinico-molecular patient data against all this rapidly advancing biomedical knowledge. MH Guide allows quick variant interpretation using referenced curated data including evaluation of quality parameters. Molecular Health technologies can assist clinicians in making informed decisions about the benefits of established therapies.
On this basis, we have concluded first contracts with statutory health insurances in Germany. The aim is to reduce the number of non-responders and toxic side effects, thus improving the overall cost of treatment as well as clinical outcomes and quality of life. Primary endpoint will be the change of the therapy recommendation in the tumor board after opening the MH side results in comparison to the previous recommendation.
Disclosure: The authors are employees of Molecular Health but for the senior author (JML) who is an advisor

P1682 LABORATORY PREDICTORS OF CLINICAL-PATHOLOGICAL RESPONSE AFTER NEOADJUVANT TREATMENT IN RECTAL CANCER

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Introduction: In locally advanced rectal cancer, the ability to predict tumor response to neoadjuvant radiochemotherapy is of great clinical importance, since patients with complete pathologic response (CPC) have a better prognosis.
Aims and Methods: The objective of this study is to determine if there is an association between the laboratory variables and the clinical-pathological tumor response in patients with adenocarcinoma (ADC) of the rectum, submitted to neoadjuvant radiochemotherapy, followed by surgical tumor resection.
Retrospective study of patients with rectal ADC who received neoadjuvant radiochemotherapy, followed by surgical tumor resection between March 2012 and October 2017. Analysis of laboratory values (hemoglobin, platelets, creatinine, alkaline phosphatase, albumin, CEA and CA 19.9) from tumor downstaging and CPC. Statistical analysis was performed using SPSS v24.
Results: 89 patients were included, 60.7% were male, with a mean age of 63.8 ± 10.42 (40–86) and 79.8% of them was performance status 0. The majority of patients underwent surgery between 6 to 10 weeks after neoadjuvant radiochemotherapy (58.4%). There was a good response to neoadjuvant radiochemotherapy in 41.6% of the patients, tumor downnstaging in 83.1% and CPC in 23.6%. There was a statistically significant association between the lower levels of CA 19.9 pre-treatment and tumor downnstaging ($p = 0.032$), as well as in CPC ($p = 0.007$). In the categorization of CA 19.9 values (cut off ≤ 17 and > 17), there is an association between this variable and tumor downnstaging (OR 0.241; 95% CI 0.074–0.788; $p = 0.019$), as well as the complete pathological response (OR 0.189, 95% I 0.04–0.88, $p = 0.034$).
Conclusion: Of the laboratory variables commonly evaluated in the pre-treatment phase with neoadjuvant radiochemotherapy, the only one with association with tumor domnstaging and CPC are CA 19.9 levels. Lower CA 19.9 values can predict responses to neoadjuvant radiochemotherapy more favorable.
Disclosure: Nothing to disclose

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P1683 THE RELATION OF SPHINGOLIPID IN THE CHANGE OF INTESTINAL BARRIER AS AGING, PRELIMINARY STUDY

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Introduction: The gut barrier protects the body from potentially harmful compounds and microorganisms and a loss of gut barrier integrity can lead to increased intestinal permeability causing leaky disease such as irritable bowel syndrome. A key factor contributing to abnormalities in permeability is aberrant structuring of tight junction proteins that support gut barrier function. However, disruption of the intestinal barrier is associated with aging is uncertain.

Aims and Methods: The overall goal of the current study was to investigate the role of aging on colonic permeability and the relation between the change of sphingolipid which was known to be related with epithelial permeability and gut tight junction.

Colonic mucosal biopsies were acquired from old (≥65 years old) and young (20–40 years old) human, old IBS patients and young IBS patients. The change of inflammation (TNF-α, IL1ß, and IL-10) and tight junction (claudin2, occludin, and ZO-1) were measured by qreal-time PCR. Sphingolipid was measured by using a UPLC system. Data were expressed mean ± SE and analysed using Student's unpaired T-test for samples comparison. A p value < 0.05 was considered significant.

Results: The statistical difference was shown in IL-10 and claudin2 mRNA between old and young control group ($P < 0.05$). The IL-1ß, IL-10, occludin and ZO-1 mRNA was shown significant difference between young control and young IBS group ($P < 0.05$). The IL-1ß, IL-10, claudin2, occludin and ZO-1 mRNA was shown significant difference between old control and old IBS group ($P < 0.05$). Acid sphingomyelinase (ASM) was significantly increased in colonic mucosa as aging and patients with IBS ($P < 0.05$).

Conclusion: Overall, the data presented here show that increased ASM activity in aging and IBS patients might be related with the disruption of intestinal barrier. Further studies are needed to be clarify the relation between sphingolipid and gut tight junction.

Disclosure: Nothing to disclose

P1684 CORRELATION OF RECTAL MOTILITY AND SENSITIVITY ABNORMALITIES WITH CLINICAL SYMPTOMS AND EMOTIONAL DISORDERS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is conceptualized as a condition of visceral hypersensitivity and gastrointestinal motility abnormalities. Great number of studies have shown a higher prevalence of anxiety and depression in patients with IBS patients.

Aims and Methods: We aimed to assess correlation between presence and severity of clinical symptoms, severity of anxiety and depression and high resolution anorectal manometry (HRAM) data in patients with IBS with constipation (IBS-C) and IBS with diarrhea (IBS-D).

31 patients with IBS-D and 33 patients with IBS-C (according to ROME III) were examined for severity of abdominal pain and flatulence (by visual analogue scales), stool frequency (defecation per week), severity of depression and anxiety (by Hamilton Depression Rating Scale (HRDS) and Hamilton Anxiety Rating Scale (HARS) respectively). All patients were also analyzed by HRAM using 20 channel water-perfused catheter with a polyethylene balloon (Solar GI, MMS, the Netherlands).

Results: IBS-D patients showed positive correlation of stool frequency to amplitude and % of relaxation of internal anal sphincter ($\tau = 0.33$, $p = 0.023$; $\tau = 0.31$, $p = 0.023$; respectively) as well as duration of RAIR ($\tau = 0.36$, $p = 0.007$); negative correlation of stool frequency to threshold for first ($\tau = -0.33$, $p = 0.015$), permanent ($\tau = -0.36$, $p = 0.007$) and intense ($\tau = -0.28$, $p = 0.037$) urge to defecate.

Patients with IBS-C showed negative correlation of stool frequency to average and maximum resting pressure of the anal sphincter ($\tau = -0.28$, $p = 0.039$; $\tau = -0.32$, $p = 0.018$ respectively) and duration of RAIR ($\tau = -0.30$, $p = 0.028$).

All patients showed positive correlation of severity of anxiety to duration of squeeze of anal sphincter ($\tau = 0.36$, $p = 0.007$) and to threshold for the rectoanal inhibitory reflex (RAIR) ($\tau = 0.32$, $p = 0.017$); depression severity to threshold for first sensation ($\tau = 0.38$, $p = 0.004$) and to threshold for intense urge to defecate ($\tau = 0.29$, $p = 0.032$). The patients also showed negative correlation of depression severity to maximum of absolute anal squeeze pressure in both IBS group ($\tau = -0.27$, $p = 0.049$).

In addition, positive correlation of severity of anxiety to stool frequency and severity of flatulence ($\tau = 0.33$, $p = 0.008$ and $\tau = 0.44$, $p = 0.001$ respectively) was observed.

Conclusion: According to HRAM, rectal motility and sensitivity abnormalities correlate with severity of stool disorders, as well as flatulence intensity. Comorbid emotional disorders aggravate already existing motility and sensory abnormalities and enhance the clinical symptoms. This data allows to suggest that all IBS patients should be tested for anxiety and depression. Antidepressant and anxiolytic drugs might be an important part of IBS treatment for these patients.

Disclosure: The authors declare no conflict of interest.

P1685 RECTO-ANAL SENSORIAL AND MOTOR CHARACTERISTICS IN TYPE 2 DIABETICS WITH OR WITHOUT COMPLAINTS OF CONSTIPATION: A COMPARATIVE STUDY

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Introduction: Constipation is a very frequent complaint in type 2 diabetic patients[1] and some authors believe that alterations in recto-anal thresholds may be present in individuals with these symptoms[2].

Aims and Methods: The aim of this study was to compare rectal sensorial and motor characteristics of type 2 diabetics with and without constipation.

Recto-anal manometry was performed in 35 type 2 diabetics, without signs of autonomic neuropathy, 15 with complaints of constipation and 20 without this symptom, matched by age and gender.

Results: In diabetics with complaints of constipation vs. without complaints, the values were the follow: rectal resting pressure, 11.5 ± 1.8 vs. 12.1 ± 2.3mmHg; $p = 0.8$; internal anal sphincter resting pressure, 40.0 ± 4.7 vs. 43.6 ± 6.1mmHg, $p = 0.6$; minimum rectal sensibility, 65.5 ± 6.8 vs. 78.6 ± 9.2ml, $p = 0.2$; first urge, 107.58 ± 14.1 vs. 119.3 ± 13.1ml, $p = 0.5$; intense urge, 132.0 ± 14.2 vs. 145.3 ± 15.5ml, $p = 0.5$; maximum tolerable rectal capacity, 197.0 ± 22.6 vs. 208.6 ± 19.0ml, $p < 0.7$. The relaxing percent during the recto-anal reflex was 40.9 ± 6.0% vs. 30.5 ± 4.5%, $p > 0.05$. The sphincter pressure during the squeeze was significantly lower in diabetics with symptoms 67.2 ± 11.2 mmHg than without it, 109.7 ± 16.4mmHg, $p < 0.03$; but during the squeeze endurance, 88.0 ± 11.7 vs. 114.9 ± 17.4mmHg, was statistically similar. The anal sphincter fatigue during the squeeze endurance, 0.29 ± 0.41 vs. -0.26 ± 0.40 mmHg/sec was similar. When comparing the recto-anal characteristics according to the severity of constipation, there were no statistic differences between diabetics with slight to moderate or severe to very severe symptoms.

Conclusion: 1-In type 2 diabetics with complaints of constipation the resting rectal pressure, the volume for minimum rectal sensibility, first urge, intense urge and maximum tolerable rectal capacity, and the relaxing degree during the recto-anal inhibitory reflex were statistically similar to diabetics without the symptoms. 2-The pressure augment during the squeeze was higher in diabetics without constipation. 3-In general recto-anal sensorial and motor thresholds were similar in type 2 diabetics with or without constipation.

Disclosure: Nothing to disclose

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P1686 NEURO-GLIAL MODULATION ASSOCIATED WITH PELVIC ORGANS CROSS-SENSITIZATION: EFFECT ON CHRONIC VISCERAL NOCICEPTION

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Introduction: Irritable bowel syndrome (IBS) and bladder pain syndrome (BPS) often overlap, and are both characterized by visceral hypersensitivity reproduced by pelvic organ distension. Since pelvic organs share a common innervation, it is likely that those syndromes involve a cross-sensitization of the bladder and the colon in response to distension.

Aims and Methods: The aim of this project was to assess the involvement of spinal neuro-glial interactions in the development and the sustainment of bladder and colon cross-sensitization. Chronic cross-organ sensitization was obtained in C57BL/6 conscious mice using ultrasound-guided intravesical administration of acetic acid under brief isoflurane anesthesia. Colonic sensitivity was assessed in conscious mice by measuring abdominal contraction during isobaric colo-rectal distension. Myeloperoxidase (MPO), used as a marker of colonic inflammation, was measured on colon. Colonic permeability was measured using Ussing chamber. C-Fos protein expression, used as a marker of neuronal activation, was counted in the spinal cord (level L6-S1) using immunohistochemistery.

CX3CR1-GFP^{+}mice were used to identify and count microglia cells in the L6-S1 dorsal horn of the spinal cord. IL1beta mRNA was assayed on the spinal cord using qRT-PCR. Expression of NK1 receptor was quantified in the spinal cord by western-blot.
Results: We developed a chronic cross-sensitization model in conscious mice. In this model, intravesical administration of acetic acid induced a transient increase in colonic permeability, and a long lasting colonic hypersensitivity to distension, that involved neuroglial interaction and NK1 receptors.
Conclusion: We developed a chronic cross-sensitization model in conscious mice. In this model, intravesical administration of acetic acid induced a transient increase in colonic permeability, and a long lasting colonic hypersensitivity to distension, that involved neuroglial interaction and NK1 receptors.
Disclosure: Nothing to disclose

P1687 REPEATABILITY OF THE FRUCTOSE BREATH TEST IN FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Intolerances to fermentable sugars, collectively referred to as FODMAPs, are common in functional gastrointestinal disorders (FGID), and reduction of the intake of these sugars results in significant symptom relief in selected patients (1). Breath tests are in widespread use for the diagnosis of sugar intolerances and have been shown to be useful in the prediction of the outcome of dietary modulation (2). However, studies of the repeatability of breath tests have not been reported.
Aims and Methods: The aim of this single-centre, prospective study was to assess the repeatability of the fructose breath test using appropriate statistical tools in successive patients with FGID. Sixteen male and female patients with functional dyspepsia and/or irritable bowel syndrome, as defined by Rome III criteria, received fructose 35g in the morning after a standardized 24h low-FODMAP diet on two separate days at least 14 days apart. At each occasion, breath samples for measurement of hydrogen and methane concentrations were collected (Quintron BreathTracker SC®, USA) and GI symptom intensities (abdominal bloating, flatulence, fullness, nausea, diarrhoea, abdominal cramps or pain, borborygmi, and gastroesophageal reflux) were scored hourly on a 3-point Likert scale for 5 hours after fructose ingestion. All patients, irrespective of symptom or gas responses, were evaluated. The areas-under-the-curve (AUC) of the aggregate GI symptom scores and of the breath hydrogen and methane concentrations were calculated and repeatability was assessed using limits of agreement and intraclass correlation coefficients (3). Additionally, the numbers of patients with intolerance (aggregate symptom score increased by >2) or malabsorption (rise in hydrogen >20ppm or in methane >10ppm) were determined and the absolute agreement and kappa values were calculated. The repeatability of measurements refers to the variation in repeat measurements made on the same subject under identical conditions, by the same instrument or method, the same observer and that the measurements are made over a short period of time.
Results: For the aggregate GI symptom score and the hydrogen and methane gas concentrations, repeatability was ''moderate'', with intraclass correlation coefficients of 0.7, 0.57 and 0.57, respectively. Fructose intolerance was present in 9 of 15 patients (60%) in the first and second breath tests, with an absolute agreement in classification between both breath testing sessions for 13 of 15 patients (87%), resulting in a kappa value of 0.72 ($p = 0.003$). Malabsorption of fructose occurred in 6 of 15 patients (40%) in the first test and in 7 of 15 patients (47%) in the second test. There was absolute agreement in malabsorption classification between both breath testing sessions for 8 out of 15 patients (53%), corresponding to a kappa value of 0.05 ($p = 0.42$).
Conclusion: The fructose breath test methodology shows repeatability in the range of what is considered adequate for clinical testing. When the arbitrarily defined thresholds used in clinical practice are applied, classification of intolerance based on symptoms shows good repeatability, while classification of malabsorption based on gas concentrations varies considerably. Based on these results, the fructose test can be recommended as a sensory provocation test, but current clinical definitions of malabsorption yield unreliable results and need to be revisited.
Disclosure: Grant support:Forschungsstftung Hirslanden, Zurich, Switzerland

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P1688 DIETARY FODMAPS SUCH AS FRUCTO-OLIGOSACCHARIDES AND LACTOSE CAN INCREASE ABDOMINAL SENSITIVITY AND THE NUMBER OF MUCOSAL MASTOCYTES IN MICE; A STUDY ON UNDERLYING MECHANISMS

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Introduction: Irritable Bowel Syndrome (IBS) is characterized by abdominal pain, often associated with diet. Limiting the consumption of FODMAPs (fermentable oligos-, di-, mono-saccharides, and polyols), unabsorbed in the small intestine and fermented by the gut microbiota, improves symptoms in 70% of IBS patients. However, the mechanisms behind this effect remain unclear. Our hypothesis is that bacterial metabolites resulting from fermentation of FODMAPs, such as aldehydes (glycation agents), can cause symptoms via the formation of pro-inflammatory advanced glycation end-products (AGEs) in the tissue. In addition, mast cells, and specifically their proximity to nerve endings in the colon, have been strongly implicated in IBS. We used the FODMAP representatives lactose (disaccharide), and fructo-oligosaccharides (FOS) in an animal model to evaluate the effects of these dietary FODMAPs on gut sensitivity. We also aimed to evaluate the involvement of AGEs and the mucosal mast cell population in the effects induced by these interventions.
Aims and Methods: Three groups of mice (C57BL/6 ♀) were treated daily for 21 days with an oral gavage of saline or saline solution containing 5 mg of lactose and/or 5 mg of pyridoxamine for lactose experiments, additionally, three groups of mice (C57BL/6 ♀) followed diets for 21 days; control (AIN-93M), 10% FOS (AIN-93M; part of starch replaced by FOS), and 10% FOS + 1mg/ml pyridoxamine in drinking water. Visceral sensitivity in lactose-treated animals was measured using electromyography during a colorectal distension procedure. Abdominal sensitivity in FOS-treated animals was evaluated non-invasively by mechanical stimulations with von Frey filaments (0.16, 0.6 and 1.4 g). In both sets of animals, mucosal mast cell (MMC) numbers and Receptor of AGEs (RAGE) expression in proximal colon were evaluated by immunofluorescence.
Results: Lactose treatment led to an increased visceral sensitivity (average response +40% at distension 0,08ml compared to control, $p < 0.01$). The FOS-enriched diet induced abdominal hypersensitivity versus control (33% vs 15% for 0.6g stimulation, 52% vs 33% for 1.4g stimulation). Co-administration of pyridoxamine prevented these effects in both experiments. Proximal colon epithelial RAGE expression was higher in lactose-treated animals (± 40% increase in signal intensity), and mucosal mast cell numbers increased (0.74 v 0.54 mast cell/crypt). Similarly, RAGE expression and MMC numbers were higher ($p < 0.05$) in the FOS group compared to the control group (± 40% increase in signal intensity and 1.27 vs 0.67 mast cells/crypt respectively). No differences were observed between control and FOS+pyr groups. These increases were prevented by co-administration of pyridoxamine, in both treatment sets.
Conclusion: This study shows that an increased FODMAP intake induces an abdominal hypersensitivity and an increase in the number of mucosal mast cells in mice, two pathophysiological factors characteristic of IBS. The prevention of these effects by anti-glycation agent pyridoxamine implies the role of glycation processes and the generation of AGEs in the origin of these effects. Given the similar results obtained with both FODMAP representatives, this work suggests a common mechanism responsible for the adverse effects observed, namely, the generation of glycation agents derived from FODMAP fermentation by the gut microbiota.
Disclosure: Nothing to disclose

P1689 ADENOSINE A_{2B} RECEPTOR REGULATES COLONIC FLUID SECRETION IN MICE

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Introduction: Adenosine is an extracellular purine nucleoside signaling molecule responsible for diverse actions in gastrointestinal systems, such as intestinal secretion, motility, inflammation and sensation. Previous studies suggest that adenosine receptors, especially A_{2B} receptor regulate colonic water secretion (1, 2). However, the available evidences that A_{2B} receptor modulates fluid secretion have been limited and the results using pharmacological agents specific for its receptor or genetically modified mice have not been demonstrated.
Aims and Methods: Our aims in this study are to investigate the effect of adenosine receptors on colonic water secretion *in vivo* and to determine the genetic evidence for the involvement of A_{2B} receptor. Assessment of intestinal fluid content was examined by mouse intestinal loop model, as described previously with some modifications (3).
Results: Adenosine solution injected into lumen increased fluid volume in murine colon in a dose-dependent manner. Pharmacological analysis using specific receptor agonists showed that A_{2B} receptor agonist BAY60-6583 significantly stimulated colonic fluid volume. We also found that A_1 receptor agonist *N*6-cyclopentyladenosine (CPA) slightly increased water contents, while A_3 receptor agonist IB-MECA produced a small reduction in it. However, these results were not significant. CGS21680, an agonist for A_{2A} receptor did not affect intestinal fluid contents. Moreover, we confirmed that the adenosine injected into lumen

did not increase fluid volume in mice genetically deficient in A_{2B} receptors compared with the case of wild-type mice.
Conclusion: Taken together, these results suggest that A_{2B} adenosine receptor regulates colonic water secretion and this receptor could be a therapeutic candidate for constipation or diarrhea related diseases.
Disclosure: We belong to endowed research division of LTT Bio-Pharma Co., Ltd.

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P1690 HYPERPLASIA OF ENTERIC GLIAL PROCESS TOWARD THE SENSORY NEURON AND INCREASED NETRIN-1 EXPRESSION IN THE COLONIC SUBMUCOSA IN A RAT MODEL OF VISCERAL HYPERSENSITIVITY

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Introduction: Elongation of enteric neuron toward the gastrointestinal mucosal surface leads to visceral hypersensitivity, which is one of the pathogenesis of irritable bowel syndrome (IBS). Among a variety of physiological roles of enteric glial cell (EGC), we reported that activated EGC in the myenteric plexus of the colon contributes to motor hypercontraction according to the stress intensity (*Neurogastroenterol Motil*, 2015). However, it is unknown how submucosal plexus, particular in submucosal EGC involves in neuronal elongation. Although netrin-1 is a well-characterized chemoattractant involved in neuronal guidance in the developing enteric nervous system, it also remains unknown which layer of the colon netrin-1 has crucial roles in under stress circumstances.
Aims and Methods: We used the Wistar Kyoto rats (WKY), a model of visceral hypersensitivity, and Wistar rats (control). Distal colonic segments were obtained from each rat, and the respective layer (mucosa, submucosa, and muscle) were separately striped from the whole colonic tissues and prepared. According to the layers, we compared mRNA expression of glial fibrillary acid protein (GFAP), netrin-1, nerve growth factors (NGF), glial cell-line derived neurotrophic factor (GDNF), and GAP43, a neurogenesis marker by real-time RT-PCR. To analyze EGC morphology and its interaction with intrinsic primary afferent neuron (IPAN), whole mount submucosal plexus preparations were used for immunohistochemistry for EGC (GFAP), IPAN (calbindin), netrin-1, and a receptor of netrin-1 (DCC, deleted in colorectal cancer).
Results: mRNA expressions of netrin-1 (3.2-fold), NGF (2.2-fold), GDNF (1.6-fold), and GAP43 (3.0-fold) were significantly increased in submucosal layer in the WKY group compared to the control, while there were no changes in the mucosa and muscle layers between WKY rats and controls. GFAP mRNA expression was increased in the submucosal layer of the WKY rats (3.0-fold) compared to the control. In the submucosal layer of the WKY rats, hyperplasia of EGC processes dramatically appeared. In morphology of EGC processes, thick elongation, ramified and spine formation toward the IPAN (calbindin-positive) were remarkably found in the WKY group rather than the control. Netrin-1 was expressed in both EGC and the neuron, while netrin-1 receptor was expressed in the neuron alone.
Conclusion: Submucosal layer of the colon has important roles under stress circumstances. In the submucosal layer, both hyperplasia of EGC processes toward the sensory neuronal body and increased neuronal elongation factors (netrin-1, NGF, and GDNF) may be involved in peripheral mechanisms of visceral hypersensitivity in IBS.
Disclosure: Nothing to disclose

P1691 ANO-RECTAL SENSORIAL AND MOTOR CHARACTERISTICS IN TYPE 2 DIABETICS WITH OR WITHOUT COMPLAINTS OF GASTRO-OESOPHAGEAL REFLUX: A COMPARATIVE STUDY

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Introduction: Some investigations shore up that there is an important overlap between the diverse functional disorders in the digestive tract.[1,2] In diabetics, gastro-oesophageal reflux and anorectal symptoms are frequent.
Aims and Methods: The aim of this study was to compare rectal sensorial and motor characteristics between type 2 diabetic individuals with and without complaints of gastro-oesophageal reflux.
Recto-anal manometry was performed in 32 type 2 diabetic, without signs of autonomic neuropathy, 12 with complaints of gastro-oesophageal reflux and 20 without this complaint, matched by age and gender.
Results: In diabetics with complaints, resting rectal pressure was slightly higher than others without complaints, 13.6 ± 1.2 vs 9.6 ± 1.6mmHg, but the difference was no significant, $p = 0.07$. In both groups, diabetics with complaints vs without complaints, other rectal manometric characteristics were the follow: minimum rectal sensibility, 56.7 ± 6.7ml vs. 80.0 ± 7.6ml, $p < 0.05$; first urge, 80.8 ± 6.1 vs. 132.3 ± 13.5ml, $p < 0.002$; Intense urge, 108.3 ± 6.0 vs. 152.8 ± 14.7ml, $p < 0.005$; maximum tolerable rectal capacity, 169.2 ± 15.6 vs. 225.5 ± 20.8ml, $p < 0.03$. The relaxing percent during the recto-anal reflex and the sphincters pressures during the squeeze and squeeze endurance were statistically similar. The anal sphincter fatigue during the squeeze endurance was 1.16 ± 0.55 vs. -0.53 ± 0.29 mmHg/sec. When comparing the characteristics according to the degree of reflux, slight to moderate vs. severe to very severe complaints, the resting external sphincter pressure was 31.0 ± 3.4 vs 58.3 ± 5.8mmHg, $p < 0.002$; and minimum rectal sensibility was 41.6 ± 6.0 vs. 63.7 ± 6.6mmHg, $p < 0.03$.
Conclusion: 1-In type 2 diabetics with complaints of gastro-oesophageal reflux the volume for minimum rectal sensibility, first urge, and intense urge and for maximum tolerable rectal capacity were lower than in diabetics without the symptoms. 2-The anal sphincter fatigue was higher in diabetics with complaints. 3-The volumes for minimum rectal sensibility and for maximum tolerable rectal capacity were higher in diabetics with more severe symptoms.
Disclosure: Nothing to disclose

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P1692 ENHANCED CONNECTIONS OF SUBMUCOSAL GLIA AND NEURONAL OUTGROWTH TOWARD INTO THE MUCOSA IN ACCORDANCE WITH THE AXON GUIDANCE MOLECULES AND NEUROTROPHIC FACTOR MAY LEAD TO VISCERAL HYPERSENSITIVITY AFTER MILD IRRITATION WITH STRESS

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Introduction: Neuronal elongation toward the colonic mucosa leads to visceral hypersensitivity, which is one of the pathogenesis of irritable bowel syndrome (IBS). Activated enteric glial cell (EGC) in the myenteric plexus of the colon contributes to motor hypercontraction in maternally separated (MS) rats of IBS model (*Neurogastroenterol Motil*, 2015). Axon guidance molecules include attraction factors and repulsion factors, and interactively regulate the direction of neuronal sprouting in accordance with neurotrophic factor in the developing enteric nervous system. However, it is unknown how EGC, axon guidance molecules, and neurotrophic factor in the submucosal plexus involve in visceral hypersensitivity.
Aims and Methods: We used MS rats of IBS model (maternal separation stress for 3 hours starting on postnatal days 2–14). As an irritated condition, MS rats ($n = 4$–8) at the adulthood received intracolonic injections of acetic acid (2 mL, 0.6%) to cause the colonic mucosal irritation (irritated rats). One week later, distal colonic segments were obtained from each rat, and both mucosal layer and submucosal layer were separately stripped from the whole colonic tissues, and prepared to evaluate respectively. According to each layer, we compared mRNA expressions of glial fibrillary acid protein (GFAP), netrin1, an attraction factor, semaphorin3A, a repulsion factor, nerve growth factors (NGF), and GAP43, a neuronal outgrowth marker by real-time RT-PCR. To histologically analyze the submucosal plexus (network formation of EGC and neuron), whole mount submucosal plexus preparations were used for immunohistochemistry for GFAP (EGC), PGP9.5 (pan-neuronal marker), and netrin1.
Results: Glial processes were remarkably elongated and glia-glial connections were clearly enhanced in the submucosal plexus of the irritated rats, while they were faintly found in the non-irritated rats and control rats. Neuronal connections were also increased and enhanced along with the glia-glial connections. In the submucosal layer of the irritated rats, mRNA expressions of GAP43 (2.6-fold) and GFAP (3.4-fold) were higher than those in the non-irritated rats and untreated rats. As well as the submucosal layer, mRNA expressions of GFAP (2.3-fold) was tended to be increased in the mucosal layer of the irritated rats. However, there was no change in GAP43 mRNA expression in the irritated rats. In the submucosal layer of the irritated rats, mRNA expressions of netrin1 (1.7-fold) and NGF (2.5-fold) were significantly increased compared to those in the non-irritated rats. However, these expressions were not changed in the mucosal layer. Different from the attraction factor, mRNA expression of semaphorin3A was decreased in the mucosal layer of the non-irritated rats by chemical irritation, although it was significantly increased in the submucosal layer. Netrin1 was localized in the cytoplasm of neuron and EGC in the submucosal plexus. Neuronal outgrowth into the mucosa was histologically confirmed by GAP43 immunoreactivity in the acetic acid-treated rats.

Conclusion: Enhancement of glia-glial connections in the submucosal plexus in accordance with the axon guidance molecules both in the mucosa and submucosa affects neuronal outgrowth toward the colonic mucosa, which may lead to visceral hypersensitivity after mild irritation with chronic stress.
Disclosure: Nothing to disclose

P1693 MUCOSAL FEATURES AND MOLECULAR MECHANISMS UNDERLYING CHRONIC CONSTIPATION IN PATIENTS WITH PARKINSON'S DISEASE

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Introduction: Chronic constipation (CC) in Parkinson's disease (PD) is a severe, usually laxative-resistant condition often worsening the patient's quality of life. To date, the molecular mechanisms underlying PD/CC pathogenesis are only partially understood.
Aims and Methods: The present study aimed to investigate neuropathological and neurochemical features in colonic mucosal biopsies of PD/CC patients compared to non-parkinsonian CC patients and asymptomatic controls by examining markers of intestinal epithelial barrier (IEB) and of enteric submucosal neurons and glia. PD/CC patients (n = 6; 2F, 51–79 yrs), CC patients (n = 6; 4F, 31–60 yrs) and control subjects (screening colonoscopy) (n = 6; 3F, 33–64 yrs) were enrolled. Colonic biopsies (n = 6) were collected from each subject. Total proteins were extracted from n = 4 biopsies and analyzed by Western blot to quantify: glial fibrillary acid protein (GFAP, as index of glial activation) and vasoactive intestinal polypeptide (VIP) and its receptors VPAC1 and VPAC2 as markers of subsets of vaso-secretomotor neurons. In addition, n = 2 biopsies were analyzed by immunohistochemistry to evaluate tight junction (TJ) proteins, i.e. *Zonula occludens-1* (ZO-1) and occludin, as indicators of IEB structural integrity. The relative density of TJ immunofluorescence was scored as follows: 4, normal; 3, slightly modified; 2, altered; 1, markedly reduced; 0, no expression.
Results: Western blot data showed no significant differences in VIP protein expression levels in PD/CC *vs.* CC *vs.* controls (One-Way ANOVA, P = 0.3). Similarly, VPAC1 and VPAC2 expression did not appear significantly different among groups (P = 0.8 and P = 0.1, respectively). However, VIP and VPAC2 expression levels showed a trend to decrease in both PD/CC and CC groups vs. controls. Also GFAP expression did not show significant differences among the three groups (P = 0.5). ZO-1 immunoreactive pattern displayed a normal network in the mucosa of control subjects and PD/CC patients (score = 4), whereas in CC patients ZO-1 immunoreactivity was markedly decreased (score = 2). In contrast, occludin immunoreactivity in PD/CC patients was almost exclusively expressed at the base of the cells and it appears weaker (score = 1–2) than in CC patients and controls (score = 4).
Conclusion: The present study showed that occludin, but not ZO-1, is reduced in PD/CC and CC patients, whereas there were no significant changes in VIP, VPAC1, VPAC2 and GFAP protein expression in PD/CC and CC patients *vs.* controls. Taken together our data support the concept of selective protein abnormalities in IEB which may contribute to distinct mechanisms in PD/CC.
Disclosure: Nothing to disclose

P1694 A PROSPECTIVE EVALUATION OF GASTROINTESTINAL SYMPTOMS AND DYSMOTILITY IN SUBJECTS WITH AND WITHOUT HYPERMOBILITY SPECTRUM DISORDERS

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Introduction: Hypermobility Spectrum Disorders (HSD) are a continuum of connective tissue disorders characterized by joint hypermobility (JH). Recent studies demonstrated that HSD are often associated with gastrointestinal (GI) symptoms. A higher prevalence of HSD has been demonstrated in patients with functional compared to organic GI disorders, pointing towards neuromuscular dysfunction of the GI tract as a possible underlying mechanism.
Aims and Methods: We prospectively evaluated whether subjects with (undiagnosed) HSD present with different symptom patterns and GI motility compared to non-HSD subjects, in an unselected tertiary GI patient population in whom organic pathology had previously been excluded. Sixty-two subjects (53 female; mean age: 40), referred for comprehensive GI motility assessment using gastric emptying test, esophageal, antroduodenal, and/or colonic manometry study, were consecutively included. Brighton criteria were used to diagnose HSD, and JH was assessed using the Beighton score. A Beighton score ≥ 6 was used as the cut-off for clinically significant JH. GI and psychological symptom scores, and quality of life were assessed using the Gastrointestinal Symptom Rating Scale, Hospital Anxiety and Depression Scale, and Rand Health Survey Short Form-36.
Results: Eighteen subjects (29.0%) met criteria for HSD. No significant differences between HSD and non-HSD subjects were found for age, BMI, GI symptom severity, depression/anxiety, and mental as well as physical quality of life. Esophageal, gastric, antroduodenal, and/or colonic dysmotility was not significantly more prevalent in the HSD group vs. the non-HSD group (72.2% vs. 43.2%, p = 0.091). However, subjects with clinically significant JH (*i.e.*, Beighton score ≥ 6) more often showed abnormal GI motility compared to subjects with Beighton < 6 (83.3% vs. 46.8%, p = 0.028). The odds of having any form of GI dysmotility were 5.7 times higher (95%-CI: 1.121; 28.788) in cases with Beighton ≥ 6 than Beighton < 6.
Conclusion: In patients with functional GI disorders referred for extensive GI motility analysis, HSD patients did not present with gastric, esophageal, antroduodenal, and/or colonic dysmotility significantly more often than non-HSD patients. However, the clinical phenotype of JH was a significant predictor for GI dysmotility. Therefore, the present study supports a possible role for neuromuscular dysfunction as a pathophysiological mechanism underlying GI symptoms in HSD.
Disclosure: Nothing to disclose

P1695 HISTOPATHOLOGIC SIGNS OF NEURON DEGENERATION IN INDIVIDUALS WITH GASTROINTESTINAL SYMPTOMS MAY BE FOUND IN CONVENTIONAL STAINING IN BOTH SUBMUCOSAL AND MYENTERIC NERVE PLEXA

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Introduction: Gastrointestinal symptoms are common in the population, many times with unknown reasons. Previous research has described that enteric neuropathy may be the etiology in some cases. Parkinsonism is one disease which often presents itself with gastrointestinal symptoms, especially constipation, where enteric neuropathy may be suspected. Studies of the enteric nervous system and microscopic details of enteric neuropathy have often been performed and described in the myenteric plexa, using full-thickness intestinal biopsy and immunostaining. Since full-thicknes biopsy demands surgery or other advanced methods (Ohlsson et al 2017), and immunostaining is rather time-consuming, diagnosing of enteric neuropathy is often not performed. This leaves the patient without any diagnosis and explanation to the symptoms, and thereby without specific treatment.
Aims and Methods: The aim of the present study was to examine if pathologic changes are present also in the submucosal plexa, and whether these changes could be identified with conventional hematoxylin & eosin (HE) staining. In 20 deceased cases of Parkinson's disease/ Parkinsonism with gastrointestinal symptoms, the intestinal tract was investigated for potential neuroganglionic disease. Ten cases of non-Parkinson, intestinally asymptomatic individuals, were used as controls. Small specimens from the jejunum were sampled, as well as specimens from the colon. The material was treated with standard histopathological procedures, i.e. fixed in formaldehyde solution, dehydrated and embedded in paraffin, then sectioned at 4 μmeter thickness and stained with HE and with immunostaining for alpha-synuclein.
Results: In 15 of these cases of Parkinson's disease, there were atrophic/pycnotic nerve plexus cells, i.e. signs of ganglionic degeneration in the submucosal and/or myenteric plexa, mostly in both. In some of the cases, the degenerative signs were mild, however corroborated by findings of positive alpha-synuclein immunostaining. In the remaining 5 cases, there was no marked micromorphologic signs of degeneration in the HE staining, but immunostaining revealed minimal alpha-synuclein deposits in 3 of these cases. None of the controls showed any signs of ganglionic degeneration.
Conclusion: It seems possible to identify a morphologic intestinal disease substrate in individuals with Parkinson's disease, showing signs of ganglion cell pycnosis and degeneration, visible in both submucosal and myenteric plexa. This finding may serve to indicate a potential of diagnosing a dysfunction in the autonomic nervous system by conventional histopathological methods, which could be the target of a therapeutic approach. Pathologic changes also in the more easily available submucosal plexa which can be reached endoscopically, and not only in the deeper myenteric plexa, facilitate the diagnosing. These histopathologic findings have to be examined along with assessment of long-term gastrointestinal symptoms and autonomic dysfunction, not only in Parkinson's disease, but also in patients with idiopathic symptoms and dysfunction.
Disclosure: Nothing to disclose

Reference

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P1696 MANAGING GASTROINTESTINAL MANIFESTATIONS IN PATIENTS WITH POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME – A UK DISTRICT GENERAL HOSPITAL EXPERIENCE

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Introduction: Postural tachycardia syndrome (POTS) is a heterogeneous clinical syndrome characterised by a rapid increase in heart rate ($\geq$ 30 bpm) that occurs within 10 minutes upon standing, in the absence of orthostatic hypotension and other medical conditions or medications. Gastrointestinal (GI) symptoms are common in patients with POTS and impact on their quality of life. Our objective is to evaluate common GI symptoms, diagnostic work up, final diagnosis and management strategy in POTS.

Aims and Methods: We reviewed the complete medical records of all patients (aged 16 years and older) referred to a District General Hospital Gastroenterology Clinic over a four year period (2014–2017) with GI symptoms and known or suspected POTS. Patients without confirmed POTS were excluded.

Results: A total of 85 patients were included, with a mean age of 28.4 years, 92.9% were female. Constipation, bloating and abdominal pain were the most common GI symptoms in POTS. Gastrointestinal endoscopy, high-resolution manometry, gastric emptying studies and colonic transit studies were most commonly performed investigations. Among 85 patients, 59 (69%) had confirmed or suspected GI dysmotility. Twenty four patients (28%) had delayed colonic transit studies.

Conclusion: Non-functional GI symptoms prevalence is high among POTS patient therefore careful evaluation is required to provide an adequate diagnosis. The majority of patients with POTS and GI symptoms have a functional disturbance and reduced GI motility, however a small proportion have organic disease which needs systematic evaluation. Dietary modifications and laxatives are the main of treatments. Novel laxatives such as prucalopride and linaclotide are effective in managing dysmotility symptoms in patient with POTS.

Disclosure: Nothing to disclose

P1697 COLONIC-TRANSIT TIME AS PREDICTOR OF OUTCOME OF COLONIC MANOMETRY IN PATIENTS WITH CHRONIC CONSTIPATION

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Introduction: Chronic constipation is categorized into normal- (NTC) and slow-transit constipation. Therefore, patients not responding to therapy are often referred to tertiary centers in order to evaluate colonic transit time (CTT) and colonic manometry (CM). Colonic manometry (CM) is of additive value in the diagnostic workup of colonic motility, however, CM is an invasive, demanding procedure and is not readily available in all centers. Colonic transit time (CTT) as measured with radio-opaque markers is a less invasive procedure but it is claimed that colonic motor disturbances occur in both normal- and slow-transit and therefore, the relationship between colonic motor disturbances on CM and colonic transit time remains unclear.

Aims and Methods: The aim of this study was to assess the predictive value of CTT for colonic motor abnormalities on 24-hours colonic manometry in patients with chronic constipation in order to evaluate whether CTT studies might be helpful in determining for which patients CM is indicated. Prospectively collected data from patients undergoing both a CTT study as well as 24-hours ambulatory CM in our tertiary referral center were reviewed. Healthy volunteers were studied to obtain control values. CTT was measured using radio-opaque markers (X ray at day 4 after ingestion of 20 markers at day 0). A catheter with 6 solid-state pressure sensors was positioned endoscopically and clipped to the mucosa in the right colon in order to perform 24-hours ambulatory CM. CM was defined as abnormal when less than three high-amplitude propagating contractions (HAPC's), i.e. propagating waves with amplitude $\geq$80 mmHg over at least three sensors, were identified. Results are shown as mean $\pm$ SD and proportions and were compared using independent-samples T-test and chi square statistics.

Results: Data of 88 patients (77 women; 42.9 $\pm$ 13.8 years) and 12 healthy controls (10 women; 47 $\pm$ 14.4 years) were evaluated. Slow colonic transit (SCT) was based on CTT. Mean number of HAPCs per 24 hours was significantly lower in patients showing SCT compared to patients with normal colonic transit and controls (1.9 $\pm$ 2.2 vs. 4.8 $\pm$ 1.6 and 5.3 $\pm$ 3.0, $p < 0.001$ and $p < 0.001$ respectively). In total, 70 patients showed SCT, of which 49 (70.0%) showed abnormal CM. All 18 patients with normal colonic transit at CTT had normal CM. Therefore, the positive predictive value (PPV) of CTT for colonic hypomotility was 70% and the negative predictive value (NPV) was 100%.

Conclusion: This study shows that in the evaluation of patients with chronic constipation normal colonic transit, as measured by radio-opaque marker study, excludes abnormal colonic manometry with a NPV of 100% (i.e. based on number of HAPCs), whereas slow transit is a strong indicator for finding motor disturbances on colonic manometry. Therefore, colonic transit studies appears to be helpful in selecting patients with chronic constipation for colonic manometry to further characterize colonic motility.

Disclosure: Nothing to disclose

P1698 GUT DYSBIOSIS IS A PROMINENT FEATURE OF CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

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Introduction: Chronic intestinal pseudo-obstruction (CIPO) represents a severe form of chronic gut dysmotility. CIPO patients manifest with recurrent intestinal sub-occlusive episodes and severe symptoms causing significant morbidity and mortality. The intestinal microbiota is an important stimulator and regulator of gut motility. However, it is unknown whether gut microbiota is altered in CIPO and whether it is associated with the clinical presentation.

Aims and Methods: 1) To characterize the gut microbiota of patients with CIPO. 2) To identify demographic or clinical features associated with microbiota profiles. This is a prospective pilot study of CIPO patients and healthy controls at 2 tertiary centres in Hamilton, Canada and Bologna, Italy. Demographic and clinical data were collected by standardized questionnaires. Fecal microbiota analysis was performed using *Illumina* 16S rRNA gene sequencing.

Results: Fecal samples from 15 patients with sporadic CIPO (7 female, median age 38.6 $\pm$ 15 years) and 4 healthy age and sex-matched controls (2 female, 39.5 $\pm$ 9 years) were collected. Mean Body Mass Index was similar between groups (19.6 $\pm$ 3.3 vs. 21.7 $\pm$ 2.9 kg/m^2). A subset of CIPO patients (6/15) were on Total Parenteral Nutrition (TPN). Median age at onset of CIPO was 19 years (range 3–53). Most patients (11/15) had a history of intestinal resection. Overall, the microbiota profiles of CIPO patients were significantly different compared to healthy controls (Adonis test). CIPO patients exhibited marked dysbiosis, with a reduced relative abundance of Firmicutes, and a significant increase in Proteobacteria ($Q = 0.004$), mainly *Escherichia* species ($Q = 0.003$), compared to healthy controls. Bacterial richness (Chao index) and diversity (Shannon index) were significantly reduced in CIPO patients. There were no associations of microbiota profiles with clinical characteristics, as dysbiosis was present regardless of etiology, history of intestinal resection or TPN.

Conclusion: This is the first prospective series aimed at characterizing the intestinal microbiota of sporadic CIPO patients. We demonstrate that gut dysbiosis is a prominent feature of CIPO and is present regardless of clinical characteristics. It consists primarily in a predominance of the phylum Proteobacteria at the expense of Firmicutes. This provides a rationale for the evaluation of microbiota-based therapies for patients with CIPO.

Disclosure: Nothing to disclose

P1699 SYSTEMATIC REVIEW AND META-ANALYSIS: PREVALENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN IRRITABLE BOWEL SYNDROME

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Introduction: Small intestinal bacterial overgrowth (SIBO), with excessive and/or abnormal type of bacteria in the small bowel may play a role for the manifestation of Irritable bowel syndrome (IBS). We aimed to compare the prevalence of small intestinal bacterial overgrowth (SIBO) in patients with IBS and controls.

Aims and Methods: Using the search terms 'small intestinal bacterial overgrowth (SIBO)' and 'Irritable Bowel Syndrome (IBS)' or 'small intestinal bacterial overgrowth (SIBO)' and 'Functional gastrointestinal disorders (FGIDs)', 21 case-control studies that met inclusion criteria were identified when searching relevant databases. Prevalence rates for SIBO, relevant demographic and geographic data, and information on the diagnostic modalities were extracted and prevalence rates and 95% confidence intervals (CI) of SIBO in IBS and controls calculated. In addition, the influence of the diagnostic modality (breath tests, aspirate or biopsy and culture or both) was determined.

Results: The final dataset combined 21 independent studies that recruited 2,422 adult patients with IBS and 2,879 controls. Sixteen studies employed breath tests (five utilized glucose breath tests (GBT), seven utilized lactulose breath tests (LBT), two utilized xylose breath tests and one each utilized sucrose and fructose breath tests) and five studies utilized culture methods. Across all testing methods, the prevalence of SIBO in patients with IBS compared with controls was increased with an OR = 3.29 (95% CI 1.91–5.67), $p < 0.001$. In patients with IBS prevalence of SIBO was 37.04% (95% CI 35.11–38.96) as compared to 19.26% (95% CI 21.01–24.07) in controls. When the method of detection was

limited to breath tests, the prevalence of SIBO in IBS was 44.25% (95% CI 48.86–46.63) compared to 23.71% (95% CI 21.53–25.89) in controls. In contrast, based upon culture techniques, the prevalence of SIBO in IBS was 13.96% (95% CI 11.49–16.43) vs 5.03% (95% CI 3.9–6.17) in controls when the cut off value was 10^5 cfu/ml (colony forming unit/ml), and 33.51% (95% CI 30.14–36.88) vs 8.18% (95% CI 6.76–9.61) in controls when the cut off value was 10^3 cfu/ml. There was no evidence that the association between SIBO and IBS was influenced by publication bias. Only studies using culture and aspirate to diagnose SIBO have uniformly reported the prevalence of IBS in different subtypes. In IBS diarrhoea (IBS-D) the prevalence of SIBO was 25.91%, higher than that in IBS mixed (IBS-M) and IBS constipation (IBS-C) at 18.9% and 17.48% respectively.
Conclusion: Regardless of the diagnostic modalities, prevalence of SIBO is significantly increased in patients with IBS, especially in IBS-D when compared to controls. However, while culture-based diagnostic methods for SIBO are the gold standard, they yield substantially lower SIBO prevalence rates in IBS as compared to breath tests. This suggests that breath tests may overestimate the prevalence of SIBO and have insufficient diagnostic specificity for SIBO. While better diagnostic tests are required, it is critical to determine if SIBO in IBS is the cause for symptoms or a consequence of other abnormalities of gut function.
Disclosure: Nothing to disclose

P1700 THE INFLUENCE OF THE DURATION OF THE DIABETES MELLITUS ON THE ANORECTAL FUNCTION

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Introduction: Diabetic enteropathy is one of the complications of diabetes. Long duration of the diabetes predisposes to different complications including those in the anorectal region.
Aims and Methods: The aim of the study was to evaluate the anorectal function with the use of the high-resolution anorectal manometry depending on the duration of the disease. Diabetic patients group with the disease history $\geq$ 10 years (group 1), the group with the disease history $<$ 10 years (group 2) and the control group included 35, 15 and 20 subjects, respectively. All patients completed the questionnaire (demographic and clinical data). The anorectal manometry was performed with the use of ManoScan 360 Sierra Scientific Instruments System. The following manometric parameters were evaluated: the maximum anal resting pressure (MRP), the maximum anal squeeze pressure (MSP), cough reflex, the push/strain maneuver, rectal sensation test and rectoanal inhibitory reflex (RAIR). Apart from the above mentioned parameters the following factors were also evaluated: length of the high pressure zone (HPZ), duration of sustain squeeze, anorectal pressure gradient, residual anal pressure (CR), rectal pressure during the push maneuver and the rectal compliance. Moreover, other parameters were calculated: MRP/MSP, MRP/CR (CR-residual anal pressure). Data are presented as mean $\pm$ SD.
Results: Patients with the diabetes history of $\geq$ 10 years reported anal region discomfort and incomplete evacuation more often than patients with the diabetes history of $<$ 10 years (13; 25 versus 1;6; $p < 0.03$, $p < 0.04$ respectively). MRP was 79.73 ± 23.52 mmHg, 96.85 ± 22.77 mmHg for group 1 and 2 patients respectively and 94.07 ± 12.96 mmHg for the control group; $p < 0.02$. MSP was 148.41 ± 62.51 mmHg, 203.31 ± 79.82 mmHg for group 1 and 2 patients respectively and 230.04 ± 59.79 mmHg for the control group $p < 0.01$. Group 1 and 2 patients had lower anorectal pressure gradient (-26.05 ± 26.33; -27.81 ± 38.01 respectively) and MRP/CR (1.19 ± 0.48; 1.29 ± 0.46 respectively) compared to the control subjects (-5.52 ± 29.56; 1.69 ± 0.56 respectively); $p < 0.05$; $p < 0.01$. Significant difference was found in the first sensation threshold between the group 1 and 2 patients (50.86 ± 28.11 ml, 38.00 ± 15.21 ml) and control group (28.50 ± 3.66 ml) $p < 0.01$.
Conclusion: Patients with the diabetes duration $\geq$ 10 years reported anal region discomfort and incomplete evacuation more often. Diabetic patients with the disease history $\geq$ 10 years had weakened function of external and internal anal sphincters than diabetic patients with diabetes history $<$ 10 years and control subjects. All diabetic patients had lower parameters used for the evaluation of push/strain maneuver (anorectal pressure gradient and MRP/CR) suggesting the appearance of dyssynergia more often. All had impaired visceral sensation manifested by higher threshold sense of the first sensation. The higher threshold of the above mentioned parameter was noted in the group of diabetic patients with the disease history $\geq$ 10 years compared to the group with the disease history $<$ 10 years.
Disclosure: Nothing to disclose

P1701 EVALUATION OF ANORECTAL FUNCTION IN DIABETES MELLITUS PATIENTS WITH DIABETES ENTEROPATHY SYMPTOMS

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Introduction: Diabetic enteropathy is one of the complications of diabetes. Symptoms such as chronic constipation, diarrhea or incontinence are important but often underestimated issues in interdisciplinary medical care.
Aims and Methods: The aim of the study was to evaluate the anorectal function with the use of the high-resolution anorectal manometry depending on the selected diabetic enteropathy symptoms.
Diabetic patients group with incontinence, constipation, chronic diarrhea and control group included 13, 15, 15, 20 subjects, respectively. All patients completed the questionnaire (demographic and clinical data).
The anorectal manometry was performed with the use of ManoScan 360 Sierra Scientific Instruments System. The following manometric parameters were evaluated: the maximum anal resting pressure (MRP), the maximum anal squeeze pressure (MSP), cough reflex, the push/strain maneuver, rectal sensation test and rectoanal inhibitory reflex (RAIR). Apart from the above mentioned parameters the following factors were also evaluated: length of the high-pressure zone (HPZ), duration of sustain squeeze, anorectal pressure gradient, residual anal pressure (CR), rectal pressure during the push maneuver and the rectal compliance. Moreover, other parameters were calculated: MRP/MSP, MRP/CR (CR-residual anal pressure). Data are presented as mean $\pm$ SD.
Results: MRP was 69.03 ± 26.15 mmHg, 81.89 ± 17.69 mmHg, 78.14 ± 26.49 mmHg for patients with incontinence, constipation and diarrhea respectively and 94.07 ± 12.96 mmHg for the control group; $p < 0.01$; $p < 0.04$; $p < 0.05$ respectively. MSP was 120.50 ± 72.57 mmHg, 140.63 ± 47.84 mmHg, 148.96 ± 77.10 mmHg for patients with incontinence, constipation and diarrhea respectively and 230.04 ± 59.79 mmHg for the control group; $p < 0.01$; $p < 0.01$; $p < 0.01$ respectively. Patients with diabetes and chronic constipation had lower anorectal pressure gradient (-30.64 ± 26.74) and MRP/CR (1.35 ± 1.69) compared to the control subjects (respectively -5.52 ± 29.56; 1.69 ± 0.56); $p < 0.03$; $p < 0.04$. Whereas patients with chronic diarrhea had only MRP/CR lower (1.28 ± 0.46); $p < 0.04$ from all the parameters used to evaluate the push/strain maneuver. Significant differences were found in the first sensation threshold between the symptomatic patients (50.00 ± 29.72 ml, 58.67 ± 37.20 ml, 38.00 ± 13.20 ml) and control group (28.50 ± 3.66 ml) $p < 0.01$; $p < 0.01$; $p < 0.02$ for incontinence, constipation and diarrhea respectively. Patients with diabetes and chronic constipation had higher threshold sense of urge to defecate (106.00 ± 47.48 ml) than control subjects (74.00 ± 9.40 ml) $p < 0.05$. RAIR was statistically significantly more often absent in the group of diabetic patients with incontinence, $p < 0.003$. Diabetic patients with incontinence and diabetic patients with chronic diarrhea had lower volumes of RAIR first time detection (31.54 ± 30.23 ml; 36.67 ± 30.39 ml) than the control subjects (52.50 ± 14.10 ml) $p < 0.01$; $p < 0.04$ respectively.
Conclusion: All diabetic patients with the symptoms of enteropathy had weakened function of external and internal anal sphincters. All diabetic patients had lower parameters used for the evaluation of push/strain maneuver (anorectal pressure gradient and MRP/CR) suggesting the appearance of dyssynergia more often. All had impaired visceral sensation manifested by higher threshold value of first sensation. Higher threshold value of urge to defecate was noted only in patients with chronic constipation. The absence of RAIR was more often noted in patients with incontinence.
Disclosure: Nothing to disclose

P1702 THE EFFECT OF PROBIOTIC ADMINISTRATION IMMEDIATELY AND ONE MONTH AFTER COLONOSCOPY IN DIARRHEA-PREDOMINANT IBS PATIENTS

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Introduction: Irritable bowel syndrome (IBS) is one of the most common disorders among young adults. Various studies have demonstrated that use of probiotics can reduce the overall symptom of IBS, thus our aim was to evaluate the efficacy of probiotics products in the reduction of IBS symptoms after colonoscopy
Aims and Methods: Our patients were divided among three groups, including immediate probiotics users (21F, 12M, 32.97 ± 10.79 years old), start use of probiotics one month after colonoscopy (19F, 13M, 30.941 ± 8.52 years old), and placebo group (22F, 12M, 35.15 ± 11.20 years old). All the patients were interviewed for having common IBS symptoms (stool consistency and frequency, gas, abdominal pain, and flatulence) at baseline, 3rd month of follow up and 6th month of follow up.
Results: The mean reduction in abdominal pain was 3.05 ± 1.21, 3.86 ± 0.94 and 3.82 ± 0.63 in the control group, immediate probiotic users and one month after colonoscopy, respectively (P value $<$ 0.001). On the other hand, the symptoms of the disease, such as stool consistency, the frequency of defecation and flatulence (except gas) in the first quarter, in the two treatment groups were significantly improved more than in the control group (P value $<$ 0.05). In contrast, in the second quarter, stool consistency, abdominal gas and bloating were improved only in the immediate probiotics users compared to the control group (P value $<$ 0.05), but the frequency of defecation was not significantly different in the treatment group receiving the probiotics month after colonoscopy compared to the placebo users (P value $>$ 0.05).
Conclusion: According to our results, use of probiotics had the beneficial effect on IBS symptoms. Furthermore, it can be said, however, reductions in symptoms and pain in the two treatment groups were not significantly different, but after six months of treatment, the effect of probiotics in patients who immediately use it after colonoscopy was more visible and more stable.
Disclosure: Nothing to disclose

P1703 A SMARTPHONE APPLICATION FOR SYMPTOM ASSESSMENT AND DATA COLLECTION IN MEDICAL TRIALS: EXAMPLE FROM AN IBS DRUG INTERVENTION TRIAL

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Introduction: Patient-reported outcome measures (PROMS) are crucial to assess the efficacy of therapeutic interventions, especially for disorders such as Irritable Bowel Syndrome (IBS), without a well-defined organic substrate and lack of validated biomarkers. The reliability of paper diaries is often affected by recall bias and fake compliance. To acquire more valid data, electronic diaries have been developed and implemented in recent years. However, little has been reported on the compliance rates of these diaries so far, and when available, the rates vary widely between studies.

Aims and Methods: Our aims were 1) to determine the compliance rate to a smartphone application in a randomised placebo-controlled trial (RCT) and 2) to identify sociodemographic and clinical patient characteristics associated with compliance rate.

The PERSUADE study (peppermint oil versus placebo) uses a smartphone application for patients to register their daily symptoms. IBS patients (ROME IV) were instructed to fill out this digital dairy during a 8-week treatment period. In addition, patients were asked to complete electronic questionnaires (via email, not smartphone), regarding demographics and life style, symptom severity (IBS-SSS), Quality of Life (IBS-QoL), and anxiety and depression (GAD-7, PHQ-9). Compliance rate was defined as the percentage of days completed in the diary.

Results: 154 (79.1% female, mean age 33.8) patients have been included so far. The mean compliance rate was high (86.6%, 10.5 SD). No association was found between age, gender, educational level, and compliance. Interestingly, the number of adverse events was positively associated with compliance (B 0.01, $p = 0.04$), whereas anxiety was inversely associated with compliance (B -0.05, $p = 0.01$). Moreover, overall compliance declined over time ($F(5.8, 886.4) = 6.07$, $p < 0.00$).

Conclusion: This study demonstrates that compliance to this smartphone application is, on average, more than 80%. However, the compliance rate decreased over time, which might suggest that this method is less suitable to measure treatment efficacy over long periods of time.

Disclosure: The PERSUADE trial in part funded by WillPharma.

P1704 ADHERENCE TO DIET LOW IN FERMENTABLE CARBOHYDRATES AND TRADITIONAL DIET FOR IRRITABLE BOWEL SYNDROME: WHAT ARE THE CHALLENGES AND OPPORTUNITIES?

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Introduction: Dietary interventions in irritable bowel syndrome (IBS) include a diet low in fermentable oligo-, di-, monosaccharides and polyols (FODMAPs) and a traditional IBS diet, which focuses on eating habits more than dietary composition.

Aims and Methods: We aimed to evaluate how well IBS patients adhere to common dietary guidelines, which specific food groups prove troublesome to replace, and which dietary shifts predicted a symptom response. This is a post-hoc analysis of a previously published RCT (Böhn *et al Gastroenterology* 2015), in which IBS patients ($n = 66$) were randomised to a 4-week low FODMAP diet or a traditional IBS diet. Participants completed 4-day diet diaries before and near the end of the intervention, and reported symptoms using the IBS symptom severity scale (cut-off for responder status was an improvement by 50 points). We evaluated compliance and general changes to the diet by principal component analysis, and described which specific food groups were reduced, replaced, or retained during the intervention. Discriminant analysis was used to investigate dietary changes predictive of responder status.

Results: Compliance with the low FODMAP guidelines was good and consistent: all patients had a comparable shift in the diet's principal components. High FODMAP fruits, nuts, and grains were largely replaced by low FODMAP equivalents (97%, 100%, and 54% of baseline consumption, $p < 0.001$, Table 1). Intake of confectionery and snacks was reduced by 69% ($p < 0.001$). High FODMAP vegetables were reduced by 88%, but poorly replaced, leading to a 17% loss of total vegetable intake. Total energy intake fell by 25% in the low FODMAP arm ($p < 0.001$). The traditional IBS diet did not lead to a major shift in the diet's principal components. Despite the traditional IBS guidelines, there remained high consumption of coffee (73% of baseline consumption), alcohol (54%), cabbage, onions, and legumes (67%, Table 1). Pizza and carbonated beverages were fully excluded. Total energy intake fell by 11% in the traditional IBS diet arm ($p = 0.15$). In both diets, responder status was predicted by reduced consumption of alcohol and coffee and increased consumption of water and tea ($p = 0.03$).

Conclusion: In both the low FODMAP diet and traditional IBS diet, certain food groups were difficult to replace. Close dietary guidance may enhance the efficacy of these diets.

Product	Reduced	Replaced	Retained	P-value	Main replacement
Low FODMAP diet					
Grains	17	54	29	<0.001	Gluten-free equivalents
Dairy products	48	28	24	<0.001	Lactose-free equivalents
Fruits (e.g. apples)	0	97	3	<0.001	Fruits (e.g. oranges)
Cabbage/onions/legumes	49	38	12	0.002	Leaf & root vegetables
Nuts (e.g. cashews)	0	100	0	<0.001	Other nuts & seeds
Confectionery	69	–	31	<0.001	–
Traditional IBS diet					
Coffee	27	–	73	0.004	–
Alcoholic beverages	46	–	54	0.005	–
Carbonated beverages	80	–	20	0.013	–
Cabbage/onions/legumes	0	33	67	0.08	Leaf & root vegetables
High-fat foods	12	2	86	0.002	Low-fat equivalents

[Table 1: Selection of products to be avoided according to the respective guideline. Values are percentages of baseline consumption.]

Disclosure: Nothing to disclose

Reference

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P1705 EFFECTS OF ALKALINE-REDUCED DRINKING WATER ON IRRITABLE BOWEL SYNDROME WITH DIARRHEA: A RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED PILOT STUDY

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Introduction: The purpose of this study was to investigate whether the ingestion of alkaline-reduced water (ARW) is helpful in improving the symptoms of diarrhea-predominant irritable bowel syndrome (IBS).

Aims and Methods: Twenty-seven patients (male, 25.9%; mean 41.7 years-old) with diarrhea-predominant IBS were randomly allocated to two groups. For eight weeks, the ARW group ($n = 13$) ingested at least 2 liters/day of ARW, while the control group ($n = 14$) ingested placebo water. IBS symptom scores (quality-of-life, abdominal pain/discomfort), stool form and frequency were assessed before and after treatment via questionnaires.

Results: Eight patients (61.5%) in the ARW group and six patients (42.9%) in the control group indicated that their symptoms had improved in more than four out of the eight weeks of treatment ($p = 0.449$). The IBS quality-of-life score significantly improved from 57.2 to 30.8 in the ARW group; this improvement was significantly greater than the slight improvement from 48.7 to 42.2 observed in the control group ($p = 0.029$). The abdominal pain score improved from 1.8 to 0.9 in the ARW group, and from 1.8 to 1.1 in the control group, with no significant group difference ($p = 0.232$).

Conclusion: Drinking ARW for eight weeks improves the quality-of-life in patients with diarrhea-predominant IBS.

Disclosure: Nothing to disclose

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P1706 FOCUSSED EDUCATION ON IBS IS A HELPFUL INTERVENTION TO REDUCE ANXIETY AND IMPROVE SYMPTOMS

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Introduction: Patient self-management is central to IBS therapy and recommended in most guidelines. Self-help allows better understanding of the condition and promotes patient implementation of evidenced-based diet, lifestyle and behavioural changes that can improve symptoms. However, co-existent anxiety may limit the response to self-help programmes. We report the impact of anxiety and IBS symptoms following a dedicated education program.
Aims and Methods: We present preliminary data from a randomised controlled trial of two forms of educational therapy in IBS, live group sessions versus individual online education. The educational programme involved six consecutive sessions over 10 weeks. Sixty nine patients (53 f, mean age 34, range 19–69) were invited to participate. All had baseline and post-treatment HAD score and IBS-SSS to assess anxiety/depression and bowel symptoms severity, respectively. Fourteen patients completed online education and 27 the live group sessions.
Results: Forty-one patients completed the educational programme. There were 14 patients with IBS-C, 14 IBS-D and 13 IBS-M. HAD scores at baseline demonstrated 36 patients had anxiety, 12 (29%) borderline and 24 (59%) overtly high scores; for depression there were 7 (17%) with borderline scores and 10 (24%) patients case-level scores. Fifteen (37%) patients had both anxiety and depression. Mean baseline IBS-SSS was 369 (range 160–480). There was no correlation between anxiety and symptom severity scores at baseline ($r = 0.17$, $p = 0.36$). Table 1: IBS subtypes.
At the end of treatment, anxiety had improved in 5/12 patients as well as in 10/24 borderline cases. No significant reduction in depression was recorded at the end of the internvetion (2/17 cases improved). Mean anxiety scores fell from 15 at baseline to 8 ($p < 0.001$). IBS-SSS fell from 369 at baseline to 273 ($p < 0.001$). There was an excellent correlation between reduction in anxiety scores and reduction in IBS-SSS scores ($r = 0.453$, $p = 0.23$).
Conclusion: Anxiety is highly prevalent in patients with IBS. Education is an effective means for reducing anxiety and improving symptom severity. Identifying and reducing anxiety is a key part of managing IBS patients. Self-management programmes are effective in addressing this objective and may be the key mechanism through which such programmes help.

Variable	Patients at baseline (69)	Patients at follow-up (41)
Age (mean)	34	32
Sex (f)	77%	91%
IBS-D	48%	35%
IBS-M	29%	32%
IBS-C	23%	33%

[Table 1]
Disclosure: Nothing to disclose

P1707 INTESTINAL MICROBIOME IN IRRITABLE BOWEL SYNDROME BEFORE AND AFTER GUT-DIRECTED HYPNOTHERAPY

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Introduction: Irritable bowel syndrome (IBS) is a disorder with brain-gut-microbiome alterations. Gut-directed hypnotherapy (GHT) has been shown to improve quality of life and symptoms in IBS. This therapy targets psychological coping, central nervous processing and brain-gut interaction. Studies have also demonstrated effects of hypnosis on the intestinal microenvironment, gastric functions such as intestinal transit, and the mucosal immune system. So far, no study has examined the effect of GHT on the intestinal microbiome.
This study aimed at examining psychological distress, IBS symptoms, and microbial alterations before and after GHT.
Aims and Methods: 38 IBS patients (Rome-III criteria, mean age 44 years, 27 female, 11 male, 22 diarrhea-dominant, 12 alternating-type and 4 constipation-dominant IBS) were assessed with validated questionnaires in psychological (perceived stress, PSQ; psychological distress, HADS-D; quality of life, visual analogue scales) and IBS symptom-related variables (IBS severity, IBS-SSS; single symptoms, visual analogue scales) and fecal samples were collected before and after 10 weekly sessions of GHT. Faecal samples underwent microbial 16S rRNA analyses (regions V1-2, Illumina MiSeq) via QIIME pipeline.
Results: Significant reductions in psychological distress (7.0 [5.0–10.5] Median [Q1-Q3] vs. 5.0 [3.0–7.3], $p = .001$) and symptom severity (322 [264–373] vs. 264 [184–333], $p = .001$), and increased quality of life (105 [91–134] vs. 151 [120–195], $p = .001$] were observed after GHT. No differences were observable in microbial alpha diversity before and after GHT (chao1 2591 vs. 2581, $p = .92$).
Conclusion: Reductions in IBS symptoms and psychological burden were observed after gut-directed hypnotherapy. No systematic alterations were found in intestinal microbiota. Hypnosis seems to act predominantly by central modulation.
Disclosure: Nothing to disclose.

P1708 COLONIC DIVERTICULA: RISK FACTOR FOR COLORECTAL ADENOMAS?

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Introduction: There are conflicting data concerning the association between diverticular disease and colorectal cancer (CRC).
Aims and Methods: The aim of this study was to determine whether colonic diverticula are associated with colorectal adenomas.
In a case-control, retrospective study, we analysed the colonoscopy reports of complete colonoscopies with the diagnosis of colonic diverticula of all patients referred for screening colonoscopy between January 2011 and January 2016. As a control group, a same number of complete colonoscopies performed for colorectal cancer screening and without the diagnosis of colonic diverticula were randomly selected in the same period of time. Patients who met any of the following criteria were excluded from study participation: positive fecal occult blood test, history of previous colorectal surgery, CRC, known colonic polyps or polyposis syndromes. Advanced adenomas were defined as adenomas $\geq$10 mm and/or villous architecture and/or high-grade dysplasia.
Results: A total of 414 patients were included in this study, 207 in each group. In the group with colonic diverticula, the mean age was 67.2 ± 8.9 years, 52.2% female ($n = 108$). In the control group the mean age was 63.3 ± 10.6 years, 48.8% female ($n = 101$). One or more adenomas were detected in 30.4% ($n = 63$) of the patients in the colonic diverticula group and 26.1% ($n = 54$) in the control group ($p = 0.326$). One or more advanced adenomas were detected in 10.6% ($n = 22$) of the patients in the colonic diverticula group and in 6.8% ($n = 14$) in the control group ($p = 0.293$). One or more adenomas were found exclusively in a proximal location in 10.6% ($n = 22$) of patients in the colonic diverticula group and in 7.7% ($n = 16$) in the control group ($p = 0.689$). One or more adenomas were found exclusively in a distal location in 15.9% ($n = 33$) of the patients in the colonic diverticula group and 11.6% ($n = 24$) in the control group ($p = 0.572$).
Conclusion: No significant association was found in this series between colonic diverticula and colorectal adenomas or advanced adenomas. There was no association between colonic diverticula and proximal or distal adenomas.
Disclosure: Nothing to disclose

P1709 ASSOCIATION BETWEEN COLONIC DIVERTICULA AND THE DETECTION OF ADENOMAS AND SERRATED POLYP SUBTYPES DURING SCREENING COLONOSCOPIES OF INDIVIDUALS WITH AN AVERAGE RISK FOR COLORECTAL CANCER

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Introduction: Colonic diverticular disease is one of the most frequently diagnosed diseases of the lower gastrointestinal tract and includes a broad spectrum of disease manifestations ranging from asymptomatic diverticula to diverticulitis with associated complications like abscess formation and perforation. Studies investigating the association between colonic diverticula and colorectal polyps and cancer (CRC) have reported conflicting results.
Aims and Methods: We aimed to evaluate this association for all relevant different histological polyp subtypes, i.e. hyperplastic polyps (HPs), sessile and traditionally serrated adenomas (SSAs and TSAs, respectively), clinically relevant serrated polyps (crSPs), non-advanced and advanced adenomas, in an exclusive colonoscopy screening cohort. We conducted a retrospective analysis of individuals $\geq$50 years with average risk for CRC who underwent a screening colonoscopy between 01/01/2012 and 14/12/2016 at a tertiary academic hospital and 6 community-based private practices. Exclusion criteria were conditions with increased risk for CRC (e.g. chronic inflammatory bowel disease, history of CRC, hereditary cancer syndromes), previous colonoscopy at the same institution, and incomplete procedures.
Results: 4196 colonoscopies were included (mean age 63.4 ± 7.6 years, 48.6% men). Individuals with diverticula were significantly older (65.6 ± 8.0 years vs. 62.0 ± 7.0 years, $p = 0.001$), whereas there was no gender difference (40.2% vs. 37.2%, $p = 0.093$). Detection rates of HPs and non advanced adenomas were significantly higher in patients with diverticula (19.4% vs. 15.8%, $p = 0.001$, and 32.3% vs. 27.4%, $p = 0.003$, respectively). No differences were found with respect to detection rates of SSA, TSA and crSP. Corresponding odds ratios (OR) were 1.340 (95%-CI 1.133–1.584, $p = 0.001$) for the detection of HPs overall and 1.459 (95%-CI 1.208–1.763, $p < 0.001$) in the distal colon as well as 1.355 (95%-CI 1.144–1.604, $p < 0.001$) for non advanced adenomas in the distal colon. The mean numbers of different histological polyp subtypes per person with at least one of the histological polyp subtype detected were not different in the presence or absence of diverticula.
Conclusion: Hyperplastic polyps and non-advanced adenomas, but not advanced polypoid lesions were detected more frequently in the presence of colonic diverticula during screening colonoscopies of individuals with an average risk for

colorectal cancer. Our results suggest careful inspection especially of the distal colon when diverticula are present during colonoscopy.
Disclosure: Nothing to disclose

P1710 CHANGES IN ASSOCIATION BETWEEN INHIBITORY MOTOR NEURONS AND CALCITONIN GENE-RELATED PEPTIDE IN COLONIC DIVERTICULOSIS

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Introduction: Colonic diverticular disease (DD) ranges among the most common benign disorders of the gastrointestinal tract (GI). Despite its ever-growing burden on the national health systems, high prevalence and complicated clinical management, over the years DD has drawn relatively little research effort and has repeatedly been named the "neglected disease"[1].
The etiology of DD is known to involve structural remodeling of the enteric nervous system (ENS) [2]. The ENS is an integrative network located along the wall of the GI tract. More than 30 neurotransmitters have been identified in the ENS which then interact to intricate peristatltic movements, initiating local reflexes to regulate motility and secretion [3].
Calcitonin gene-related peptide (CGRP) is a potent smooth muscle relaxant playing a significant role in the non-adrenergic non-cholinergic regulation of the GI tract motility. CGRP acts through a heteromeric receptor composed of a G-protein coupled receptor called calcitonin receptor-like receptor (CRLR) and a receptor activity-modifying protein 1 (RAMP1) [4] resulting in a further activation ofvasoactive intestinal peptide (VIP) and nitric oxide (NO) – two of the primary relaxant neurotransmiters of the intestinal musculature [5].
Aims and Methods: The aim of the study was to reveal associations between CGRP and vipergic and nitriergic neurons within myenteric (MP), inner (ISP) and outer (OSP) submucosal plexuses of the ENS, suggesting an altered relaxation mechanism during DD.
Control (n = 10, age: 50–75 years) and asymptomatic DD (ADD) (n = 10, age: 57–76 years) sigmoid samples were obtained from patients undergoing surgery for non-obstructing colorectal carcinoma if colonic diverticula were present and patient had no previous anamnesis of DD associated symptoms. Symptomatic DD (SDD) samples (n = 10, age: 39–80 years) were obtained from patients who underwent sigmoid resection or left hemicolectomy after recurrent attacks of diverticulitis. Double immunohistochemical staining for NO synthase 1 (NOS1) or VIP and CGRP or its receptors – calcitonin receptor-like receptor (CRLR) and receptor activity modifying protein 1 (RAMP1) – was performed on full-thickness sections of sigmoid colon and analysed with quantitative fluorescence microscopy.
Results: According to our data, along the wall of the sigmoid colon NOS1 and VIP positive neurons were found to be distributed unevenly – NOS1 positive neurons were mainly located within the myenteric plexus, while VIP positive neurons predominated throughout submucosal plexuses. Both NOS1 as well as VIP positive neurons were found expressing a significant amount of CRLR and RAMP1, demonstrating a close association with CGRP positive fibers and susceptibility to CGRP activation.
Quantification of fluorescence intensity revealed decreased CGRP levels within the enteric ganglia of the sigmoid colon of DD patients. In the MP, as well as in the ISP, the amount of CGRP decreased by 51.7% ($p < 0.0001$) and 52.4% ($p < 0.0001$), respectively. In the OSP, the decrease was less expressed and reached 27.8% ($p = 0.04$).
CRLR levels were increased within the enteric ganglia of SDD patients. Compared to CGRP, this reflected an opposite trend between the experimental groups. The greatest increase of 41.3% ($p < 0.0001$) was found in the OSP, whilst in MP and ISP CRLR was increased by 29.3% ($p = 0.008$) and 22.7% ($p = 0.022$), respectively.
Conclusion: In conclusion, CGRP has all the necessary components for direct activation of nitriergic and vipergic neurons within both enteric plexuses and this disbalance in neuronal activation may cause the disordered myorelaxation in DD.
Disclosure: Nothing to disclose

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P1711 DIVERTICULAR DISEASE: REAL-LIFE PREVALENCE AND ASSOCIATED RISK FACTORS IN A HIGH-VOLUME ENDOSCOPIC UNIT

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Introduction: Diverticular disease, a prevalent condition in the general population, is frequently asymptomatic, but may also cause abdominal pain, diarrhea, and occult as well as overt bleeding, which are also common indications for endoscopic evaluation of the lower gastrointestinal tract. The Diverticular Inflammation and Complication Assessment (DICA) endoscopic classification has been shown to constitute a valid parameter to predict the risk of diverticulitis occurrence/recurrence in patients suffering from diverticular disease of the colon[1].
Aims and Methods: The aim of the present study was to determine the prevalence of diverticular disease in the population that undergoes a colonoscopy, and to identify clinical and demographic factors that are associated with an increased risk for this condition. Prospectively recorded and codified data of all lower endoscopies performed in adult patients at our Endoscopy Unit from April 2009 to March 2018 was retrieved and the following variables were analyzed: age, sex, indication to perform endoscopy, exam completion (cecum visualization), and endoscopic findings. For patients who underwent several endoscopic examinations, only the index endoscopy was considered (complete colonoscopy). Incomplete evaluations (due to poor intestinal cleansing, exam suspension for all reasons, and cecum intubation failure) were excluded from the analysis.
Results: A total of 36981 colonscopies were performed at our tertiary hospital during the study period; 11019 cases of multiple endoscopic controls in the same patient or of incomplete exams were excluded from the analysis. Of 25962 patients (F = 13003, 50.1%), mean age 60.9 (range 18–102.55), who underwent lower endoscopy, diverticular disease was found in 7936 patients (30.6%), with similar frequencies in male vs female patients. With respect to patients without diverticular disease, patients with this condition were older (mean age 58.17 ± 14.3 vs 67.23 ± 10.8, $p < 0.001$, respectively); abdominal pain (20.4%vs 18.3%), positive fecal occult blood test (23.2% vs 20.1%), and anemia (5.3% vs 4.1%) were significantly more frequent indications for colonoscopy in patients with diverticular disease with respect to those without ($p = 0.0001$ for all), whereas significantly less patients with diverticular disease ($p < 0.05$ for all) had positive family history of colorectal cancer (4.0% vs 6.9%), diarrhea (5.3% vs 6.5%), lower gastrointestinal bleeding (18.8% vs 21.8%), constipation (9.5% vs 10.4%) and a change in bowel habits (1.8 vs 2.2%) as the indication for colonoscopy. DICA classification, used in our center since March 2017, was available for 1347 patients; 754, 379, and 214 patients were grouped in DICA 1, 2, and 3, respectively. Polyps were more frequently found in association with diverticular disease (27.1% vs 23.0%, $p = 0.0001$), but neoplasms were significantly more frequent in patients without diverticular disease (1.4% vs 2.2%, $p = 0.0001$) than in patients with diverticula.
Conclusion: A frequent finding in all-cause colonoscopy, diverticular disease is associated with increasing age and with a lower incidence of colorectal cancer. The latter is probably due to the fact that patients with diverticular disease usually undergo colonoscopy at an earlier age, and for symptoms such as rectal bleeding, which allow for prompt polyp detection and removal.
Disclosure: Nothing to disclose

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P1712 THE EFFICACY OF LACTOBACILLUS REUTERI 4659 IN REDUCING ABDOMINAL SYMPTOMS AND INFLAMMATORY BIOMARKERS IN ACUTE UNCOMPLICATED DIVERTICULATIS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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Introduction: Diverticular Disease (DD) is the most frequent abnormality in the digestive tract mainly in developed countries.
Acute Uncomplicated Diverticulitis (AUD) is defined as the inflammation of a colon diverticulum, often involving colic wall and pericolic fat. Conventional treatment of AUD includes antibiotic therapy, usually Ciprofloxacin and Metronidazole, fasting and fluid therapy.
At the state of the art, no RCT versus placebo studies have been performed aimed at evaluating the clinical efficacy of probiotics in AUD, and so no definitive results have been achieved yet.
Aim of our RCT study is to test the efficacy of *Lactobacillus Reuteri* 4659 (*L. Reuteri*), a specific strain with anti-inflammatory effect in association with conventional antibiotics in treating AUD compared to conventional antibiotic therapy plus placebo.

Primary outcome of the study is the reduction of abdominal pain and inflammatory markers (C-RP) in the group treated with *L. Reuteri 4659* supplementation compared to placebo.
Secondary outcome is the comparison of the days of hospitalization between the two groups.
Aims and Methods: A double-blind, placebo RCT was conducted in 88 (34M/54F mean age 61.9 +- 13.9 years) consecutive patients who came to the Emergency Department of Foundation Policlinico A. Gemelli Hospital with a diagnosis of AUD. All patients performed routine blood test, dosage of C – reactive protein value and they were randomly assigned to two groups:
- Group A (44 patients, 26F), treated with ciprofloxacin 400mg twice a day and metronidazole 500mg three times a day for one week, with a supplementation of L. Reuteri 4659 twice a day for 10 days.
- Group B (44 patients, 28F), treated with ciprofloxacin 400mg twice a day and metronidazole 500mg three times a day for one week plus placebo twice a day for 10 days.
All patients filled a daily Visual Analog Scale (VAS) for abdominal pain, with a range value from 0 (asymptomatic) to 10, and C-RP value was determined on admission and at discharge.
Results: All patients completed the study. No side effect were observed.
As regards the VAS values: between day 1 and 3, group A decreased 4.5 points of VAS scale, group B decreased 2.36 points of VAS scale ($p < 0.0001$); between day 1 and 5 group A decreased 6.6 points of VAS scale, group B decreased 4.4 points of VAS scale ($p < 0.0001$); between day 1 and 7 group A decreased 7.6 points of VAS scale, group B decreased 5.6 points of VAS scale ($p < 0.0001$); between day 1 and 10 group A decreased 8.1 points of VAS scale, group B decreased 6.7 points of VAS scale ($p < 0.0001$).
Regarding C-RP value, the difference between the admittance value and the discharge value was 45.3 mg/l for group A and 27.49 mg/l for group B ($p < 0.0001$).
Finally, group A has a mean of 4 days of hospitalization, meanwhile group B has a mean of 4.7 days of hospitalization ($p < 0.0001$).
Conclusion: Our RCT showed that the supplementation with *L. Reuteri 4659* in the standard AUD therapy, significantly reduce abdominal pain and inflammatory markers compared to placebo group, conducting also to a shorter hospitalization period, thus influencing also with an economical factor.
These interesting results could be due to the fact that *L. reuteri 4659* modulate cytokine production and reduce LPS-induced intestinal inflammation, expression levels of IL-6 and TNF-"mRNAs, and TLR4.
Disclosure: Nothing to disclose

P1713 MULTIDIMENSIONAL PROGNOSTIC INDEX PREDICTS MORTALITY IN HOSPITALIZED ELDERLY PATIENTS WITH DIVERTICULAR DISEASE

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Introduction: Diverticular Disease (DD) has a chronic burden in Western aged people affected by other comorbidities. The multidimensional prognostic index (MPI) ia a validated non disease-specific prognostic index based on a comprehensive geriatric assessment in older patients. The aim of this study was assess the prognostic accuracy of MPI on long-term mortality in hospitalized elderly patients with DD.
Aims and Methods: In this prospective study with a 12-month follow-up, 41 hospitalized elderly patients (median 71 years, 33–92), affected by DD were enrolled. Within 48 hours since admission, the MPI score was calculated in all patients according to a validated algorithm that included information on basal and instrumental activities of daily living, cognitive status, nutritional status, the risk of pressures sores, co-morbidity, number of drugs and co-abithation. The patients were stratified in threee risk groups: low (MPI-1 value $\leq$0.33), medium (MPI-2 value 0.34–0.66), and high (MPI-3 $\geq$ 0.67) risk. The adjusted age-adjusted Charlson comorbidity index (ACCI) was calculated for all patients to assess the burden of comorbidities on survival. Kaplan-Meier curves of the survival probability according to the MPI was assessed to explore the association between MPI score baseline and mortality of the patient hospitalized.
Results: All patients had a median MPI of 0.44 (range 0.12–1.00). Patients were divided according their MPI grade: 11 patients (29%) were included in MPI-1 group, 16 patients (42%) in MPI-2 group, and 13 patients in MPI-3 group. Twelve-month mortality was significantly ($p < 0.05$) higher in MPI-3 group (9/11. 82%) than in MPI-2 (5/16, 31%) and MPI-1 (2/11, 18%) groups, with no difference between MPI-1 and MPI-2. Age, ACCI and MPI were predictive of mortality.
Conclusion: Our study demonstrated that MPI is a useful tool to estimate the risk of twelve-month mortality in hospitalized elderly patients affected by DD.
Disclosure: Nothing to disclose

P1714 EVALUATING GASTROINTESTINAL MORPHOLOGY AND ENTERIC NERVOUS SYSTEM VIABILITY IN THE *DYSTONIA MUSCULORUM* MOUSE MODEL OF HEREDITARY SENSORY AND AUTONOMIC NEUROPATHY TYPE VI

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Introduction: Hereditary sensory and autonomic neuropathy type VI (HSAN-VI) is a newly identified neuronal disorder caused by mutations in the human dystonin gene (*DST*). Patients may present with joint contractures, problems with eating and breathing, motor deficits, autonomic irregularities, as well as gastrointestinal symptoms such as chronic diarrhoea, and abdominal pain. Similarly, a mouse mutant known as *dystonia musculorum* (Dst^{dt}) also arises due to mutations in the dystonin gene. In our studies, we have also come to recognize certain gastrointestinal pathologies present within this mouse model. At the level of gross morphology, we have observed discolouration of the gastrointestinal tract, as well as an accumulation of gas, which often causes distension of the ileum, cecum, and colon.
Aims and Methods: As HSAN-VI and Dst^{dt} are primarily sensory neurone disorders, we hypothesize that the underlying cause for these gastrointestinal defects is due to impairments in the enteric nervous system. Here we aim to assess gut morphology by hematoxylin and eosin staining, evaluate the myenteric and submucosal plexuses by wholemount immunofluorescence staining, and assess function by GastroSense 750 tracking via *in vivo* imaging system.
Results: In late stage Dst^{dt} mice (postnatal day 15) we have observed small, but significant reductions in ileum villi width and crypt length, as well as decreased smooth muscle wall thickness at all levels of the gastrointestinal tract. Despite the reduced muscle size, motility as assessed by tracing of the fluorescent GastroSense 750 marker appears to be normal in Dst^{dt} mice. Investigation of the enteric nervous system also reveals no difference in markers for cell death (as determined by cleaved caspase 3, FluoroJade C, and TUNEL staining), though total number of neurones per ganglia still remains to be characterized.
Conclusion: Thus far we have observed no major changes to the enteric nervous system of Dst^{dt} mice. Although we have determined that dystonin isoforms are expressed in the enteric nervous system, their role my not be as critical to neuronal survival as in dorsal root sensory neurones. It may also be that autonomic dysfunction (possibly by the vagus nerve) could be responsible for observed gastrointestinal defects. Investigation into higher nervous system centres inputting onto the gut will be performed in future work.
Disclosure: Nothing to disclose

P1715 GASTROINTESTINAL BLEEDING AFTER LEFT VENTRICULAR ASSIST DEVICE IMPLANTATION IS ASSOCIATED WITH A SHIFT TOWARD A PRO-ANGIOGENIC PHENOTYPE IN THE ANGIOPOIETIN AXIS

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Introduction: Gastrointestinal bleeding (GIB) occurs in approximately 20% of continuous-flow left ventricular assist device (CF-LVAD) recipients after device implantation, predominantly from angioectasias in the upper GI tract or small intestine. While a higher risk of GIB has been observed in CF-LVAD recipients with lower device pulsatility, a mechanism linking changes in hemodynamics to an increased rate of GIB has not been established. In a recent study LVAD implantation was associated with increased angiopoietin-2 (Ang-2) levels, a growth factor that promotes vascular destabilization, suggesting that alterations in the molecular regulation of angiogenesis may play a role in GIB in this population.
Aims and Methods: The aims of our study were to:
1. Compare levels of angiopoietin-1 (Ang-1), a growth factor with vascular protective effects, vascular endothelial growth factor A (VEGF-A), an inducer of angiogenesis, and Ang-2 in (a) CF-LVAD recipients vs. control patients and (b) in CF-LVAD recipients that developed GIB after device implantation vs. those who did not;
2. Assess whether CF-LVAD pulsatility and pulse pressure are correlated with levels of Ang-1, VEGF-A, and Ang-2.
To achieve our aims we recruited 24 participants from our institution, 12 with CF-LVADs (six of whom developed GIB after device implantation) and 12 age-matched controls with no history of heart failure or GIB. Each participant provided a peripheral venous blood sample. We measured VEGF-A and Ang-2 levels in serum samples with a magnetic bead immunoassay panel (MILLIPLEX®, EMD Millipore) and Ang-1 levels with an enzyme-linked immunosorbent assay kit (Abcam). Statistical analyses were performed with SPSS version 22.
Results: In CF-LVAD recipients as compared to controls, Ang-2 levels were higher (9674 pg/mL vs. 4456 pg/mL, respectively; $P = 0.001$) and Ang-1 levels were lower (5639 pg/mL vs. 8239 pg/mL, respectively; $P = 0.023$). There was no

difference in VEGF-A levels between the two groups. In CF-LVAD recipients who developed GIB after device implantation as compared to those who did not, Ang-1 levels were lower (4021 pg/mL vs. 7258 pg/mL; $P = 0.028$). Neither levels of Ang-2 nor VEGF-A differed between the two groups. While there was no correlation between CF-LVAD pulsatility index and levels of Ang-2, Ang-1, or VEGF-A, pulse pressure was negatively correlated with levels of Ang-2 ($r = -0.578$, $P = 0.003$) and positively correlated with levels of Ang-1 ($r = 0.496$, $P = 0.014$). There was no correlation between pulse pressure and VEGF-A.
Conclusion: CF-LVAD recipients in our study demonstrated a shift toward a pro-angiogenic phenotype in the angiopoietin axis, a main regulatory pathway of angiogenesis, with increased serum levels of Ang-2 and lower serum levels of Ang-1 as compared to controls. Additionally, lower serum levels of Ang-1 were associated with GIB following CF-LVAD implantation, suggesting a role for alterations in the regulation of angiogenesis in GIB in this population. Lastly, lower pulse pressure was associated with higher Ang-2 levels and lower Ang-1 levels, suggesting a link between the lower pulse pressures that follow CF-LVAD implantation and changes in the regulation of angiogenesis.
Disclosure: Nothing to disclose

P1716 WHOLE TRANSCRIPTOMIC ANALYSIS IN TURKISH PATIENTS WITH ACHALASIA

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Introduction: Achalasia is an esophageal motor disorder characterized by incomplete relaxation of the lower esophageal sphincter (LES) and by the absence of esophageal peristalsis. Patients typically present with regurgitation, dysphagia, retrosternal pain, and marked weight loss. Exact pathogenesis of the disease still remain to be clarified while it has been known for more than 300 years. However, the most widely accepted hypothesis of the development of achalasia is that a viral infection or some other environmental factors trigger autoimmune response resulting in chronic inflammation that leads to myenteric neuronal loss and neuronal fibrosis in susceptible subjects who may be genetically predisposed. Therefore genetic factors may play an important role in its pathogenesis.
Aims and Methods: The aim of our research was to reveal candidate genes involved in pathogenesis of achalasia. We obtained 12 achalasia and 5 intact esophageal resection tissues from patients operated on because of achalasia and esophagus cancer respectively. We characterized whole-transcriptome profiles (47.231 gene transcripts) by using Illumina Human HT-12 v4.0 Expression Beadchips. Expression data were analyzed with Genome Studio data analysis software.
Results: We detected that 733 differentially expressed genes, of these, 519 were up-regulated in cases. Pathway analysis by KEGG online tool revealed that mostly upregulated genes were involved in the pathways of focal adhesion and smooth muscle contraction. Moreover miR-targeted genes expressed in muscle cell, epithelium and lymphocytes were also mostly upregulated.
Conclusion: To the best of our knowledge, our research is first transcriptomic study in Turkish patients with achalasia. We here firstly identify the candidate genes in pathogenesis of achalasia. However, further analysis is needed to reveal the gene interactions with each other and other pathways.
Disclosure: this study was supported by grants from Marmara University, Scientific Research Research Projects Committee (Project No:SAG–B-030114-0005)

P1717 CIRCULAR RNA_009414 /MIR-30C-2-3P AXIS PROMOTES GASTRIC CANCER VIA BCL9/WNT/β-CATENIN SIGNALING PATHWAY

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Introduction: Circular RNA (circRNA) _009414 is emerging as a vital regulatory molecule in the progression of different types of cancer and miR-30c-2-3p is reported to be embedded in BCL9's first exon. However, their function and specific mechanisms of action have not been fully elucidated.
Aims and Methods: The aim of this study was to identify a novel circRNA-microRNA-mRNA functional network in gastric cancer. Quantitative real-time polymerase chain reaction (qRT-PCR) was used to assess the relative expression of circRNA_009414 and miR-30c-2-3p in normal (GES-1) and gastric cancer cell lines (SGC-7901, AGS) as well as in tumor tissues. Gain and loss of function approaches were carried out to investigate the potential roles of circRNA_009414/miR-30C-2-3P in cell proliferation and apoptosis. Moreover, BCL9 was validated to be the target of miR-30C-2-3P, and miR-30C-2-3P targeted circRNA_009414 via luciferase reporter assay and RNA-pulldown. Western blotting was used to evaluate the protein expression of related signaling pathway. Finally, we confirmed the function in nude mice.
Results: In our study circRNA_009414 and BCL9 were increased in gastric cancer cell lines and tissues, while miR-30c-2-3p was decreased in gastric cancer cell lines and tissues. Overexpression of circRNA_009414 and BCL9 promoted cell proliferation and inhibited cell apoptosis, whereas knockdown them inhibited these effects. Overexpression of miR-30c-2-3p inhibited cell proliferation and inhibited cell apoptosis, while knockdown it promoted these effects. By further examining the underlying mechanism, we showed that circRNA_009414/miR-30c-2-3p axis inhibited expression of BCL9. RNA-pulldown confirmed that circRNA_009414 could bind to BCL9 and thus further suppress the expression. BCL9 downregulation subsequently inhibited the Wnt/β-catenin including c-myc and β-catenin.
Conclusion: Taken together, our results point to a novel regulatory pathway circRNA_009414/miR-30C-2-3P/ BCL9/ Wnt/β-catenin in gastric cancer which may be potential target for cancer therapy.
Disclosure: Nothing to disclose

P1718 ROLE OF HIGHLY DEREGULATED MICRORNAS IN GASTROINTESTINAL STROMAL TUMORS

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Introduction: MicroRNAs are a class of small non-coding RNAs involved in post-transcriptional regulation of gene expression. Deregulated microRNA profiles and their contribution to carcinogenesis have been observed in different types of cancer, making them a promising tools for cancer diagnosis and targeted therapy. However, their involvement in pathogenesis of the most common mesenchymal tumors of gastrointestinal tract – gastrointestinal stromal tumors (GISTs) – is not well defined yet.
Aims and Methods: The aim of this study was to evaluate the role of highly deregulated microRNAs in pathogenesis of gastric GISTs. Investigated microRNAs (hsa-miR-375, hsa-miR-200b-3p, hsa-miR-490-3p) were selected from sequencing and TaqMan Low Density Array validation data from our previous study on microRNA profiling in GIST. Potential targets of selected microRNAs were predicted using TargetScan (Release 7.1) database. Further functional analysis in GIST representing GIST-T1 cell line was performed after transfections of microRNA mimics and mimic negative control using a lipofection approach. Changes in target gene expression were detected using TaqMan primers and probes, protein expression analysis was performed using Western Blot technique. Alterations in cell viability and migration rate were evaluated by MTT and Wound Healing Assays. Statistical analysis was performed using the computing environment R.
Results: Increased amounts of hsa-miR-375 significantly reduced expression of its potential target gene *KIT* ($FC = 0.57$, $p < 0.05$), however KIT protein expression remained unchanged in GIST-T1 cell line. Overexpression of hsa-miR-200b-3p significantly reduced *EGFR* and *ETV1* gene expression ($FC = 0.7$ and $FC = 0.81$, respectively, $p < 0.05$) and significantly reduced levels of EGFR protein ($FC = 0.55$, $p < 0.05$). Analysis of physiological changes of GIST-T1 cells revealed that only hsa-miR-375 significantly reduced both viability and migration rate of GIST-T1 cells, while hsa-miR-200b-3p significantly reduced cell migration rate and showed slight, but not significant impact on cell viability. Hsa-miR-490-3p did not affect expression of its predicted target genes and was not further investigated.
Conclusion: Analysis of highly deregulated microRNAs in GIST-T1 cell line showed that microRNA hsa-miR-375 potentially targets known GIST associated oncogene KIT and therefore affects cell viability and motility. Another microRNA hsa-miR-200b-3p might be involved in GIST pathogenesis by targeting oncogenes EGFR and ETV1. Therefore, microRNAs hsa-miR-375 and hsa-miR-200b-3p should be further investigated as a potential components of GIST pathogenesis and a promising tools for targeted therapy in GIST.
Disclosure: Nothing to disclose

P1719 GRANULOMATOUS GASTRITIS : CLINICAL AND PATHOLOGICAL FEATURES

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Introduction: Granulomatous gastritis is an infrequent lesion characterized by the presence of granulomas in the gastric mucosa. Etiopathogenic diagnosis is obtained only by combining morphological examination with clinical and laboratory investigations. The purpose of our study is to evaluate the clinical features and to determine the etiologies of granulomatous gastritis.
Aims and Methods: This is a retrospective study of all cases of granulomatous gastritis noted in the histopathological examination of gastric biopsies, collected between 2012 and 2016 in the department of gastroenterology in the university hospital of Monastir. The clinical, endoscopic, histological characteristics as well

as the associated lesions and the etiology retained of gastritis granulomatosis were noted.
Results: Fourteen cases of gastric granulomatosis included 6 men (42.9%) and 8 women (57.1%) with an average age of 39 years (21–65 years). The indication for endoscopy was dominated by epigastric pain in 6 cases (42.9%), chronic diarrhea in 4 cases (28.6%), anemia in 2 cases (14.3%) and vomiting in 1 case (7.1%). The discovery of granulomatous gastritis was fortuitous in 1 case.
Oeso-gastro-duodenal fibroscopy was abnormal in the majority of cases (92.8%), it showed antral gastropathy in 12 cases (erythematous gastritis in 6 cases and nodular gastritis in 6 cases). The granuloma was unique in 4 cases (28.6%) and multiple in 10 cases (71.4%). The location of the granuloma was antral in 8 cases, fundic in 1 case, and antro-fundic in 5 cases. Associated chronic gastritis was noted in 13 cases (92.9%). Regarding the etiology, eight of our patients (57.1%) had Crohn's disease and two, gastric tuberculosis (14.3%). In two cases, *H. pylori* was the cause of granulomatous gastritis. In the remaining patients, the final diagnosis was sarcoidosis (n = 1), lichen planus (n = 1). Six patients (42.9%) had Hp positive histological status.
Conclusion: In our series, Crohn's disease and tuberculosis dominate the etiologies of granulomatous gastritis. An association between *H. pylori* and granulomatous gastritis cannot be excluded and the confirmation of this link is based on the disappearance of this histological lesion after the eradication of this bacterium.
Disclosure: Nothing to disclose

P1720 CHARACTERIZATION OF IMMUNE CELLS INFILTRATING THE CORPUS MUCOSA OF THE STOMACH IN AUTOIMMUNE ATROPHIC GASTRITIS

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Introduction: Autoimmune atrophic gastritis (AAG) is an organ-specific autoimmune disease affecting the corpus-fundus mucosa of the stomach. Little is known regarding the pathogenic mechanisms underlying AAG. Chronic T cell-induced activation of B cells seems to be responsible for the local production of antiparietal cell autoantibodies, peripheral hallmark of AAG.
Aims and Methods: Aim of our study was to characterize immune cells infiltrating the gastric corpus mucosa of patients with AAG in comparison to control subjects. We isolated lamina propria mononuclear cells (LPMCs) from gastric corpus of six patients with AAG (mean age 58.3 ± 13.5 years, F:M ratio 2.0:1) and ten patients with functional dyspepsia (mean age 56.1 ± 15.1 years, F:M ratio 2.3:1) enrolled as controls. Freshly isolated LPMCs were stained with the following antibodies: CD45, CD3, CD4, CD8, CD19, CD56, CD66b and CD68, then analyzed by flow cytometry in order to identify $CD4^+$ and $CD8^+$ T cells, B cells, natural killer cells, neutrophils and macrophages.
Results: As shown in Table 1, the percentage of gastric B cells was significantly ($p < 0.05$) higher in patients with AAG (mean 26.7 ± 6.4%) than in those with functional dyspepsia (mean 9.9 ± 1.7%). Conversely, the frequency of all other immune cell types did not significanty differ between AAG and those with functional dyspepsia (Table 1).

Cell type	Autoimmune atrophic gastritis (n = 6)	Functional dyspepsia (n = 10)	P value
CD45+ LPMCs, mean ± SEM	39.8 ± 7.0%	29.6 ± 2.6%	NS
CD3+ T cells, mean ± SEM	41.5 ± 10.3%	61.9 ± 8.9%	NS
CD3+ CD4+ T cells, mean ± SEM	15.2 ± 3.1%	14.8 ± 2.3%	NS
CD3+ CD8+ T cells, mean ± SEM	43.6 ± 13.2%	48.2 ± 7.6%	NS
CD19+ B cells, mean ± SEM	26.7 ± 6.4%	9.9 ± 1.7%	< 0.05
CD56+ natural killer cells, mean ± SEM	2.3 ± 0.9%	4.5 ± 1.5%	NS
CD66b+ neutrophils, mean ± SEM	7.6 ± 3.1%	11.9 ± 2.8%	NS
CD68+ macrophages, mean ± SEM	4.3 ± 0.5%	10.2 ± 2.5%	NS

[Table 1. Frequencies of the main immune cell type subsets in the lamina propria of gastric corpus]
Conclusion: Amongst all the main gastric immune cell type subsets, we here described an increased frequency of lamina propria B cells in the gastric corpus of AAG patients. Further studies are needed to better clarify the putative pathogenic role of gastric B cells in AAG.
Disclosure: Nothing to disclose

P1721 EVALUATION OF A NEW ASSAY FOR THE QUANTITATIVE DETERMINATION OF CALPROTECTIN IN HUMAN FECES (CALIAGOLD)

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Introduction: The objective of this study is to evaluate the analytical and clinical performances of a new assay for the quantitative determination of calprotectin in human feces (CALiaGold) on SENTiFIT 270 analyzer. The presence of calprotectin in human stool specimens is intended as an aid in the assessment of intestinal mucosal inflammation. The assay results can be useful in distinguishing organic, inflammatory disease of the gastrointestinal tract (inflammatory bowel disease, IBD, e.g. Crohn's disease or ulcerative colitis, UC) from functional disease (irritable bowel syndrome, IBS), in patients with chronic abdominal pain, and as an aid to IBD monitoring.
Aims and Methods: The CALiaGold test is a particle enhanced turbidimetric immunoassay (PETIA) and allows quantification of calprotectin in fecal extracts. Fecal samples are dissolved in the extraction buffer using the CALiaGold Tube device. The extracts are incubated with reaction buffer and mixed with polystyrene nanoparticles coated with calprotectin-specific antibodies (immunoparticles). Calprotectin in the sample mediates immunoparticles agglutination. Sample turbidity, measured by light absorbance, increases with calprotectin-immunoparticle complex formation and is proportional to the calprotectin concentration. The detected light absorbance allows quantification of calprotectin concentration via interpolation on an established calibration curve.
Results: The Limit of Blank (LOB) (1 saline sample × 20 replicates × 3 runs) was 12.2 ug/g. The Limit of Detection (LOD) (1 sample at 4-fold LOB concentration × 20 replicates × 3 runs) was 18.3 ug/g. The Limit of Quantitation (LOQ) (8 dilution levels starting from sample at concentration 100 ug/g × 10 replicates × 1 run) was 21.3 ug/g at%CV lower than 20%. The Intra Assay (3 runs × 3 samples × 20 replicates) gave 6.6% CV at 50.7 ug/g (Level 1), 4.3% CV at 115.5 ug/g (Level 2), and 6.7% CV at 1576.4 ug/g (Level 3). Total imprecision study (44 testing days × 2 runs × 2 observations × 4 level samples – during total time of 66 days) gave 6.7% CV at 59.1 ug/g (Level 1), 3.3% CV at 161.3 ug/g (Level 2), 2.0% CV at 509.9 ug/g (Level 3), and 2.3% CV at 1435.2 ug/g (Level 4). The test was linear up to 2249.5 ug/g, considering the% bias versus theoretical concentration lower than ± 10% for each dilution point of linearity curve. Reagent on board stability was up to 66 days, obtaining% bias versus Time 0 (mean value) -4.6% at 60.0 ug/g (Level 1), 0.0% at 161.4 ug/g (Level 2), -0.6% at 509.5 ug/g (Level 3), and -0.2% at 1433.2 ug/g (Level 4). This test (y) was compared with Bühlmann fCAL turbo on Architect c16000 (x) that uses the same methodology and gave the following results: y = 8.17 + 1.00x; correlation coefficient (r) = 0.979; number of samples = 114. The test is not affected by the presence of conjugated bilirubin up to 0.5 mg/L, hemoglobin up to 0.07 g/L, lipids up to 1.2 g/L. There is not Hook effect/antigen excess up to 1323.9 ug/g. High concentration samples (up to 10000 ug/g) were flagged by the instrument (no false negative results).
Conclusion: Analytical and clinical performances of CALiaGold assay on SENTiFIT 270 analyzer meet the requirements for its use as quantitative determination of calprotectin in human feces. Specificity and precision make this assay very suitable for routine measurement of this analyte.
Disclosure: Nothing to disclose

P1722 SUSPICIOUS PATHOGENIC BACTERIA WITH HIGH AFFINITY BINDING WITH IGA IN THE STOMACH

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Introduction: *H. pylori* may not the only one that could colonize in the gastric mucosa, and the other potential pathogens may trigger gastric disease except for *H. pylori*. [1] Hosts select gastrointestinal microbiota mainly by secretary of immunoglobulin A (IgA). [2] IgA binds those bacteria invading into the mucosal epithelium and threating the host, therefore identifying the IgA-coated bacteria can give an insight into the potential pathogens in the stomach. [3]
Aims and Methods: To investigate the IgA-coated gastric bacteria, gastric juice specimens without bile, blood and other contamination were collected from 12 individuals during endoscopy examination. Six cases were diagnostic with chronic atrophic gastritis and the others were non-atrophy gastritis. We used Flow Cytometer to separate the IgA positive and IgA negative bacteria in gastric juice. Firstly, bacterial flora from the gastric juice were extracted by centrifugation. Then gastric microbiota were strained with FITC-conjugated Goat Anti-Human IgA alpha chain (Abcam) and Goat IgG FITC – Isotype control after fixing and washing. Sorting of IgA+ and IgA- bacteria was performed by flow cytometer (BD FASC Aria III). V4 region of 16S rDNA gene sequencing was performed by MiSeq sequencer (Illumina). Species relative abundance in the IgA positive (P group), negative (N group) and the total bacterial flora (T group) was acquired by bioinformatics analysis. IgA-coating index (ICI) was use to assess the affinity of bacteria with IgA.
Results: The proportion of IgA positive bacteria in the gastric juice of atrophic gastritis was higher than that from non-atrophic gastritis juice (35.55% vs. 23.15%), though there was no statistical difference. ICI of *Rothia aeria* and *Rothia dentocariosa* were as high as 19.2 and 18.2 respectively, while the ICI of *H. pylori* was about 6.8. And other species with a higher ICI than *H. pylori* were *Streptococcus anginosus* (8.6), *Streptococcus infantis* (7.9), and *Prevotella*

melaninogenica (6.9). The average relative abundance of those species in T group were higher than *H. pylori*. And Kruskal test indicated significant different average relative abundance of those species between group N and P.
Conclusion: The high affinity of *Rothia aeria, Rothia dentocariosa, Streptococcus anginosus, Streptococcus infantis and Prevotella melaninogenica* with IgA in the stomach indicates that they may be the potential pathogens in the stomach.
Disclosure: Nothing to disclose

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P1723 AUTOIMMUNE GASTRITIS: FREE RADICALS PRODUCTION BUT NOT OXIDATIVE STRESS-RELATED GENOMIC DAMAGE

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Introduction: Reactive oxygen Species (ROS) are physiologically produced within the organism but, when their concentration increases, exceeding the physiologic capacity of repair, they induce ''oxidative stress'', a condition that can be seen in many chronic inflammatory processes and in autoimmune diseases as well. The most relevant damage, hitting genomic DNA, involves the formation of 8-hydroxydeoxyguanosine (8-OHdG), a biomarker identified in gastric carcinogenetic processes and gastric cancer[1].
Aims and Methods: This study, which, in our findings, is the first one to consider the relation between oxidative stress and gastric autoimmune disease, was aimed at investigating the presence, the entity and the characteristics of oxidative stress in autoimmune atrophic gastritis (AAG) compared with multifocal *H.pylori* related gastritis (MAG) and superficial non atrophic gastritis (SG).
The study included 90 patients sub-grouped in 40 with AIG, 24 with MAG and 26 SG. dROMs test for the detection of ROS was performed in the serum of 37 AIG and 9 MAG patients and the test levels were subclassified in borderline, mild, moderate, high and very high. The levels of 8-OHdG were investigated by HPLC in gastric biopsies of 40 AIG patients, 24 MAG and 26 SG. The OLGA staging system was used for staging gastric damage. Levels of PgI, PgII and gastrin (ELISA) were evaluated in AIG patients. Statistics was performed using Kolmogorov-Smirnov test, t test, chi square and Fisher's exact test. We also performed linear regression, ROC curves, Odds Ratios, sensitivity and specificity tests.
Results: ROMS levels in AIG and MAG were similar, with medium/high levels in 62% and 55.5% of the cases, respectively. 8-OHdG values were lower in AIG and SG with respect to MAG (mean ± SEM: 17 ± 3, 20 ± 3 and 32 ± 6 adducts/105dG, respectively), with a statistically significant difference overall ($p = 0.016$), strongly supported by the difference between AIG and MAG ($p < 0.01$). A trend towards a significant difference ($p = 0.06$) was found comparing OLGA 1–2 AIG vs OLGA 2–3. Lastly, a cut-off for 8-OHdG between AIG/SAG and MAG was calculated (AUC 68%, sensitivity 83%, specificity 50%, positive predictive value 82%, negative predictive value 52%), with 93% of AIG and 50% of MAG presenting levels lower than the cut-off. The OR of patients with 8OH-dG above the cut-off of having AIG was 0.08 ($p = 0.0002$).
Conclusion: Both AIG and MAG present high levels of oxidative stress. However, when the genomic oxidative damage is expressed as 8-OHdG, a carcinogenesis biomarker, AIG presents much lower levels of oxidative genomic damage than MAG that, conceptually, could correlate with the lower risk of neoplastic evolution of AIG.
Disclosure: Nothing to disclose

Reference

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P1724 THE IMPORTANCE OF EOSINOPENIA IN PREDICTION OF TREATMENT RESPONSE IN PATIENTS WITH CHOLANGITIS

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Introduction: We aim in this study to compare the effectiveness of eosinopenia in predicting response to cholangitis treatment with C-reactive protein and procalcitonin which are the other inflamatory reagents.
Aims and Methods: Patients who applied to our unit between September 2016 and September 2017 who have cholangitis diagnosis (cholangitis group) and who do not have cholangitis but have undergone ERCP by reason of choledoch stone (control group) were prospectively examined in our study. After having compared both groups in terms of eosinophil counts at time of application, additionally the relationship between eosinophil level and other inflamatory reagents (CRP and Procalcitonin) of the patients in cholangitis group during the period they are hospitalized at time of application was examined.
Cholangitis diagnosis and severity classification have been performed with Tokyo criteria (1) and examined in 3 groups according to disease severity. The patients with eosinohil count < 100 were considered as eosinopenic.
Results: 62 patients in cholangit group [(age average 66.9 ± 1.85 years old; 21 female (%41.2)], and 57 patients in the control group [(age average 57.3 ± 2.3 years old; 31 female (%73.8)] were examined (For age $p < 0.05$; For type $p < 0.05$). The average eosinophil count in the cholangitis group at time of application was 55.7 ± 10.5 10^3/uL while this count was significantly higher in the control group (201.8 ± 19.2 10^3/uL) ($p < 0.001$). 25 of the patients were Grade-1 (40%), 27 were Grade-2 (17%) and 10 were Grade-3 (17%) according to cholangitis severity. The higher the disease severity, eosinophil levels decrease and any statistical significance was not determined. (respectively 86.4 ± 22.4 10^3/uL, 40.1 ± 10 10^3/uL, 21.3 ± 7.6 10^3/uL; $p = 0.19$). ERCP process was applied on all patients (median 0 within (0–5) days) and the patients were followed-up for 3.5 ± 0.1 days in average after the ERCP. All patients were discharged with full recovery, eosinophil values tended to increase while CRP and Procalcitonin values tended to decrease to a statistically significant extent beginning from the second day.
ROC curve analysis suggested that the optimum eosinophil level cut-off point for cholangitis was 100.5 10^3/uL, with sensitivity, specificity, positive and negative predictive value of 87, 65, 72, and 81%, respectively (area under the receiver-operating characteristic curve = 0.877). According to this evaluation, eosinophenia is existing in 87% of the patients with cholangitis and this ratio was determined as 36.8% in the control group when the eosinopenia threshold is taken as < 100.510^3/uL ($p < 0.001$).
CRP upper limit was taken as 5 mg/L and this was taken as 0.15 ng/mL for Procalcitonine in the hospital laboratory where the study was performed. According to this, there was a distinct recovery in the number of patients whose eosinopenia recovered in 1st, 2nd, 3rd day beginning from hospitalization and at time of discharge (last day) (percentage of patients with eosinopenia is respectively 87, 68, 45, 45, 39%) while the ratio of patients whose CRP and Procalcitonin values became negative and recovered was determined lower (1.6% for 1st day, 3.2% for 2nd day, 3.2% for 3rd day, 4.8% at time of discharge for CRP and PCT).
Conclusion: Eosinopenia is an inflamatory reagent that may be used in patients with cholangitis. Its inexpensiveness and applicability everywhere are the most significant advantages.
Disclosure: Nothing to disclose

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P1725 EFFICACY OF HEMOSPRAY AND ENDOCLOT IN THE TREATMENT OF GASTROINTESTINAL BLEEDING: RESULTS FROM A TERTIARY REFERRAL CENTER

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Introduction: Gastrointestinal (GI) bleeding frequently leads to hospital admission and is associated with relevant morbidity and mortality, particularly in the elderly. Due to the increasing administration of direct oral anticoagulants in the last years and the emerging role of antiplatelet agents treatment of gastrointestinal bleeding may be challenging. Hemostatic powders (HP) represent novel ''touch-free'' and easy to use items for the management of gastrointestinal bleeding.
Aims and Methods: Our aim was to analyze the short-term (ST-within 72 hours-) and long-term (LT-within 30 days-) success for achieving hemostasis with HP and to directly compare the two agents Hemospray (HS) and Endoclot (EC) in their hemostatic efficacy. Data were prospectively collected on patients who received HS and EC between September 2013 and September 2017 for endoscopic hemostasis in our center. Patients were followed-up for at least one

month after index endoscopy and data analysis was performed after follow-up was completed.
Results: HP was applied in 154 consecutive patients (mean age 67 years) with GI bleeding in our center. Patients were followed up for at least 1 month (mean FU: 3.2 months). The majority of HP applications were in the upper GI tract (89.0%) with the following bleeding sources: peptic ulcer (35%), esophageal varices (7%), tumor bleeding (11.7%), reflux esophagitis (8.7%), diffuse oozing bleeding and erosions (15.3%). Overall ST success with HP was achieved in 125 pts (81.2%) and LT success in 81 patients (67%). Re-bleeding occurred in 26.6% of all patients treated with HP. In 72 patients (47%), HP was applied as a salvage hemostatic therapy, here ST and LT success were 93.1% and 64.3%, respectively, with re-bleeding in 31.9% of patients. As a primary hemostatic therapy, ST and LT success were 81.7% and 69.2%, respectively, with re-bleeding occurring in 21.9%. Subgroup analysis showed a ST and LT efficacy for cancer bleeding of 83.3% and 86.7%, for peptic ulcer disease of 81% and 56.2% and in patients under therapeutic anticoagulation of 80% and 60.5%. There was no statistical difference in the ST or LT efficacy between EC and HS for the various indications; however, HS was more frequently applied for upper GI bleeding ($p = 0.04$).
Conclusion: Both HS and EC allow for effective hemostasis with high ST success when applied as primary or salvage therapy. No differences in ST, LT success and re-bleeding between HS and EC were detected.
Disclosure: Nothing to disclose

P1726 HEMOSPRAY USE IN ACUTE GASTROINTESTINAL BLEEDING- A 4-YEAR SINGLE-CENTRE EXPERIENCE

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Introduction: Upper GI bleeding (UGIB) has a mortality of about 10% in United Kingdom (UK) despite advances in treatment. The current guidelines recommend dual modality of treatment which could include injection of adrenaline, argon photocoagulation or using endoscopic clips to achieve haemostasis. A recent addition to therapeutic options is Hemospray. Since June 2013, there have been reports from UK that it is useful as an adjunct in treatment of UGIB with most reporting success rates of 77%-85%. It has been suggested that it may not be reliable when used as the only mode of treatment.
Aims and Methods: We aimed to report our experience of using Hemospray in our centre over last 4 years (2013 to 2017). A retrospective review was carried out to select relevant patients between July 2014 and July 2017, using the trust endoscopy database. We looked at electronic records of patients who underwent an endoscopy & needed Hemospray as a mode of treatment for managing an acute gastrointestinal (GI) bleed. All relevant clinical data was compiled using electronic records.
Results: 45 consecutive patients (M = 31), with median age 72 years (range 35–91y) were included. The mean haemoglobin prior to endoscopy was 92 g/L. 40% were on anticoagulants or anti-platelets on admission. Of all patients who needed Hemospray, 43 had gastroscopies, 1 ERCP and 1 had colonoscopy. The details of diagnosis are in Table 1.
- 39 (86%) patients had Hemospray as adjunct therapy & all patients had complete haemostasis documented at the end of index procedure.
- It was used as the only modality of therapy successfully in 6 patients (4 with malignancy and 2 iatrogenic bleeds).
- Overall, 6/45 patients had a documented rebleed after discharge but within 4 weeks; 4 had bleeding vessels and were on warfarin or Ticagrelor; 2 patients had tumour related recurrent bleeding.
- Forrest classification applicable to 22 patients -1A (n = 3, 15%), 1B (n = 10, 46%), 2A (n = 3, 15%), 2B (n = 3, 15%), 2C (n = 2, 9%).
- 100% (n = 7) of UGIB related to malignancy responded to Hemospray (adjunct and monotherapy included).
- 30-day mortality was 24%(n = 11) with 3 deaths directly attributed to GI bleeding, 4 palliative secondary to malignancy and 4 multifactorial in elderly patients.

Conclusion: Our 4-year experience suggests that Hemospray can be a useful adjunct to conventional endoscopic therapy for acute GI bleed with success rates comparable to previous reports (nearly 85% in our cohort), with a rebleed rate of 14%. Rebleeding was observed to be higher when patients were on antiplatelets or anticoagulants. Our findings also suggest it could be useful as monotherapy for bleeding related to malignancies where other therapy may be impractical. More studies with larger numbers are needed to add to the evidence base.

Diagnosis	Number (n = 45)
Duodenal Ulcer	14 (32%)
Oesophageal/gastric ulcer	4(9%)
Malignancy related	7(15%)
Iatrogenic bleeding	7 (15%)
Other including unclear cause of bleed	13(29%)

[Table 1]
Disclosure: Nothing to disclose

P1727 70-DAY MORTALITY OF ADMISSIONS TO INTENSIVE CARE UNIT WITH UPPER GASTROINTESTINAL BLEEDING

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Introduction: Acute upper gastrointestinal bleeding (AUGIB) is a common hospital presentation. The incidence of UGIB in New Zealand is reported as 59.2 per 100,000 adults per year (1). The estimated mortality rate ranges between 6% and 10% (2), but can be even higher in patients admitted to the intensive care unit (ICU). There is very little data on what predicts outcomes of patients with UGIB requiring intensive treatment.
Aims and Methods: The aim of this study is to determine the 30-day mortality of UGIB post-ICU admission and potential risk factors that predict an outcome.
A retrospective analysis of all patients admitted to ICU at Middlemore Hospital with AUGIB from 2010 to 2015 was performed. The following characteristics were examined – demographics; comorbidities; mode of presentation; haemodynamic; urea, lactate, and coagulation profile at presentation; Rockall score; precipitating factors (anti-platelets; anticoagulation, NSAID's); cause of UGIB; endoscopic findings; and transfusion requirement. The primary outcome was 30-day mortality post-ICU admission. The secondary outcome was risk factors that independently predicted mortality.
Results: A total of 80 patients with AUGIB were admitted to ICU. Median age was 61 years (interquartile range 52–72). Bleeding from peptic ulcer was the most common endoscopic diagnosis (70%), followed by oesophageal varices (17.5%). Overall 30-day mortality was 11% (9/80), of which 78% (7/9) had UGIB as their primary cause of death. Logistic regression revealed high Rockall score and high lactate were significant independent predictive factors for 30-day mortality. On Receiver Operating Characteristic (ROC) analysis, these two variables, when combined, had the greatest accuracy (area under ROC curve 0.94, sensitivity 90%, specificity 90%) for predicting 30-day mortality
Conclusion: Patients presenting with AUGIB requiring intensive treatment have a high mortality rate of 11% at 30 days and, in the majority, this was due directly to GIB. High Rockall score and lactate at admission to ICU were the strongest independent predictors of 30-day mortality in patients presenting with AUGIB and should be used as prognostic markers to predict an outcome.
Disclosure: Nothing to disclose

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P1728 REBLEEDING AND MORTALITY ARE HIGHER IN PATIENTS WITH GASTROINTESTINAL BLEEDING TREATED WITH ANTICOAGULANTS THAN ANTI-PLATELETS

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Introduction: Antithrombotic (AT) drugs increase the risk of overt gastrointestinal bleeding (GIB) but their effects on clinical outcomes are not well established.
Aims and Methods: The aim of this study was to determine the effect of antiplatelet (AP) and anticoagulant (AC) drugs on rebleeding and mortality in patients with gross GIB.
This was a prospective study on all patients admitted to the American University of Beirut Medical Center with melena, hematochezia, hematemesis, or coffee ground emesis between Jan. 2013 and Feb. 2018. The patients' characteristics and clinical outcomes were compared among the following groups: (a) patients on any one or more antiplatelet (AP) only (aspirin, clopidogrel, ticagrelor, prasugrel, and dipyridamole), (b) patients on any anticoagulant (AC) only (warfarin, heparin, low molecular weight heparins, direct acting oral anticoagulants), (c) patients on combination therapy (AP and AC), and (d) patients on no AT therapy.
Clinical features associated with rebleeding and mortality were assessed using the Chi-Square and Student's t-tests, respectively. Stepwise Cox proportional hazards regression analysis was used to adjust for potentially confounding variables when assessing the association between mortality, rebleeding, and the following: type of AT therapy, age, Charlson Comorbidity Index (CCI), blood transfusion, severe GIB (systolic blood pressure < 100 mmHg, > 2 units of blood transfused or ≥ 2 units drop in Hb), stigmata of recent hemorrhage (SRH), and endoscopic therapy.
Results: Complete follow-up information for a mean of 22 months was available for 447 patients. The clinical characteristics of patients are shown in table 1. Patients on any AT were significantly older and had higher CCI than controls.

Abstract No: P1728

Table 1: Clinical characteristics and outcomes of patients based on antithrombotic medications on admission

		No antithrombotics (Control group) (170)	Antiplatelets only (148)	Anticoagulants only (75)	Antiplatelet and anticoagulant (54)	Total (447)
Age (SD)		60 (19)	74 (11) **	72 (17) **	75 (10) **	
Charlson Comorbidity Index (SD)		1 (2)	2 (2) *	2 (2) *	2 (1) *	
Male	N (%)	106 (62%)	104 (70%)	44 (59%)	30 (56%)	284 (64%)
Upper GIB	N (%)	105 (62%)	70 (47%)	41 (55%)	26 (48%)	242 (54%)
Lower GIB	N (%)	48 (28%)	60 (41%)	22 (29%)	19 (35%)	149 (33%)
Blood Transfusion	N (%)	83 (49%)	87 (59%)	55** (73%)	40** (74%)	265 (59%)
Severe Bleeding	N (%)	77 (45%)	76 (52%)	40 (53%)	30 (56%)	223 (50%)
Stigmata of recent hemorrhage	N (%)	50 (29%)	52 (35%)	26 (35%)	9 (17%)	137 (31%)
Endoscopic Therapy	N (%)	42 (25%)	47 (32%)	24 (32%)	21 * (39%)	134 (30%)
Rebleeding	N (%)	39 (23%)	23 (16%)	19 (25%)	8 (15%)	89 (20%)
Death	N (%)	22 (13%)	30 (20%)	31 ** (41%)	19 ** (35%)	102 (23%)

*: $p < 0.05$; ** $p < 0.01$ compared to control

The overall rebleeding and mortality rates were 20% and 23%, respectively. Of 277 patients admitted on AT drugs, 23 died in-hospital, and 169 were discharged on AT drugs.

After adjusting for confounders, predictors for mortality were: older age (HR = 1.037 per year increase, $p < 0.0001$), higher CCI (HR = 1.442, $p < 0.0001$), severe GIB (HR = 1.83, $p = 0.007$), and being on AC only (HR = 1.9, $p = 0.037$), while independent predictors of rebleeding were: older age (HR = 1.03 per year increase, $p < 0.0001$), higher CCI (HR = 1.4, $p < 0.0001$), severe bleeding (HR = 2.0, $p = 0.002$), and being on AC only (HR = 1.8, $p = 0.07$).

Compared to patients on AP only, patients on AC only were more likely to receive blood transfusions ($p = 0.03$) and to die ($p = 0.001$) (table1). After adjusting for confounders, the AC only group had a higher rebleeding rate (HR = 2.3, $p = 0.003$) and higher mortality (HR = 2.3, $p = 0.002$) compared to the AP only group.

Discharge AT drugs had no independent effect on mortality or rebleeding.

Conclusion: Overall re-bleeding and mortality in patients with GIB remain high and seem to be associated with AC therapy. The findings may inform risk stratification and decisions regarding continuation or discontinuation of AC.

Disclosure: Nothing to disclose

P1729 ENDOSCOPIC RADIOFREQUENCY ABLATION IS AN EFFECTIVE THERAPY IN PATIENTS WITH SYMPTOMATIC ANAEMIA SECONDARY TO GASTRIC ANTRAL VASCULAR ECTASIA

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Introduction: Gastric antral vascular ectasia (GAVE) is a rare cause of gastrointestinal bleeding (GIB). Patients often require regular blood transfusions and long-term oral or intravenous iron supplementation to manage symptomatic anaemia impacting on quality of life. Endoscopic therapy (ET) for GAVE includes argon plasma coagulation (APC), laser therapy and endoscopic band ligation. In some patients, these measures are not successful with significant effects on their health and quality of life. Radio-frequency ablation (RFA) may provide a solution in these patients.

Aims and Methods: A single-centre prospective study to evaluate the efficacy and safety of RFA in patients with GAVE refractory to first line ET.

The primary outcome was an increase in haemoglobin (Hb) 3 months after treatment. Secondary outcomes were a reduction in frequency of blood transfusions and/or iron (PO or IV) in the 3 months before and after RFA treatment. Endoscopic surface area (SA) regression of GAVE was analysed by 3 experts estimating % change in SA following treatment by examining images before and after treatment.

Methods: Patients who remained anaemic and/or transfusion or iron dependent after other ET were eligible. Other causes of GIB were excluded. Treatment with RFA was with focal RFA at 12J/cm2 with 3 applications to visible areas of GAVE under conscioussedation. Patients had up to 2 RFA treatments 6 weeks apart. Data were collected before and after treatment.

Results: 20 patients had RFA for refractory GAVE. The median age was 69 years (IQR 62–82). 17/20 (85%) were female. 13 were previously treated with APC, 4 with laser and 3 with band ligation. In the 3 months prior to treatment, 11/20 were on oral iron, 6/20 were on IV iron. 14/20 required regular blood transfusions prior to treatment, with 11 of these on both iron supplementation and blood transfusions. The median number of RFA treatments was 2 (IQR 1–2).

No patients had recorded complications of RFA. The mean pre-treatment Hb was 95.1g/L (95% CI 87.4–102.6g/L). The mean Hb at 3 months after final RFA treatment was 112g/L (95% CI 103.9 -120.1g/L). The mean change in Hb was +12.6 g/L (95% CI 11.7–24.3g/L) ($p < 0.0001$) (paired t-test)).

Post treatment, only 3/14 (21%) of the patients who required blood transfusions prior to the procedure had ongoing transfusions. Only 5/17 (29%) patients who were previously on iron had ongoing iron needs.

The mean surface area regression when scored by 3 expert endoscopists was 64.2.% (95% CI 56.3–72.1).

Conclusion: RFA for patients with symptomatic anaemia secondary to GAVE refractory to previous ET is a novel treatment therapy for a difficult cause of GIB. This feasibility study shows that this approach can significantly reduce blood transfusion dependence and iron supplementation in some patients with improved Hb after treatments. The required number of treatments is small and it appears safe.

Disclosure: Nothing to disclose

P1730 MANAGEMENT OF ANTIPLATELET AND ANTICOAGULANT THERAPY IN PATIENTS WITH NONVARICEAL UPPER GASTROINTESTINAL HEMORRHAGE

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Introduction: Acute nonvariceal upper gastrointestinal hemorrhage (NVUGIH) is a frequent event with an estimated incidence of 40–150/100,000/year. The European Society of Gastrointestinal Endoscopy (ESGE) has published guideline recommendations on the management of antiplatelet (APT) and anticoagulant therapy (ACT) in patients with NVUGIH [1].

Aims and Methods: Patients who underwent esophago-gastro-duodenoscopy (EGD) at a single university hospital between 01/01/2016 and 31/12/2017 were screened for cases of NVUGIH. Inclusion criteria were endoscopically diagnosed NVUGIH and prior exposition to antiplatelet agents (APA) and/or anticoagulation (AC). Exclusion criteria were variceal bleeding, negative findings in EGD, and outpatient setting because of missing information on follow-up.

Following definitions were used to assess the management of APA and AC according to the ESGE guidelines:

Primary prophylaxis: APA should have been withheld. Resumption of APA was not included in the definition.

Secondary prophylaxis: APA should have been withheld and then resumed in case of high-risk endoscopic stigmata, or continued without interruption in case of low-risk endoscopic stigmata.

Dual antiplatelet therapy (DAPT): Both APAs should have been continued without interruption in case of low-risk endoscopic stigmata, or in case of high-risk endoscopic stigmata and high thrombotic risk. In case of high-risk endoscopic stigmata and low thrombotic risk, the second APA should have been withheld and low-dose acetyl salicyl acid (ASA) as first APA should have been continued without interruption.

ACT should have been withheld and then have been resumed within 15 days irrespective of thrombembolic risk.

Endoscopic stigmata were classified as high risk in case of Forrest Ia, Ib, IIa, and IIb and as low risk in case of Forrest IIc and III. High arterial thrombotic risk was defined as acute coronary syndrome < 12 months, elective implantation of a bare metal stent < 4 weeks, or drug eluting stent < 6 months. Major bleeding was defined as haemoglobin ≤8 g/dl on the day of endoscopy (day 0), drop of haemoglobin of ≥2 g/dl between day 0 and day 1 or need for transfusion of packed red blood cells. Blood products included platelets, fresh frozen plasma, and single or combination of coagulation factors. Follow-up was defined as time period between index endoscopy and hospital discharge or death.

Results: 316 out of 9,948 (3.2%) patients met inclusion criteria. Of these 68.4% were male, median age was 70.5 years (IQR 62–78). Management of APA for primary or secondary prophylaxis was assessed as not following guideline

recommendations in 37/83 (45%) patients. Age, gender, treating specialty, major bleeding, use of blood products, Charlson comorbidity index, admission to intensive care unit, need for reendoscopy, rebleeding or endoscopic stigmata were not associated with management of APA. Management of ACT was assessed as not following the guideline recommendations in 68/127 (53.5%) patients. After including the use of heparin in therapeutic dosage, number decreased to 61/127 (48%). In univariate analysis, age (66 years, IQR 57–74.75, vs. 73 years, IQR 66–78, $p=0.005$) and treating specialty (internal medicine 61.8% vs. 88.1%, $p=0.003$) were significantly associated with inappropriate management of ACT. All other patients received combination therapy.
Conclusion: Management of APA or AC in patients with NVUGIH was not according to current ESGE guidelines in a significant number of patients. Efforts need to be made to improve management of these patients as they are at an increased risk for cardiovascular events.
Disclosure: Nothing to disclose

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P1731 COFFEE GROUND VOMIT: DOES IT JUSTIFY AN URGENT ENDOSCOPY?

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Introduction: Coffee ground vomit is vomit that looks subjectively like coffee grounds. It is thought to occur due to the presence of coagulated blood in the vomit and hence is a common indication for inpatient admission and thereafter endoscopy. In an increasingly stretched inpatient endoscopy service it is important not to over burden it with endoscopies that could be performed safely as an outpatient.
Aims and Methods: Therefore, our aim is to evaluate the need for inpatient gastroscopy in patients who are deemed to have coffee ground vomiting. We hypothesize that patients with coffee ground vomiting do not have significant upper gastro intestinal bleeding requiring endoscopic intervention.
A single-center, retrospective analysis was performed on patients endoscopied for the primary indication of coffee ground vomiting. Data was collected and scrutinized from the Electronic Patient Records (EPR) and Unisoft endoscopy-reporting tool at Barnet and Chase Farm Hospitals, Royal Free London for 12 months of 2017. Gastroscopy reports were studied to see whether endoscopic therapy was required (defined as use of adrenaline injection, banding, clips, haemospray or gold probe). EPR was subsequently used to assess whether these patients had a significant drop in their haemoglobin (Hb) defined as a Hb drop $\leq$20g/dl. Two independent researchers carried this out.
Results: There were 2618 gastroscopies during the study period. Of these, 37 were indicated due to coffee ground vomiting with 29 being performed as an inpatient. Of these 29 patients, 27 (93%) had a significant drop in their Hb level prior to gastroscopy. One (3%) patient required endoscopic therapy. This patient had significant co-morbidty of ischaemic heart disease, hypertension, aortic valve replacement as well as a drop in Hb.
In total, 12 patients had a diagnosis of oesophagitis, 3 had erosive gastritis, 3 non erosive gastritis, 1 oesophageal ulcer, 3 duodenal ulcers, 3 non erosive duodenitis, 1 pyloric ulcer and 1 hiatus hernia. 4 gastroscopies were completely normal. There were no patients with cancer diagnosis. Each diagnosis was reported separately if the report contained more than one diagnosis.
Conclusion: From this study we conclude that in the majority of patients endoscoped for coffee ground vomit do not require intervention during endoscopy. This study confirms our hypothesis and adds weight to the notion that patients with coffee ground vomiting do not necessarily require inpatient gastroscopy despite a significant Hb drop. If findings from this study were to be repeated in other centers we may be able to discharge stable patients with coffee ground vomiting to early OPD endoscopy thus reducing length of stay and pressure on already stretched inpatient emergency workload.
Disclosure: Nothing to disclose

P1732 ORAL ANTICOAGULANTS AND UPPER GASTROINTESTINAL BLEEDING: POTENTIAL RISK FACTORS AND OUTCOMES – A SINGLE-CENTRE EXPERIENCE

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Introduction: Acute nonvariceal upper gastrointestinal bleeding (AUGIB) is a common medical emergency requiring prompt management. Available data suggest that use of oral anticoagulants (OAC) is associated with more frequent AUGIB, mostly peptic ulcer-related, and more severe outcomes.
Aims and Methods: To identify patients with AUGIB who use OAC and determine the severity of bleeding, outcomes and potential contributing factors for adverse outcomes. Retrospective, prospective analysis of all patients over 18 years of age consecutively admitted for AUGIB in a tertiary centre in Latvia – Riga East Clinical University Hospital from November 2013 to December 2014. Patients were asked to complete a questionnaire regarding their history of OAC use and INR control. Data were collected on bleeding-related interventions, length of hospital stay and outcomes. Bleeding severity on endoscopy was evaluated according to Forrest classification. Data was analysed using SPSS 20.0.
Results: Two hundred thirty-six patients with AUGIB were identified (138 (58%) men and 98 (42%) women, mean age 62 ± 17.36 years). Twenty-seven (11.4%) patients used OAC (mean age 73 ± 11.3 years), mostly warfarin (n = 22, 82%). Only 5 (18%) of OAC users were on new OAC – dabigatran (n = 3, 11%) and rivaroxaban (n = 2, 7%). Sixty-seven percent of OAC users received this therapy for $>$ 2 years, most commonly because of permanent atrial fibrillation. Among OAC users 8 (30%) were on double antithrombotic (OAC+antiplatelet) therapy. The most common diagnoses in patients using OAC were haemorrhagic gastropathy (n = 5, 17%) and Mallory-Weiss syndrome (n = 5, 17%) and peptic ulcer disease (PUD), with Forrest IA, IIA and IIB bleeding with equal frequency (n = 4, 14% in each). Despite previously experienced spontaneous haemorrhages (n = 5, 18%) and episodes of severe bleeding, such as gastrointestinal bleeding, epistaxis and post-traumatic bleeding, (n = 8, 29.6%), most OAC users with AUGIB were not regularly controlling INR levels. One hundred eight patients (45.7%) were hospitalized in intensive care unit (ICU), most often with Forrest IIB PUD bleeding – 36 (33.3%). Of those hospitalised in ICU one was using OAC. There was no statistically significant difference in severity of PUD bleeding between OAC users and non-users ($r=-0.189$, $p=0.004$, *Pearson Correlation)*. There was also no statistically significant difference between OAC users and non-users in length of ICU stay ($p>0.05$, *Chi-Square Test*) and total length of hospital stay. Transfusion of red blood cells was required in 133 (56.3%) cases, fresh frozen plasma in 106 (44%) cases and cryoprecipitate in 39 (16.5%) cases. Surgery was performed in 37% of patients. Ninety-seven (41,1%) of all patients received vitamin K intravenously. Twenty-four (10%) patients died, two of them (8.3%) were OAC users.
Conclusion: OAC use was not associated with more severe ulcer bleeding, longer hospitalization in ICU or longer total hospital stay. OAC use-related bleeding could be minimised with thorough patient education about risks and regular INR control.
Disclosure: Nothing to disclose

P1733 GASTROINTESTINAL BLEEDING, A SERIOUS COMPLICATION OF PATIENTS WITH ACUTE CORONARY SYNDROME

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Introduction: Gastrointestinal bleeding (GIB) is frequent in patients receiving anti thrombotic treatment. This situation is more delicate in patients with an acute coronary syndrome (ACS). There is no specific recommendation whether antiplatelet medications should be interrupted or not. The aim of this study is to evaluate the clinical outcome and therapeutic features of patients who developed a GIB during an ACS.
Aims and Methods: We retrospectively reviewed the medical files of patients with ACS who were complicated with GIB from January 2012 to December 2017. Clinical, biological and endoscopic findings were collected.
Results: One hundred sixty-five patients were included in our study. There were 68% males and 32% females. The median of age was 52 years. The average time between the ACS onset and GIB was 5 days. All patients had dual antiplatelet therapy (DAPT). Haemorrhage was externalized by hematemesis in 72% of the cases, melena in 28% and rectal bleeding in 12%. Upper endoscopy showed: erosive gastritis (24%), bulbar ulcer (28%), antral ulcer (16%), œsophagitis (20%), erosive duodenitis (2.6%),esophageal ulcer (8%), esophageal varices (2.6%), gastric varices (4%) an portal hypertensive gastropathy (2.6%). Colonoscopy revealed: diverticulosis coli (20%), angiodysplasia colic (45%) and colic polyps (35%). DAPT was maintained in all patients because of the high thrombotic risk. Patients had intravenous proton pump inhibitors and endoscopic management (adrenaline injection, argon plasma coagulation, variceal banding). Bleeding stopped in the majority (89.3%) of patients. Eight (10.7%) patients died after endoscopic haemostasis failure or because of an early recurrence.
Conclusion: GIB is a severe complication that can occur in patients with ACS. Management is based on medical treatment and endoscopic haemostasis.
Disclosure: Nothing to disclose

P1734 ENDOSCOPIC APPLICATION OF HIGHLY MUCO-ADHESIVE POWDER (NEXPOWDER) FOR TREATMENT OF DIFFUSE OR REFRACTORY ACTIVE UPPER GASTROINTESTINAL BLEEDING (UGIB): PRELIMINARY RESULTS

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Introduction: Upper gastrointestinal bleeding (UGIB) frequently leads to hospital admission and is associated with relevant morbidity and mortality. Although the conventional endoscopic hemostasis was usually effective in controlling UGIB but some have difficulty in achieving successful hemostasis depending on the location and severity of hemorrhage. Conventional endoscopic hemostasis require targeted therapy on bleeding focus. However hemostatic powder do not require target approach and can apply easily to bleeding site.
Nexpowder (Nextbiomedical Co., Incheon, South Korea) is a novel highly muco-adhesive hemostatic powder designed to be a simple endoscopic technique in applying to large surface areas even in difficult positions. Nexpowder consists of oxidized dextran and modified amino acid, and is thus, biodegradable and biocompatible. When Nexpowder contacts water, the oxidized dextran reacts with the amino acid, and becomes a highly muco-adhesive gel. The gel physically adheres to the ulcer base creating a mechanical barrier to achieve hemostasis.
Aims and Methods: The aims of the current study were to evaluate 1) the feasibility of the application of the highly muco-adhesive hemostatic powder inpatient with diffuse or refractory UGIB 2) re-bleeding rate on second-look endoscopy at 1 or 3 days after the procedure, 3) persistent rate of hydrogel on ulcer base at follow-up endoscopy.
The muco-adhesive hemostatic powder (3~6g) was sprayed endoscopically onto the bleeding site using a 7.5-Fr catheter passed through the operative channel of the endoscope.
Results: Eleven patients with diffuse or refractory active UGIB requiring endoscopic hemostasis were treated with Nexpowder. The etiology of bleeding was a post-ESD bleeding in 5 patients, ampullary bleeding in 2, ulcer bleeding in 2, and tumor bleeding in 2 patients. Application of the highly muco-adhesive hemostatic powder on the bleeding source was successful in all patients with no therapy-related adverse events (AEs). Immediate hemostasis was achieved in 11/11 (100%) patients. Recurrent bleeding within 3 days was observed in 1/11 patients 9.1%. The persistence rate of Nexpowder gel was about 80% at 1 day and 20% at 3 days after the procedure.
Conclusion: Despite the small number of patients in this study, we can find that Nexpowder is an effective method in achieving immediate hemostasis when used in diffuse or refractory UGIB. Nexpowder seems to have a successful hemostatic effect because the highly muco-adhesive gel attaches to the bleeding site to form a mechanical barrier and then the adhesive gel protect the bleeding site for more than one day. Therefore, muco-adhesive Nexpowder seems to be good option in patients with diffuse or refractory UGIB.
Disclosure: Nothing to disclose

P1735 AORTO-OESOPHAGEAL FISTULA DETECTED BY UPPER DIGESTIVE ENDOSCOPY – CLINICAL PRESENTATION, ENDOSCOPIC ASPECTS AND PROGNOSIS OF A RARE ENTITY

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Introduction: Aortic esophageal fistula (AEF) can be classified as primary in the absence of previous surgery of the esophagus or aorta, and secondary in the presence of one of them. AEFs classically present with the Chiari triad: chest pain, sentinel hematemesis followed by exsanguinating hematemesis.
Aims and Methods: The aim of the study was to evaluate and characterize the clinical presentation and endoscopic findings and prognosis of AEFs detected by upper gastrointestinal endoscopy (UGE).
Between October 2014 and January 2018, 5 patients with AEFs were detected by UGE. The clinical presentation, comorbidities, endoscopic appearance, management and outcome of the patients were evaluated. Descriptive statistical analysis was performed.
Results: The mean age was 59.5 ± 11.9 years of which 4 (80%) were men.
Clinical presentation: Toracalgia-2 (40%), hematemesis-2 (40%), melena-1 (20%), abdominal pain-2 (40%) and anemia-1 (20%). In patients presenting with gastrointestinal hemorrhage, 3 (60%) cases had no hemodynamic repercussion. The lowest median value of hemoglobin in the first 24 hours was 8 g/dL.
Etiology: Primary – 3 (60%); secondary – 2 (40%).
All patients had cardiovascular comorbidities and 1 (20%) had oesophageal neoplasia. Antiplatelet agents were documented in 3 (60%) and antiplatelet agents in combination with anticoagulants were noted 1 (20%) patients.
Endoscopically, the median distance of the ulcer in the esophagus from the dental arch was 30 (Range – 22–35) cm. Active arterial bleeding was noted in 1 (20%), adherent clot to the base of the ulcer in 2 (40%) and an ulcer with evident endovascular stent mesh visible in the ulcer base in 2 (40%) patients.
The AEF were confirmed by computed tomography of the chest in all patients. Management of patients involved endovascular stent placement in 4 (80%), esophageal and endovascular stent in 1 (20%) and esophageal stent in 1 (20%) in the patient with esophageal neoplasia. There was a recurrence of bleeding in 3 (60%) patients. Mortality was documented in 4 (80%) patients after a median of 3.6 (Range – 2.9–7.5) months.
Conclusion: Aortic esophageal fistulas detected by endoscopy were more frequent in men in the 6th decade of life presenting as an ulcer in the middle third of the esophagus. The prognosis is poor despite endoscopic and endovascular interventions.
Disclosure: Nothing to disclose

P1736 EXPERIENCIE WITH N-BUTIYL-2 CYANOACRYLATE GASTRIC VARIX INYECTION IN AN UNIVERSITY HOSPITAL OF LA PLATA, ARGENTINA

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Introduction: Gastric varices are founded in 20% of patients with portal hypertension. Their bleeding rates ranges between 55 to 78%, associated to high mortality (45%). According to literature, management with N-butyl-2-cyanoacrylate shows initial hemostasis rates between 87% and 100%, while the rebleeding rates ranged between 24% and 50%. Severe complications related to the procedure (sepsis, thromboembolism, fistulas, adherence of the needle to the varix) are rare. Even though prospective studies are lacking, the linear echoendoscopy placement of coils associated to N-Butyl-2-Cyanoacrylate is a promising therapeutical option for the varix obliteration and the achievment of hemostasis. Besides, it enables to use less cyanoacrylate doses and thus decreases the risk of any complications
Aims and Methods: Retrospective, observational study of 106 patients having gastric varices who were treated in our unit with butyl-cyanoacrylate. A 0.5 ml of N-butyl-2-cyanoacrylate + 0.5 ml of lipiodol solution was used. 21 gauge sclerosis needles were used, and Olympus endoscopes. Procedures were performed under sedation with propofol.
Results: 106 patients were included, 41 women and 65 men, with a 54 year old average age (16–92 years). Portal hypertension (HTP) causes were: cirrhosis HTP (87.7%), non cirrhotic HTP (0.9%) and segmentary HTP (2.8%), 49% were Child A, 36.7% Child B, 9.4% Child C, 5 patients were not classified. Esophageal varices were classified as esophagogastric (GOV) or isolated gastric (IGV) in accordance with the classification of Sarín: 17.9% GOV-1, 44.3% GOV-2, 11.3% GOV-1 Y GOV-2, 22.6% IGV-I, 2.8% IGV-I and GOV-II).
In 94 patients having gastrointestinal bleeding, primary hemostasis was 88.6% successful, while the rest of the patients required one or more sessions, including 1 therapy combined with coils and surgical shunt after the 4 session failure. In the latter case, the endoscopic finding included active bleeding in 21 cases (19.8%), sticking clot in 11 (10.3%), red dots in 12 (11.3%), platelet plug in 34 (32%), ulcer on varix in 12 (11.3%), tumoral varices in 14 (13.2%).
Rebleeding rate during the 6-week follow-up period was 11.3%, they were re-treated with N-Butyl-2-cyanoacrylate, thus achieving the final hemostasis. In one patient, the greatest complication of treatment was thrombosis of the splenic vein.
Conclusion: The use of N-butyl-2-cyanoacrylate is a safe and efficient option for gastric varix management. To our knowledge, in accordance with the international literature, the achievements were as follows: primary hemostasis (88.6%); final hemostasis (99%), and rebleeding low risk and complications (1%). In order to obtain good results, it is essential to follow the technical recommendations during the injection methodology.
Disclosure: Nothing to disclose

P1737 A RANDOMIZED TRIAL OF MONOPOLAR SOFT-MODE COAGULATION VERSUS HEMOCLIP FOR PEPTIC ULCER BLEEDING

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Introduction: In the treatment of peptic ulcer bleeding, various endoscopic treatment modalities are used depending on ulcer size, localization and clinical status of the patient. These modalities are; injection treatments (sclerotherapy etc), thermal treatments (argon plasma coagulation, soft coagulation, bipolar or monopolar cautery etc.) and mechanical treatments (hemoklips etc.). These treatment methods have advantages or disadvantages among themselves and there isn't a recommended standard treatment approach.
Aims and Methods: The aim of this study is to compare a relatively new method monopolar hemostatic forceps soft coagulation (MHFSC) and commonly used hemoclips (HC).
Between September 2016 and February 2018, patients with upper gastrointestinal bleeding who were diagnosed with Forrest 1a, 1b, 2a stomach or duodenal ulcer on endoscopic examinations were included in the study. Proton pump infusion therapy was started at the time of diagnosis to all patients and continued until 72 hours after the procedure. Patients were randomized to MHFSC and HC groups. The rates of primer hemostasis with MHFSC and HC were approximately 96% and 78.5%, respectively and we planned a total of 56 patients per group, considering an alpha error of 0.05 and to achieve statistical power of 80%. In patients who do not have adequate haemostasis with the first method, the other method applied. Rebleeding was defined as hemorrhage within the first 7 days after endoscopic hemostasis. Patients with stomach operation history, malignant ulcers, and patients who could not be followed for 7 days after discharge were excluded. Both groups were compared in terms of initial hemostasis

success, rebleeding rate, endoscopic procedure time to achieve hemostasis, and hospitalization time.
Results: During the study period, a total of 245 patients were referred to our clinic with hematemesis or melena. Emergency endoscopy was performed within 24 hours after the presentation of 238 patients. According to the study protocol, 126 patients were excluded from the study. 112 patients were randomized to the MHFSC (n = 56) and HC (n = 56) groups. The mean age was 61.36 ± 19.3 years and 80 (71.4%) were male. There was no statistically significant difference between the two groups in terms of demographic and laboratory parameters, drug use and underlying chronic diseases.
The initial hemostasis was achieved in MHFSC alone in 55 patients (98.2%) and HC group in 45 patients (80.4%) in HC group, higher in MHFSC group (p = 0.004). All 11 patients who were not able to receive the first hemostasis in the HC group were successfully treated with hemostatic forceps. One patient who could not undergo hemostasis with hemostatic forceps was stabilized by medical treatment and hemorrhage was not observed at 24th hour control endoscopy. Rebleeding was detected in ten patients (2 MHFSC, 8 HC). In the MHFSC group, the duration of endoscopic procedure (302 ± 87.8 vs 568 ± 140.4 s, p < 0.0001) and the length of hospital stay were shorter (3,50 ± 1,03 vs 4,37 ± 1,86 days, p = 0.016). None of the patients needed transcatheter embolization or emergency surgical treatment.
Conclusion: MHFSC method is is more effective and safe treatment method than HC and can be applied more rapidly in the endoscopic treatment of peptic ulcer bleeding.
Disclosure: Nothing to disclose

P1738 SAFETY AND EFFICACY OF NALDEMEDINE IN THE TREATMENT OF OPIOID-INDUCED CONSTIPATION IN CHRONIC NON-CANCER PAIN IN SUBJECTS WITH OR WITHOUT INADEQUATE RESPONSE TO LAXATIVES

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Introduction: Opioid-induced constipation (OIC), a common side effect of opioid utilization in treating chronic non-cancer pain, is caused by the action of opioids on peripheral μ-opioid receptors in the enteric nervous system. Naldemedine (NAL), a peripherally acting μ-opioid receptor antagonist (PAMORA), has demonstrated consistent efficacy and safety in the treatment of OIC from two phase 3, randomised, placebo-controlled, double-blind clinical trials [NCT01965158 (COMPOSE-1) and NCT01993940 (COMPOSE-2)]. In both studies there were significant improvements in the frequency of Spontaneous Bowel Movements (SBMs) and in the OIC symptoms of incomplete evacuation and straining with NAL. Study subjects in these studies, who must have discontinued previous laxative therapy, were assigned to a once-daily, oral 0.2 mg dose of NAL or placebo (PBO) for 12-weeks. Other elements of study design, study participants, eligibility criteria, clinical characteristics, clinical assessments, and outcome measures, as well as results are reported by Hale et al (Hale et al. 2017). However, the effect of naldemedine on the treatment of OIC in laxative inadequate responders (LIR) has not been reported.
Aims and Methods: To understand the therapeutic effect of naldemedine in LIR relative to PBO as well as non-LIR subjects. A post-hoc analysis from pooling two phase 3, randomised, placebo-controlled, double-blind clinical trials (COMPOSE-1; COMPOSE-2) was performed in the LIR and Non-LIR subgroup. LIR was defined as subjects who were on laxative therapy prior to entering the study and those who stopped its use within 30 days prior to screening, and who signed the informed consent which required the subject to have self-reported OIC (ie, incomplete bowel movement, hard stools, straining, or false alarms). Non-LIR was defined as those subjects who did not receive laxatives or only received rescue laxatives at or after screening. SBM responders, defined as having ≥3 SBM/week with ≥1 SBM/week increase over baseline for ≥9 of 12 weeks and ≥3 of the last 4 weeks, were compared between groups. Treatment emergent adverse events (TEAEs) were defined as those that were reported after randomization and were assessed as well.
Results: A significantly higher proportion of SBM responders was observed in the NAL group as compared to PBO in both the LIR and non-LIR groups for both studies (Table 1). TEAEs were comparable between the NAL and PBO in both LIR and non-LIR groups. The most common TEAEs were gastrointestinal-related.
Conclusion: These data demonstrate that NAL is efficacious and well tolerated in the treatment of OIC in those subjects who were LIR or non-LIR. These results suggest that the effect of NAL is independent of previous laxative utilization and is a useful treatment option in the management of OIC in patients with chronic non-cancer pain.

	LIR		Non-LIR	
	Naldemedine	Placebo	Naldemedine	Placebo
	0.2 mg		0.2 mg	
	N = 317	N = 311	N = 221	N = 226
Total	46.4% (147/317)	30.2% (94/311)	54.3% (120/221)	38.9% (88/226)
95% Confidence Interval (%) [a]	40.8, 52.0	25.2, 35.7	47.5, 61.0	32.5, 45.6
Difference of Proportion (SE) [b]	16.2 (3.82)		15.6 (4.66)	
95% Confidence Interval for Difference	8.7, 23.7		6.4, 24.7	
P-value [c]	< 0.0001		0.0009	

[a] Clopper-Pearson method.
[b] Difference of Proportion (SE) was calculated by using the estimator given by Koch et al.
[c] P-value was calculated by Cochran-Mantel-Haenszel test adjusted by the opioid dose strata and study.
[TABLE. Proportion of Responders in Treatment Period by LIR/Non-LIR Subgroups]
Disclosure: J. Tack has provided scientific advice to Allergan, Kyowa Kirin, Shionogi, and Shire. M. Hale was a consultant to Shionogi and received a stipend for review of the clinical study report. T. Yamada is an employee of Shionogi Inc. who may or may not own stock options. J. Wild received a stipend from Shionogi Inc. for review of the clinical study report.

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P1739 RNA SEQUENCING OF DUODENAL MUCOSA SAMPLES BEFORE AND AFTER FECAL MICROBIOTA TRANSPLANTATION DEMONSTRATES TRANSCRIPTOMIC CHANGES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME-DIARRHEA

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Introduction: The interactions occurring in the gut microenvironment following gut microbiota manipulation are believed to play an important role in the pathophysiology of irritable bowel syndrome (IBS) and yet to be studied. A previous study demonstrated the role of mucosal factors in the pathobiology of IBS by conducting RNA sequencing of colon samples showing transcriptomic changes that affect neurotransmitters, ion channels, cytokines, immune function, cell adhesion and barrier function in IBS-diarrhea (IBS-D) patients [1]. The use of fecal microbiota transplantation (FMT) in IBS-D patients improves their symptoms and manipulates their gut microbiota [2].
Aims and Methods: In this study we conducted RNA-sequencing to evaluate disease biology in Formalin-Fixed Paraffin-Embedded (FFPE) tissue samples of duodenal mucosa of the same cohort of IBS-D patients before and after FMT. Twelve IBS-D patients received freshly donated feces from their family members' donors and were instilled via a gastroscope into the descending part of the duodenum. Biopsy samples were collected before and three weeks after FMT. They were fully characterized with full transcriptome next-generation RNA sequencing (NGS) of duodenal samples, both before and after FMT. Half of the patients had idiopathic etiology (n = 6) and the remaining half had post-infectious (PI) etiology. NGS libraries were prepared with the illumina TruSeq® RNA Access protocol and sequenced on an illumina HiSeq 4000 apparatus [3]. Assembly of reads and alignment was guided by Tophat and Bowtie. Comparative analysis was done using voom/Limma package in R software version 3.4. Quality expression filter for all mRNA species was set at 3 counts per million for at least 50% of the samples evaluated. Differentially expressed genes (DEGs) were considered significant with a p-value cut-off at 0.05 and fold change greater than 1,5.
Results: Both subgroups of IBS-D patients showed different characteristics of gene expression following FMT with 85 and 108 DEGs in the idiopathic and post-infectious group, respectively. Table 1 shows the differentially expressed *common* changes in gene expression and some known gastroregulatory hormones between the two subgroups of IBS-D patients before and after FMT, and their respective up- or down-regulation after FMT.
Conclusion: RNA sequencing appears to be complementary in identifying changes in mucosal mRNA expression of genes of interest. This is the first study to show that RNA sequencing of duodenal mucosa samples demonstrates transcriptomic changes that affect immune function, cell adhesion, ion channels,

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Table 1: Differentially expressed genes common in idiopathic and post-infectious IBS-D patients before and after fecal microbiota transplantation

Gene (HGNC)	Function	Idiopathic IBS			Post-infectious IBS		
		log FC	FC A-B	P value	log FC	FC A-B	P value
C-C motif chemokine ligand 21 (CCL21)	Cytokine gene involved in immune regulation and chemotaxis	1.30	2.46	**0.008**	1.79	3.45	**0.002**
Hemicentin 2 (HMCN2)	Smooth muscle contraction, cell adhesion and cell migration. Calcium ion binding	0.76	1.70	**0.002**	0.80	1.75	**0.025**
Prostaglandin D2 synthase (PTGDS)	Prostaglandin D2 (PGD2) functions as a neuro-modulator and regulates smooth muscle contraction/ relaxation	0.73	1.66	**0.012**	0.67	1.59	**0.032**
Calponin 1 (CNN1)	Regulation and modulation of smooth muscle contraction	0.68	1.61	**0.015**	0.98	1.98	**0.006**
Cytochrome P450 family 2 subfamily C member 8 (CYP2C8)	A cytochrome P450 encoding gene	−0.83	−1.77	**0.009**	−0.68	−1.60	**0.024**
Musashi RNA binding protein 1 (MSI1)	Musashi RNA binding protein 1 (stem cell progenitor)	−0.08	−1.06	0.760	0.20	1.15	0.374
Neuronal differentiation 1 (NEUROD1)	Neuronal differentiation gene	−0.46	−1.37	0.108	0.12	1.09	0.696
Chromogranin A (CHGA)	Chromogranin A encoding gene	−0.17	−1.13	0.289	0.43	1.34	0.069
Solute carrier family 6 member 4 (SLC6A4)	Serotonin transporter gene	−0.05	−1.04	0.787	−0.67	−1.59	0.056
Somatostatin (SST)	Somatostatin encoding gene	−0.22	−1.16	0.220	0.10	1.07	0.511

HGNC: Hugo Gene Nomenclature Committee, log FC: logarithmic fold change, FC A-B: Fold change after vs. before.

cytokines, stem cells and neurotransmitters in patients with irritable bowel syndrome-diarrhea following fecal microbiota transplantation.
Disclosure: Nothing to disclose

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P1740 ASSOCIATION BETWEEN INTERSTITIAL CELLS OF CAJAL AND ANTI-VINCULIN ANTIBODY IN HUMAN STOMACH

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Introduction: Interstitial cells of Cajal (ICC) are known as the pacemaker cells of gastrointestinal tract that regulate gastrointestinal motility. It was reported that small intestinal bacterial overgrowth induce intestinal dysmotility by decreasing ICC through antibody to vinculin, a cytoskeletal protein in gut, and it can be used as a biomarker for irritable bowel syndrome. However, there are no data on relationship between ICC and anti-vinculin antibody in human stomach. Thus, this study aimed to investigate correlation between levels of circulating anti-vinculin antibody and ICC density in inner muscular layer and myenteric plexus of human stomach.
Aims and Methods: Paraffin-embedded gastric specimens from 46 patients (mean age 65.1 years ± 11, male 78.3%, female 21.7%, Diabetes Mellitus 21.7%), with gastric cancer who received gastric surgery at Kangwon National University Hospital from 2013 to 2017 were used for immunohistochemistry. Each specimen was stained with c-Kit and DOG-1 specific antibodies, then number of positive cells in inner circular muscle, and myenteric plexus were counted. Corresponding patient's blood samples were used to determine the amount of anti-vinculin antibody by enzyme-linked immunosorbent assay (ELISA).
Results: The median concentration of anti-vinculin antibody was 0.12μg/mL (IQR 0.04–0.45), the median number of ICC in inner circular muscle with positive c-Kit stain was 93 per 2.5mm^2 (IQR 54–155), the median number of ICC in myenteric plexus with positive c-Kit was 60 per 2.5mm^2 (IQR 32–89), while the number of ICC in inner circular muscle with positive DOG-1 stain was 161 per 2.5mm^2 (IQR 25–337), and the number of ICC in myenteric plexus with positive DOG-1 stain was 31 per 2.5mm^2 (IQR 7–81). Level of circulating anti-vinculin antibody correlated significantly with density of ICC in myenteric plexus ($p = 0.008$; Spearman correlation). Increased level of circulating anti-vinculin antibodies were significantly associated with reduced number of ICC in myenteric plexus, but not inner circular muscle.
Conclusion: Increased level of circulating anti-vinculin antibody was significantly correlated with decreased density of ICC in myenteric plexus of human stomach, which suggest regulation of ICC expression by anti-vinculin antibody in patients with gastrointestinal dysmotility. Further studies are needed to determine such relationship in functional dyspepsia.
Disclosure: Nothing to disclose

P1741 OVERALL SAFETY AND TOLERABILITY OF RELAMORELIN IN ADULTS WITH DIABETIC GASTROPARESIS: ANALYSIS OF PHASE 2A AND PHASE 2B TRIAL DATA

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Introduction: Relamorelin (RLM) is a pentapeptide ghrelin receptor agonist with prokinetic effects, shown in Phase 2 trials to accelerate gastric emptying significantly and improve symptoms in patients with diabetic gastroparesis (DG). Ghrelin agonists may increase appetite and glycaemia.
Aims and Methods: The aim was to assess overall safety and tolerability of RLM in adults with DG using Phase 2 trial data. Randomised, double-blind, placebo-controlled Phase 2a and 2b trials (NCT01571297, NCT02357420; results published previously) were conducted in DG patients aged 18–75 years over 4 weeks (RLM 10 μg once or twice daily [BID] or placebo BID) and 12 weeks (RLM 10, 30 or 100 μg or placebo BID) with 1- and 2-week, single-blind placebo run-in periods, respectively. Safety assessments included weight, adverse events (AEs) and laboratory tests, including blood glucose and HbA1c. Analysis of covariance on the change from baseline (CFB) values was used post hoc to assess the effect of treatment on HbA1c and glucose; a test for linear trend was also performed. All other data were summarised descriptively.
Results: Among 204 Phase 2a and 393 Phase 2b patients, mean age was 56 years, 64% were female, 90% had Type 2 diabetes and mean (range) body mass index was 32 (18–60) kg/m^2. Proportions of patients with ≥1 treatment-emergent AE (TEAE) were generally similar across treatment groups (Table). TEAEs occurring in ≥5% of RLM-treated patients included headache and dizziness in Phase

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Table 1

TEAE summary	Phase 2a placebo (n = 69)	Phase 2a relamorelin 10 μg QD PM (n = 67)	Phase 2a relamorelin 10 μg BID (n = 68)	Phase 2b placebo (n = 104)	Phase 2b relamorelin 10 μg BID (n = 98)	Phase 2b relamorelin 30 μg BID (n = 109)	Phase 2b relamorelin 100 μg BID (n = 82)
Patients with ≥1 TEAE, n (%)	30 (43.5)	32 (47.8)	25 (36.8)	49 (47.1)	46 (46.9)	63 (57.8)	45 (54.9)
Serious TEAEs, n (%)	2 (2.9)	1 (1.5)	4 (5.9)	8 (7.7)	7 (7.1)	10 (9.2)	6 (7.3)
TEAEs leading to study drug discontinuation, n (%)	2 (2.9)	5 (7.5)	1 (1.5)	3 (2.9)	3 (3.1)	8 (7.3)	9 (11.0)
TEAEs ≥5% in any treatment group, n (%)							
Constipation Diabetes mellitus	4 (5.8)	1 (1.5)	1 (1.5)	3 (2.9)	0 (0.0)	3 (2.8)	0 (0.0)
Diarrhoea Dizziness	2 (2.9)	1 (1.5)	4 (5.9)	0 (0.0)	2 (2.0)	1 (0.9)	3 (3.7)
	2 (2.9)	3 (4.5)	1 (1.5)	0 (0.0)	4 (4.1)	7 (6.4)	6 (7.3)
	4 (5.8)	1 (1.5)	1 (1.5)	1 (1.0)	0 (0.0)	1 (0.9)	5 (6.1)
Headache	2 (2.9)	2 (3.0)	5 (7.4)	3 (2.9)	4 (4.1)	6 (5.5)	2 (2.4)
Hyperglycaemia	1 (1.4)	2 (3.0)	0 (0.0)	2 (1.9)	5 (5.1)	10 (9.2)	10 (12.2)
Increased blood glucose	1 (1.4)	0 (0.0)	1 (1.5)	1 (1.0)	3 (3.1)	4 (3.7)	6 (7.3)
Urinary tract infection	4 (5.8)	2 (3.0)	2 (2.9)	7 (6.7)	7 (7.1)	8 (7.3)	7 (8.5)
Fasting blood glucose, mmol/l, mean (SD) CFB[a]							
Weight, kg, mean (SD) CFB[a]	−0.01 (1.6)	0.20 (1.6)	0.17 (2.0)	0.25 (2.6)	−0.07 (2.7)	0.59 (3.0)	0.46 (2.2)

[a]Study duration was 4 weeks for Phase 2a and 12 weeks for Phase 2b

2a, and hyperglycaemia, urinary tract infection and diarrhoea in Phase 2b. No cardiac TEAEs occurred in ≥2% of any RLM-treated group. In Phase 2b, discontinuations due to TEAEs were higher in RLM-treated patients compared to placebo. Incidence of serious TEAEs was generally similar between treatment groups. No specific serious TEAE was experienced by ≥1 Phase 2a patient; in Phase 2b, impaired gastric emptying was documented in two patients on placebo, one on RLM 30 μg and one on RLM 100 μg, and unstable angina was reported in two patients on RLM 30 μg, all assessed by the investigator as unrelated to study drug. One 100 μg RLM-treated Phase 2b patient died from urosepsis, unrelated to study drug. Treatment-emergent diabetic ketoacidosis (DKA) was experienced by three RLM-treated Phase 2b patients (one in each group), unrelated to study drug. In Phase 2a, one case of DKA occurred during the placebo run-in period (not considered treatment emergent). Over the Phase 2b study, the mean CFB to Week 12 HbA1c levels increased with RLM dose: mean (SD) values were -0.03 (0.86), 0.48 (1.03), 0.92 (1.53) and 0.81 (1.77) for placebo, RLM 10, 30 and 100 μg, respectively (test for linear trend $p < 0.0001$). A dose-related linear trend was also observed for fasting blood glucose ($p = 0.0043$). No clinically relevant changes in weight were observed (Table).
Conclusion: Phase 2 results indicate that RLM 10–100 μg BID is generally safe and well tolerated in adults with DG. Proactive glycaemic management will be incorporated into the planned Phase 3 trial due to increased blood glucose and HbA1c levels observed in RLM-treated patients.
Disclosure: MC (with compensation to his employer) and AL have received research funds to study relamorelin and serve on the Rhythm Pharmaceuticals advisory board. RM has received grants and consulting fees from Rhythm Pharmaceuticals. ST, LK, MM, KB and AI are employees of Allergan plc and own stock and stock options in the company.

P1742 COLD SENSATIONS AND HEARTBURN EVOKED BY ESOPHAGEAL INFUSION OF L-MENTHOL INDICATE EXPRESSION OF THE TRPM8 RECEPTOR IN ESOPHAGEAL C-FIBERS IN HUMANS

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Introduction: The TRPM8 receptor is best known for its responsiveness to cold and menthol, however, TRPM8 was also implicated in amplification of nociceptive sensory signals. Recent studies in animals showed that C-fibers innervating the esophagus express TRPM8. Here we evaluated the translatability of this finding in humans.
Aims and Methods: We hypothesized that the infusion of the TRPM8 activator L-menthol into the esophagus induces cold sensation in healthy subjects and that this sensation is exaggerated in patients with chronic heartburn. We used L-menthol because of its higher potency on TRPM8 compared to R-menthol or racemic mix. L-menthol (3mM), vehicle (0.05% ethanol) or acid (HCl solution, $pH = 1$) was infused (8ml/min) into the esophagus via a transnasal tube with the opening placed 5 cm above the manometrically determined LES. The intensity of sensations was recorded every 2 min. by visual analogue scale (VAS, range 0–10). The subjects were also asked to describe the quality of the sensations. 12 healthy subjects and 27 patients with chronic heartburn (> 6 months, burning sensation behind the sternum with frequency at least one day per week) were enrolled. Each subject received only one esophageal infusion.
Results: Esophageal infusion of L-menthol evoked a cold sensation behind the sternum in 11 of 12 healthy subjects (mild heartburn in the remaining subject). The intensity of sensations was relatively modest, it fully developed during the 10 min. and did not increase further during the rest of infusion. VAS score in healthy subjects at 20 min. was 1.9 ± 0.3 ($N = 12$). Surprisingly, in 11 of 12 patients with chronic heartburn, esophageal infusion of L-menthol evoked typical heartburn (cold sensation in the remaining one). The intensity of heartburn increased gradually during the whole duration of L-menthol infusion and the VAS score at 20 min was 6.0 ± 0.7 ($N = 12$, $P < 0.01$ compared to healthy subjects). Infusion of vehicle failed to evoke similar sensations ($N = 3$). For comparison, in a separate group of patients with chronic heartburn ($N = 12$) the VAS score at 10 min of acid infusion was 7.1 ± 0.8 indicating that the intensity of heartburn evoked by L-menthol is comparable to that evoked by acid infusion.
Conclusion: Cold sensations evoked by esophageal infusion of menthol in healthy subjects indicate the expression of TRPM8 in esophageal sensory nerves. A relatively intense heartburn evoked by menthol in patients with chronic heartburn indicates that TRPM8 is expressed in C-fibers and suggest that the role of TRPM8 in amplification of visceral painful sensations in humans deserves a closer look.
Disclosure: Nothing to disclose

P1743 NEWLY DEVELOPED WIRELESS GASTROSTIMULATOR FOR MINIMALLY INVASIVE GASTRIC STIMULATION: IN VIVO PILOT STUDY

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Introduction: Gastric electrical stimulation (GES) via high-frequency, low-energy pulses can provide an effective treatment for gastroparesis and obesity; however, the current available device requires surgical implantation for long-term stimulation and repeated surgical procedure after a period of time. We aimed to describe and test endoscopic implantation of newly developed wireless gastric electrical stimulator.
Aims and Methods: We developed a novel and miniature wireless gastric electrical stimulator. Endoscopic gastric implantation techniques were implemented on healthy weaner pigs under general anesthesia. We made endoscopic submucosal pocketing and inserted gastrostimulator as previously mentioned. In vivo gastric slow waves were recorded and measured during electrical stimulation. A multi-channel recorder (Acknowledge 4.4, MP150; Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity throughout the study.
Results: Electrogastrogram recordings demonstrated that gastric slow waves became more regular and of constant amplitudes when stomach tissues were stimulated, in comparison with no stimulation. The frequency-to-amplitude ratio also changed significantly with stimulation.
Conclusion: Gastric electrical stimulation is feasible by our endoscopically implanted, wireless GES device. This technique have the potential to increase the utility of GES as a treatment alternative.
Disclosure: Nothing to disclose

P1744 OESOPHAGO-GASTRIC JUNCTION OUTFLOW OBSTRUCTION: OUTCOMES OF 45 PATIENTS FROM A TERTIARY REFERRAL CENTRE

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Introduction: Oesophago-gastric junction outflow obstruction (OGJOO) is characterised by a raised integrated relaxation pressure (IRP) with preserved oesophageal peristalsis. Although in some series OGJOO is being reported more frequently than achalasia, challenges still remain understanding its aetiology, clinical significance, natural history and appropriate therapy.
Aims and Methods: From June 2015 to November 2017, a retrospective analysis of patients undergoing high-resolution manometry (HRM) using 36-channel solid-state catheter (Manoscan 360, Sierra Scientific Instruments) was performed in a tertiary referral centre in London. Patients who fulfilled the diagnostic criteria for OGJOO as per version 3.0 Chicago Classification were included. 10 single water swallows were followed with 5×1cm cubed of bread. Medical files of patients meeting the diagnosis were reviewed to determine patient demographics; clinical history, endoscopic and barium swallow findings as well as therapy and response.
Results: 45 patients were included, 28 females (62%), mean age 56 ± 2 (range 33–83 years). Most patients (84%) reported symptoms of dysphagia and chest pain (Eckardt score >3), while the others complained of heartburn, epigastric pain and/or cough. 18 patients were diagnosed based on single water swallows alone (IRP >15mmHg), 7 based only on solid swallows and 20 on both. 43 patients had Oesophago-Gastro-Doudenoscopy (OGD) recorded, 3 had Endoscopic Ultrasound (EUS) and 25 had Timed Barium Swallow (TBS). 9 patients (21%) had possible explainable aetiology: 2 Schatski ring, 2 peptic stricture, 3 slipped fundoplication, 1 Eosinophilic Oesophagitis and 1 extrinsic compression at the OGJ (seen on EUS). The rest were idiopathic. 12 patients reported regular use of opioids, including morphine, codeine and/or tramadol. Thus far, 12 patients have been treated within the same tertiary institution: 9 had botulinum toxin (botox) injections into the OGJ and 7 had Rigiflex balloon dilation to 30 and/or 35mm (4/7 of who were previously treated with botox with no response). 4 of those who were treated with botox and all patients who underwent Rigiflex dilatation improved significantly when assessed between 3 and 12 months following therapy. The median height of the barium column at 5 minutes prior to treatment was 8.2 cm (IQR = 0;11.4cm) while the median height following treatment was 0cm (IQR = 0;0cm). Overall, mean Eckardt scores for the 12 treated patients dropped from 9 (range 4–12) prior to therapy to 2 (range 0–3) after treatment.
Conclusion: : OGJOO is an increasingly recognised manometry-defined disorder. In patients who are symptomatic with no explainable cause, treating as one would achalasia with botox or Rigiflex dilatation, is associated with excellent clinical response.
Disclosure: None

P1745 OESOPHAGEAL APERISTALSIS IS UNDER INVESTIGATED IN THOSE WITHOUT ACHALASIA OR REFLUX

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Introduction: Oesophageal aperistalsis (OA) is the absence of oesophageal motility with water swallows at high-resolution manometry (HRM). Symptoms include dysphagia, regurgitation, globus, chest pain and heartburn. The main causes are achalasia and acid reflux although in many patients no cause is found. There is no consensus for the investigation of OA without achalasia; this will depend on how common the underlying aetiology is.
Aims and Methods: The objective of this study was to investigate the number of patients with an identifiable cause of OA and to investigate the number of patients in whom the most common aetiologies of OA have been determined.
We examined the reports of all patients who had undergone HRM at Guy's and St. Thomas' NHS Trust from January 2008 to July 2017. 492 patients had OA as per the Chicago Classification 2014; achalasia was defined as an integrated relaxation pressure (IRP) of >15mmHg or IRP 12–15mmHg and a barium swallow or other imaging or a previous myotomy for achalasia was identified. For those without achalasia, Gastroesophageal reflux disease (GORD) was defined according to any pH study off proton pump inhibitors. Patients without GORD or achalasia were classified as non-achalasia, non-reflux aperistalsis (NANRA). Non-achalasia patients without a pH study were excluded (n = 35). The electronic patient record of NANRA patients was then consulted to look specifically for evidence of autoimmune disorders (AD), eosinophilic oesophagitis (EoE) or previous oesophageal surgery.
Results: Among 457 included patients we defined three categories: 183 (40%) had achalasia, 185 (41%) had GORD and 89 (19%) had NANRA.
Of the 89 NANRA patients, 29% had an AD including Systemic Lupus Erythematosus, Scleroderma, Sjögren syndrome and Antisynthetase syndrome (n = 25, M:F 3:7, average age = 48). One had Myotonic Dystrophy (n = 1); 11% (n = 10) had hypersensitive oesophagus; 6% (n = 5) had surgery for atresia, oesophageal spasm, or gastric cancer; 2% (n = 2) had EoE and in 2% (n = 2) of patients AD screen and EoE screen were normal. The remaining 50% of NANRA patients (n = 44) had an unknown cause but incomplete investigations (no screen for AD: 97.7%; no biopsy: 67.4%).
Conclusion: 1. The principal cause of OA is achalasia; it shouldn't be dismissed as a cause even if the IRP is <15mmHg as 6.5% (n = 12) of patients with achalasia and OA had IRP <15mmHg but typical radiological findings.
2. GORD is present in 41% of patients but it is unclear whether it is a cause or effect of OA, therefore the finding of GORD should not stop further investigation.
3. Patients with OA are under investigated for AD and EoE. Incomplete investigations occurred in 50% of patients with NANRA, potentially losing the opportunity to identify other aetiologies. It is unclear whether NANRA patients should be routinely tested for AD or for EoE, or whether this should be done only in selected cases.
Disclosure: Nothing to disclose

P1746 RELATIONSHIP BETWEEN ESOPHAGEAL MOTILITY ABNORMALITIES AND SKIN INVOLVEMENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS: MULTIVARIATE ANALYSIS

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Introduction: Esophageal motility abnormalities (EMAs) are often seen in patients with systemic sclerosis (SSc). Several studies have shown a relationship between EMAs and skin involvements, while other studies have not.
Aims and Methods: The aim of the study was to identify predictive variables for EMAs in patients with SSc. A total of 109 patients with SSc who underwent esophageal high-resolution manometry (HRM) between May 2009 and August 2016 at Gunma University Hospital were enrolled. Esophageal motility was assessed retrospectively according to the Chicago Classification v3.0. HRM and clinical data, including the presence of autoantibodies and skin involvements, were collected. The association between EMAs and skin involvements was evaluated. SSc was divided into two types, diffuse cutaneous SSc (dcSSc) and limited cutaneous SSc (lcSSc), based on the presence or absence of the proximal extent of skin thickness. The severity of skin thickness was assessed by a modified Rodnan total skin thickness score. Chi-square or rank sum tests were used to compare variables between patients with EMAs and those with normal esophageal motility. Variables were categorized as age: <65 or ≥ 65 years, disease duration: <5 or ≥ 5 years and skin score <11 or ≥ 11; and multiple logistic regression analysis was performed. Data was expressed as median values (25%, 75%) unless stated otherwise.
Results: Forty-four patients had normal esophageal motility, eight had esophago-gastric junction outflow obstruction, one had distal esophageal spasm, 27 had ineffective esophageal motility and 29 had absent contractility. Although the prevalence of dcSSc did not differ between patients with EMAs and those with normal esophageal motility (34% vs. 20%, respectively; $p = 0.19$), patients with EMAs had a significantly higher skin score than those with normal esophageal motility [7.0 (4.0, 16.0) vs. 4.0 (2.0, 9.0), respectively; $p < 0.05$, Table]. Other variables such as age, sex, disease duration, and the presence of digital ulcers, Raynaud's phenomenon, or autoantibodies did not differ between patients with EMAs and those with normal esophageal motility. Although a significant predictive variable for EMAs was not found by multiple logistic regression analysis, a high skin score was a significant variable for absent esophageal contractility (Table).
Conclusion: A significant correlation between severe skin thickness and absent contractility was found in patients with SSc. Consequently, if such patients have a high skin thickness score, esophageal motility should be evaluated.

	Normal esophageal motility (n = 44)	Esophageal motility abnormarlity (n = 65)	Odds ratio [95% confidence interval] for absent contractility
Sex (male/female)	6/38	11/65	1.570 [0.582, 4.235]
Age (years)	60 (50, 68)	63 (55, 67)	1.216 [0.326, 4.541]
Disease duration (years)	2 (0, 6)	2 (0, 11)	1.701 [0.566, 5.112]
SKIN INVOLVEMENT			
dcSSc	9/44 (20%)	22/65 (34%)	0.771 [0.145, 4.103]
Raynaud's phenomenon	42/44 (95%)	61/65 (94%)	1.393 [0.134, 14.500]
Digital pitting ulcer or scars	12/44 (27%)	18/65 (28%)	1.082 [0.365, 3.204]
Total skin score	4.0 (2.0, 9.0)	7.0 (4.0, 16.0)	7.203 [1.614, 32.144]
AUTOANTIBODIES			
Anti-nuclear	31/44 (70%)	46/65 (71%)	0.818 [0.213, 3.136]
Anti-centromere	19/44 (43%)	26/65 (40%)	1.334 [0.305, 5.836]
Anti-topoisomerase I	8/44 (18%)	3/64 (33%)	0.837 [0.167, 4.196]
Anti-RNA polymerase III	3/39 (8%)	0/57 (0%)	N/A
Anti-U1-RNP	6/44 (14%)	10/64 (16%)	3.717 [0.805, 17.165]

[Comparison of characteristics between patients with esophageal motility abnormality and those with normal esophageal motility]
Disclosure: Nothing to disclose

P1747 PER ORAL ENDOSCOPIC MYOTOMY IN ESOPHAGEAL MOTILITY DISORDERS: OUTCOMES IN OVER 700 PATIENTS

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Introduction: Per-oral endoscopic myotomy (POEM) has revolutionized the management of esophageal achalasia and other spastic disorders of esophagus. In the absence of large studies with long-term follow-up, the role of POEM remains uncertain for the management of esophageal motility disorders. In this study, we aimed to analyse the safety and efficacy of POEM in a large cohort of patients with esophageal motility disorders.
Aims and Methods: The data of consecutive patients with achalasia and non-achalasia esophageal motility disorders who underwent POEM at a single tertiary care center from January 2013 to March 2018 were analysed. Technical and clinical success, adverse events, and operative time were analysed in all the patients.
Results: Overall, 775 patients (40.37 ± 4.39 years, Males 428) with esophageal motility disorders underwent POEM during the study period. The type of achalasia as per Chicago classification were: type I (219), type II (481), type III (30). 15 patients were classified as non-achalasia spastic motility disorder including Jackhammer esophagus in 4 and diffuse esophageal spasm in 11 patients. Overall, 356 patients had history of prior treatment. Majority of patients (71.35%) underwent anterior POEM. POEM was successfully performed in 98.45% patients. The most common reason for technical failure was submucosal failure (1.16%) followed by excessive extension of mucosal incision (0.4%). Mean operating time was 64.8 ± 31.26 minutes (16–240). Mean length of myotomy on esophageal and gastric side was 8.23 ± 2.91 cm and 3.01 ± .49 cm, respectively. Major adverse events were noticed in 9 patients (1.1%). Post-procedure Eckardt score (6.89 ± 1.52 vs 0.86 ± 0.77) and lower esophageal sphincter pressures (37.45 ± 15.14 vs 13.16 ± 5.61) were significantly lower than prior to the procedure. Clinical success was evident in 92% and 90% at 1 and 2 years, respectively. Long-term clinical success (≥3years) was achieved in 87.6% of patients. Gastroesophageal reflux disease was noticed in 58 patients (40.5%) on 24-hour pH impedance analysis. Clinical symptoms of reflux and erosive esophagitis were found in 22.4% and 18.9% of patients, respectively.
Conclusion: POEM is safe, effective and durable for the treatment of esophageal motility disorders. However, gastroesophageal reflux disease occurs in a substantial number of patients and needs to be considered while considering POEM for the management of achalasia.
Disclosure: Nothing to disclose

P1748 ABNORMAL DISTENSIBILITY ON ESOPHAGEAL ENDOLUMINAL FUNCTIONAL LUMEN IMAGING PROBE (ENDO-FLIP) IDENTIFIES ESOPHAGEAL OUTFLOW OBSTRUCTION AND DIRECTS MANAGEMENT WHEN INTEGRATED RELAXATION PRESSURE (IRP) ON HIGH-RESOLUTION MANOMETRY (HRM) IS NORMAL OR BORDERLINE

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Introduction: An important clinical role for esophageal HRM is to diagnose esophageal outflow obstruction, typically identified when IRP is higher than the upper limit of normal. However, achalasia and esophageal outflow obstruction can manifest with IRP within the threshold of normal, and borderline elevated IRP may not be clinically relevant in some instances. Evaluation of EGJ distensibility and esophageal body contractility with endo-FLIP may refine diagnosis of esophageal outflow obstruction.
Aims and Methods: Our aim was to evaluate the value of endo-FLIP in identifying EGJ outflow obstruction when IRP values are normal or borderline on esophageal HRM. Adult patients undergoing both HRM and endo-FLIP testing at a tertiary care institution were eligible for inclusion. Patients with incomplete HRM or endo-FLIP data were excluded. Patients completed questionnaires defining presenting symptoms. Endo-FLIP was performed using sequential volumetric distension of a compliant balloon placed in the distal esophagus during sedated endoscopy. Primary metrics were distensibility index (DI) from endo-FLIP (≤ 2.8 mm^2/mmHg = abnormal), and IRP from HRM (≥ 15 mmHg = abnormal; 15–20 mmHg = borderline). Chicago Classification 3.0 diagnoses, results from provocative testing during HRM (rapid drink challenge or RDC, multiple rapid swallows or MRS), and esophageal body contractility were additionally assessed. Data was analyzed to assess concordance and discordance between HRM and endo-FLIP assessments of the EGJ, and final diagnoses from each assessment.
Results: Of 85 patients (61.4 ± 1.6 yr, 61.2% F) identified over an 18-month period, 78 presented with dysphagia or suspected esophageal outflow obstruction, and the remainder had unexplained symptoms. Both IRP and DI were abnormal in 25 patients (29.4%); this was true for all patients with achalasia (6 patients). Among patients with a normal IRP, DI was normal in 21/53 (40%), while abnormal (discordant) in 32/53 (60%, p = 0.0007). When IRP was borderline, DI was also abnormal in 9/12 (75%, p = 0.3 compared to normal IRP). In borderline and normal IRP cohorts, esophageal pressurization on provocative testing was seen more often with abnormal DI (69.4% vs. 37.5%, p = 0.02); mean IRP (p = 0.6) and MRS IRP (p = 0.8) were not discriminative between abnormal and normal DI. High GERDQ scores suggesting reflux disease in the normal IRP cohort were associated with normal DI (p = 0.005), but other symptom assessments were not different between abnormal and normal DI cohorts. Of 10 patients with absent contractility and normal IRP, 5 patients (50.0%) had features of achalasia on endo-FLIP with mean DI 1.3 ± 0.4 and mean IRP 6.8 ± 0.6 mmHg, compared to true absent contractility (mean DI 5.4 ± 0.8, p = 0.007, mean IRP 7.6 ± 1.3, p = 0.6). Endo-FLIP findings resulted in a change in management in 67.8% with normal IRP, and in 75% with borderline IRP.

Chicago Classification diagnosis	Distensibility index ≤2.8 mm2/mmHg	Distensibility index >2.8 mm2/mmHg
IRP < 15 mmHg (n = 53)	***n = 32***	***n = 21***
Normal	14/24 (58.3%)	10/24 (41.7%)
Hypermotility (Jackhammer, DES)	7/9 (77.8%)	2/9 (22.2%)
IEM, fragmented peristalsis	6/10 (60.0%)	4/10 (40.0%)
Absent contractility	5/10 (50.0%)	5/10 (50.0%)
IRP 15–20 mmHg (n = 16)	***n = 12****	***n = 4****
Achalasia	2/2 (100%)	0/2
EGJOO	9/12 (75%)	3/12 (25%)
IRP≥20 mmHg (n = 16)	***n = 13***	***n = 3***
Achalasia	4/4 (100%)	0/4
EGJOO	9/12 (75%)	3/12 (25%)

*[*two patients had DES, one each with normal and abnormal DI]*
Conclusion: Endo-FLIP evaluation provides prominent gains over HRM when IRP is normal or borderline in symptomatic patients, with management implications.
Disclosure: Nothing to disclose

P1749 FOOD RHEOLOGY AND NUTRITIONAL ASSESSMENT OF DIET IN ACHALASIC PATIENTS: AN OBSERVATIONAL STUDY

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Introduction: Esophageal Achalasia (EA) is a rare disease of still uncertain etiology, characterized by absence of peristalsis and absence or incomplete relaxation of the Lower Esophageal Sphincter (LES) in response to swallowing. Dysphagia, food regurgitation and chest pain are the main symptoms of the disease with negative impact on the quality of life (QoL) and lead patients to limit food intake with possible nutritional consequences. There are no specific dietetic advices for this kind of dysphagia resulting in self-management.
Aims and Methods: Aims of the study was to evaluate diet, eating habits and nutritional status of achalasic patients, and to assess association, if any, between food rheology and symptoms. Twenty-five achalasic patients (F14, M11, mean age 54 ± 18 yrs) were enrolled in the outpatient office of gastrointestinal Pathophysiology of Policlinico Umberto I, Rome. EA was diagnosed by manometry, 19/25 patients had been previously treated by endoscopic dilatation (n = 13), Heller myotomy (n = 4), both treatments (n = 2), 6/25 patients had not yet undergone any treatment. Clinical data were collected using a symptom and QoL questionnaire, divided in two parts (MD Anderson Dysphagia Inventory and Modular Questionnaire Roma III). Patients filled in a diary for 15 days (a total of 990 meals), where they reported ingested food for each meal and the presence of symptoms according to ESS. Estimated caloric intake and composition of macronutrient were compared to Mediterranean Diet. Patients were classified according to the Eckardt Symptom Score (ESS) considering the ESS value ≥3 as a cut-off to identify the need for (re) treatment.
Results: Seventeen patients (68%) had a ESS≥3 with dysphagia and chest pain as main symptoms, 16 patients (64%) reported no weight loss, 6 (24%) reported weight loss < 5 kg and 3 (12%) reported weight loss ranging from 5 to 10 kg. ESS correlated with disability (r = 0.7; p < 0.05), and was inversely correlated with BMI (r = −0.59; p < 0.05). The mean score of QoL was 19.08 ± 12.94, corresponding to a mild degree of disability perception.
Evaluation of the usual diet in comparison with estimated caloric need showed an intake of 1620 ± 382 vs 2201 ± 546 Kcal and in comparison with the recommended macronutrient assumption the following subdivision: carbohydrates 45.4% ± 5.9 vs 55–59%, protein 20.3% ± 3.9 vs 15–18%, total fat 33% ± 3.8 vs 26–27% and fiber 14.9 ± 4.2 vs 25–30 g. Solid food caused more frequently symptoms than semiliquid and liquid ones: dysphagia (26.2% vs 3.6% vs 1%), chest pain (13.6% vs 2.1% vs 0.3%), regurgitation (7.8% vs 1.8% vs 0.5%).
Spaghetti, pizza and bread were associated with dysphagia in >50% of the meals, dry food and vegetables caused symptoms in ~30% of meals; 40% of patients reported a worsening of symptoms with cold foods, 36% of patient improvement with hot foods. Full meals were achieved by 68% of patients; 32% stopped meals for vomiting, chest pain or regurgitation (64%, 27%, 9%, respectively). The most frequent intervention to overcome symptoms was

drinking (52%), followed by repeated swallowing (21%), waiting (14%), regurgitation (13%).
Conclusion: The results of this observational study suggest that dysphagia and chest pain are main symptoms in achalasic patients even after treatment and they affect mildly the QoL. However, patients conform their diet to avoid symptoms reducing the intake of solid food and food rich in carbohydrates, leading to a hypocaloric and unbalanced diet in favour of fat and protein.
Disclosure: Nothing to disclose

P1750 PYLORIC DISTENSIBILITY MEASUREMENT PREDICTS SYMPTOMATIC RESPONSE TO INTRA-PYLORIC TOXIN BOTULINUM INJECTION

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Introduction: Recent studies reported that pyloric distensibility is altered in 30–50% (1) of gastroparetic patients. Pyloric distensibility has also been shown to correlate with gastric emptying and symptom severity.
Aims and Methods: The aim of the present study was to assess whether pyloric distensibility measurement is predictable of the symptomatic response after intra-pyloric toxin botulinum injection in gastroparesis.
Pyloric distensibility has been measured using the ENDOFLIP® system in 25 consecutive gastroparetic patients before intra-pyloric toxin botulinum injection (Botox, 200 UI). Altered pyloric distensibility was defined as a distensibility below 10 mm^2/mmHg as previously reported (1). Dyspeptic symptoms and quality of life have been prospectively investigated before and 3 months after intra-pyloric toxin botulinum injection. Dyspeptic symptoms (vomiting, nausea, gastric fullness, early satiety, bloating, epigastric pain and regurgitation) have been evaluated using a 5 point likert scale (0 = non symptoms; 4 = most severe symptoms). Total symptomatic score (TSS) was defined as the aggregation of individual symptomatic scores. Quality of life was measured using the GIQLI score ranging from 0 (worst quality of life) to 144 (best quality of life). Gastric emptying was assessed using the C13 octanoic acid breath test.
Results: Using the threshold of 10 mm^2/mmHg, 17/24 patients had altered pyloric distensibility while 8 patients had normal pyloric distensibility. In patients with altered pyloric distensibility, TSS dropped at 3 months from 13.6 to 11.0 ($p = 0.02$), while it remained unchanged in patient with normal pyloric distensibility (from 14.0 to 14.2; $p = 0.77$). Among dyspeptic symptoms, vomiting (from 1.3 to 0.5; $p = 0.03$) and gastric fullness (from 3.3 to 2.4; $p < 0.01$) were the only symptoms to be improved in patients with altered pyloric distensibility, while none of the dyspeptic symptoms were improved in patients with normal pyloric distensibility. GIQLI score improved from 65 to 74 in patients with altered pyloric distensibility ($p = 0.06$) while GIQLI score remained unchanged (from 70 to 70; $p = 0.94$) in patients with normal pyloric distensibility. In patients with altered pyloric distensibility, gastric emptying half time was 249 min before and 222 min 3 months after injection ($p = 0.18$). In patients with normal pyloric distensibility, gastric emptying half time was 227min before and 214 min 3 months after injection ($p = 0.93$). When threshold was set at 9 or 8 mm^2/mmHg, similar findings were observed.
Conclusion: Pyloric distensibility measurement before intra-pyloric toxin botulinum injection predicted symptomatic and quality of life response 3 months after injection in gastroparetic patients.
Disclosure: Nothing to disclose

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P1751 PYLORIC DISTENSIBILITY MEASUREMENT AFTER GASTRIC SURGERY: WHICH SURGERY IS ASSOCIATED WITH PYLOROSPASM?

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Introduction: History of gastric surgery is found in 10% of gastroparesis. A vagal lesion is often suspected to be responsible of pylorospasm, although there was until recently no routine test to diagnose such alteration. Recently, pyloric distensibility measurement using the ENDOFLIP® system showed that pylorospasm was found in 30–50% of gastroparetic patients (1).
Aims and Methods: The aim of the present study was to assess whether pylorospasm, diagnosed using the ENDOFLIP® system is observed in 3 different types of gastric surgeries, namely antireflux surgery, sleeve gastrectomy, and esophagectomy.
Pyloric distensibility and pressure were measured using the ENDOFLIP® system in 43 patients (19 antireflux surgery, 16 sleeve gastrectomy, and 8 esophagectomy) with dyspeptic symptoms after gastric surgery, and in 21 healthy volunteers. All patients had delayed gastric emptying, except in sleeve gastrectomy in the absence of normal values established in asymptomatic controls. Altered pyloric distensibility was defined as distensibility below 10 mm^2/mmHg as previously reported (1).
Results: Different patients groups were not different in demographic characteristics, except for body mass index that was increased in the sleeve gastrectomy group and age that was older in the esophagectomy group. Compared to healthy volunteers (distensibility: 25.2 ± 2.4 mm^2/mmHg; pressure: 9.7 ± 4.4 mmHg), pyloric distensibility was decreased in the antireflux surgery (14.5 ± 3.4 mm^2/mmHg; $p < 0.01$) and esophagectomy (10.8 ± 2.1 mm^2/mmHg; $p < 0.05$) groups, while pyloric pressure was only increased in the antireflux surgery group (18.9 ± 2.2 mmHg; $p < 0.01$). Pyloric distensibility and pressure were similar in healthy volunteers and the sleeve gastrectomy (distensibility: 20.3 ± 3.8 mm^2/mmHg; pressure: 15.8 ± 1.6 mmHg) groups. Altered pyloric distensibility was found in 18% of patients from the sleeve gastrectomy group, 58% ($p < 0.05$) of patients from the antireflux surgery group and 67% ($p < 0.05$) of patients from the esophagectomy group.
Conclusion: Antireflux surgery and esophagectomy are associated with pylorospasm although pylorospasm is not found in all these patients. Sleeve gastrectomy was not associated with altered pyloric distensibility nor altered pyloric pressure.
Disclosure: Nothing to disclose

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P1752 BENEFIT OF SMALL-DOSE ANTIDEPRESSANTS FOR FUNCTIONAL DYSPEPSIA: EXPERIENCE FROM EASTERN CHINA

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Introduction: Traditional treatment of functional dyspepsia (FD) is unsatisfactory, and the potential role of antidepressant medications also hasn't been definitely clarified.
Aims and Methods: This study aimed to evaluated the efficacy and safety of antidepressant medications for management of annoying symptoms of FD. Adult FD patients (identified by Rome III criteria) and not remitted using routine treatments were selected for this study. All patients had undergone appropriate gastrointestinal (GI) diagnostic tests and ruled out organic GI diseases seemed possible explanations for the symptoms. The symptom patterns of included patients were divided into three subtypes at initial visit: postprandial distress syndrome (PDS), epigastric pain syndrome (EPS) or both. Patients were treated with different antidepressant agents and dosage according to individual illness features. An established 4-point Likert-type scale was used to measure the response of antidepressant therapy at follow-up according to the clinical records. Patient demographics, clinical symptoms, medication history, GI diagnostic tests, and antidepressant therapy were collected. Antidepressant treatment data extracted contained the type and dose used, treatment response, and self-reported adherence.
Results: Among the total patients ($n = 1524$) referred to this specialist clinic because of refractory GI symptoms or asked for physical examination, 9.4% ($n = 144$) met the inclusion criteria for study cohort. Fourteen patients were subsequently excluded for failure to return after initiation of antidepressant therapy and 130 cases were left for analysis. The mean patient age was 50.5 years over a range of 18–83 years, and 88 patients (67.7%) were female. Thirty-eight patients (29.2%) had EPS, 64 (49.2%) had PDS, and the remaining 28 (21.6%) complained of both EPS and PDS. The mean duration of GI symptoms prior to initial evaluation was 3.8 years. Thirty-three subjects (25.4%) of all had been treated with only one antidepressant; 91 (70%) were treated with two, and 6 (4.6%) had changed medication consecutively. Antidepressant agents, in descending order of frequency were: fluoxetine, flupenthixol melitracen, sulpiride, paroxetine, citalopram, mirtazapine, sertraline, duloxetine, amitriptyline, and venlafaxine. Following initiation of antidepressants, symptom improvement was attained in 122 patients (93.8%) at some time in follow-up: remission of symptoms (score = 3) occurred in 71 patients (54.6%), and the average time to obtain remission was 3.4 months; moderate improvement (score = 2) was obtained in 33 patients (26.2%). No significant difference was detected in remission rate in relation to symptom pattern and no antidepressant regimen was significantly different for management of three FD types. Complete symptom remission occurred in 46.9% of subjects with PDS vs. 57.9% for subjects with EPS and 67.9% with both. When subjects with symptom remission were compared with the reminder, young patients ($P = 0.065$) tended to lead a poor outcome. Furthermore, when given sulpiride or fluoxetine, patients with younger age were associated with a poor outcome ($P = 0.001$ and $P = 0.005$, respectively).

However, there was no any association between gender, FD subgroups, or dyspepsia duration and response to antidepressants.
Conclusion: Low dose of antidepressant medications achieved a high response rate in FD patients, especially for older patients. Symptom remission was not related to symptom patterns or antidepressant regimens.
Disclosure: Nothing to disclose

P1753 INVESTIGATION OF AUTOIMMUNE GASTRITIS DIAGNOSED BY ENDOSCOPIC FINDINGS

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Introduction: Endoscopic features of autoimmune gastritis (AIG) are based on severe spread of atrophic gastritis in the stomach body. The endoscopic findings are different from those of atrophic gastritis associated with *H.pylori*, which is frequently found in Japan. Diagnosis of AIG is meaningful clinically because AIG can complicate autoimmune polyendocrine syndrome (APS) and can cause anemia and gastric tumor.
Aims and Methods: We investigated the significance of endoscopic findings as a lead for AIG diagnosis. Thirty-nine cases with appreciatively severe atrophic gastritis in the stomach body on endoscopic examination between January 2009 and March 2018 were studied. Gender, laboratory data (serum gastrin, parietal cell antibody (PCA), intrinsic factor antibody (IFA), pepsinogen (PG) I and II, Hb, Vit.B12, Fe), complications, *H.pylori* infection, and reason for endoscopic examination were evaluated as retrospective cohort study.
Results: We defined patients who satisfied all these criteria — severe atrophic gastritis in the stomach body, hypergastrinemia (>200pg/ml), positive reaction of PCA and/or IFA, low level of serum PG-I (<40mg/ml) — as "AIG fix". All except "AIG fix" were defined as "AIG suspect (sus)". "AIG fix" were 17 patients (43.6%). Males in "AIG fix" were 17.6%. Mean serum gastrin, PG-I, and PG-II were 3184 ± 1986pg/ml, 6.6 ± 4.5mg/ml, and 8.2 ± 2.4mg/ml. PCA- and IFA-positive rates were 88.2% and 35.3%. Low serum Vit.B12 and Fe levels were 64.7% and 29.4%, respectively, in this group. Five patients (29.4%) were complicated by some autoimmune diseases. Five patients (29.4%) were complicated by NET (Neuroendocrine tumor). Two patients (11.8%) were complicated by gastric cancer. *H.pylori*-positive by urea breath test were 3 patients (17.6%). Among "AIG sus" several patients with autoimmune disease and pernicious anemia were included.
Conclusion: It was suggested that correct diagnosis of atrophic gastritis predominating in the stomach body differing from *H.pylori*-related gastritis may be the first step in the diagnosis of AIG. However, many cases were not examined even if findings were correct. Dissemination of the diagnostic significance of AIG will be needed in the future.
Disclosure: Nothing to disclose

P1754 COMPARATIVE STUDY BETWEEN ROME III AND IV DIAGNOSTIC CRITERIA AMONG COLLEGE STUDENTS' FUNCTIONAL GASTROINTESTINAL DISORDERS EPIDEMIOLOGICAL INVESTIGATION IN CHINA

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Introduction: FGIDs are common and important disorders of the digestive system and have a worldwide distribution. Its incidence in the general population is approximately 36.1%. Rome IV criteria published in 2016 redefines FGIDs as brain-intestinal interactions, varying from a single gastrointestinal motility abnormality to neuro-gastroenterology and brain-intestinal interactions abnormality. Compared with Rome III, Rome IV has a more stringent and precise definition of FGIDs. For example, Rome IV revised frequency threshold and the nature of IBS symptoms. Rome IV adjusted and refined diagnostic criteria might impact the clinical diagnosis of FGIDs. Therefore, on the basis of the previous survey performed by our research team regarding FGIDs epidemiological investigation in students from the colleges in Zhejiang province, we compared the two criteria regarding FGIDs diagnosis, to explore the difference between the two criteria and evaluate the value, if present, in the clinical FGIDs diagnosis using Rome IV criteria.
Aims and Methods: This research was aimed at investigating the differences and the similarities between Rome III and IV diagnostic criteria in the diagnosis of Functional Gastrointestinal Disorders (FGIDs) among college students in China. According to FGIDs database of college students in Zhejiang Province established by our previous research team, further epidemiological analysis and comparisons were made using Rome IV and Rome III criteria.
Results: Among 1870 students' database information, 54.81% FGIDs met Rome IV criteria and 59.41% FGIDs met Rome III criteria. Rome IV-positive students showed a higher scoring of obsessive-compulsive, depressive and anxiety. In Rome IV group, belching disorders, irritable bowel syndrome (IBS), functional abdominal bloating/distension (FAB/D) and postprandial distress syndrome (PDS) detection rates were lower than that of Rome III group. In Rome IV group, functional diarrhea (FDr) and epigastric pain syndrome (EPS) detection rates were higher than in Rome III group. Some of the original PDS patients (11 cases, 11.11%) were included in the EPS, some of the original IBS patients (43 cases, 33.33%) were included in the FDr, and 12 cases (9.30%) of the original IBS patients were included in FC according to Rome IV criteria. A significant difference was observed in the distribution of different subtypes (PDS, EPS) of FD between two criteria ($\chi^2 = 25.63$, $P < 0.01$).
Conclusion: Rome IV criteria has more strict and accurate FGIDs definition, allowing a more accurate identification of the disease and those patients who really need treatment, resulting in a more efficient and feasible application in clinical practice and scientific research.
Disclosure: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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P1755 NORMAL MEAN NOCTURNAL BASELINE IMPEDANCE (MNBI) MAY DEFINE FUNCTIONAL HEARTBURN BETTER THAN ACID-BASED METRICS ON PH-IMPEDANCE MONITORING

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Introduction: Acid exposure time (AET) and reflux-symptom association (RSA) on pH-impedance monitoring can stratify esophageal syndromes into nonerosive reflux disease (NERD), and functional esophageal disorders (FED), including reflux hypersensitivity (RH, normal AET with positive RSA) and functional heartburn (FH, normal AET and negative RSA). Low mean nocturnal baseline impedance (MNBI) is now a recognized marker of impaired mucosal integrity that can predict therapeutic outcome from antireflux therapy. We hypothesized that MNBI could differentiate between NERD and FED, particularly FH.
Aims and Methods: Our aim was to evaluate the discriminative value of MNBI within FED categories, both conventional (diagnosed off PPI) and overlap (diagnosed on PPI therapy), compared to conventional NERD (diagnosed off PPI). Adult patients undergoing pH-impedance testing at two tertiary academic centers were approached for enrollment in this prospective study. Patients with proven GERD were tested on PPI therapy, while those with unproven GERD were tested off PPI for 7–10 days. Patients completed questionnaires defining symptoms (Reflux Diagnostic Questionnaire, RDQ), affective state (Hospital Anxiety and Depression Scale, HADS; Visceral Sensitivity Index, VSI), and functional diagnoses (irritable bowel syndrome, IBS; functional dyspepsia, FD on ROME diagnostic questionnaire). Patients with incomplete symptom data were excluded. Based on AET and RSA, FED patients were designated RH and FH, and were compared to NERD (AET > 6% off PPI therapy). MNBI was calculated by averaging baseline impedance from 3 stable 10-minute periods (1AM, 2AM, 3AM) at the 5 cm impedance channel, low if < 2292 ohms. Data were analyzed to assess differences between FED categories segregated by MNBI thresholds, and NERD.
Results: Of 93 patients (51.8 ± 1.5 yr, 74.2% F), 26 had NERD, and 67 had FED (RH = 15, FH = 52) based on ROME IV definitions. Within FED, proportion of acidic reflux episodes were higher off PPI, compared to proportion of weakly acidic reflux episodes ($p < 0.001$ for each comparison). Symptom burden, HADS, VSI and proportions of IBS and FD were similar between RH and FH, both within conventional and overlap subgroups. When MNBI was available (n = 45), FED could be subdivided into two categories using a threshold of 2292 ohms. Within RH, numbers were too small to make meaningful comparisons. Within FH, when MNBI was normal, symptom burden, depression and anxiety scores were higher compared to FED with low MNBI ($p \leq 0.04$ for each comparison). Proportions with FD were numerically higher in FH with normal MNBI ($p = 0.08$ across groups); proportions with IBS were similar. In particular, 30% with normal MNBI FH had evidence of depression on HADS compared to none with low MNBI FH ($p = 0.002$).

	FH with normal MNBI	FH with low MNBI	NERD
RDQ score	81.6 ± 8.1	59.5 ± 17.4	61.6 ± 7.7
Acid exposure time	0.6 ± 0.2*	0.9 ± 0.3*	10.9 ± 1.5
Acid reflux episodes	7.4 ± 1.4*	8.1 ± 2.1*	34.6 ± 5.8
All reflux episodes	45.3 ± 4.9	33.5 ± 4.4	53.7 ± 9.8
Mean MNBI (ohms)	3178 ± 167.4*	1443 ± 134.2*†	927.7 ± 124.2
HADS depression score	5.0 ± 0.8	1.8 ± 0.5*†	4.6 ± 0.7
HADS anxiety score	8.7 ± 0.9	5.5 ± 1.1†	7.4 ± 0.8
VSI	54.7 ± 4.5	65.8 ± 6.2	65.1 ± 4.1

*[*p≤0.05 compared to NERD; †p≤0.05 compared to FH normal MNBI]*

Conclusion: Within the ROME IV FH category, heartburn with normal MNBI defines a subgroup with higher symptom burden, and higher anxiety and depression scores despite similar metrics on pH-impedance monitoring. Our findings suggest that normal MNBI may augment diagnosis of FH by identifying absence of reflux induced mucosal injury. Further research using normal MNBI values in defining FH is warranted.

Disclosure: Nothing to disclose

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P1756 IMPROVEMENT OF MEAL-RELATED SYMPTOMS AND EPIGASTRIC PAIN IN PATIENTS WITH FUNCTIONAL DYSPEPSIA TREATED WITH ACOTIAMIDE WAS ASSOCIATED WITH ACYLATED GHRELIN LEVELS IN JAPAN

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Introduction: Recent years, functional dyspepsia is treated by two major categories of drugs; acid inhibitors such as H_2-receptor antagonists and proton pump inhibitors (PPIs), and prokinetic drugs that accelerate disturbed GI motility by modifying altered visceral sensitivity. Although PPIs are widely used as the initial treatment of choice in patients with epigastric pain, several randomized controlled studies have suggested that the efficacy of PPI therapy for FD is limited and may be confined to FD patients with co-existing EPS. Acotiamide may act directly on the gut and also indirectly through the brain-gut axis via actions in the central nervous system. Thus, it may be difficult to improve both PDS and EPS symptoms by using a single-agent therapy because of the complexity of FD. The aim of this study is to clarify whether acotiamide and rabeprazole combination therapy can improve clinical symptoms, gastric emptying and satisfaction with treatment in FD patients more effectively than acotiamide or rabeprazole monotherapy alone. We also aimed to determine whether acotiamide affects these changes via its effect on gastric emptying and appetite-related hormones such as ghrelin and leptin, and on the hypothalamic-pituitary-adrenal (HPA) axis.

Aims and Methods: We used Rome III criteria to evaluate upper abdominal symptoms, and anxiety by the State-Trait Anxiety Inventory. Gastric motility was evaluated by the ^{13}C-acetate breath test. Eighty-one FD patients were treated with acotiamide (300mg/day) (n = 35), acotiamide (300mg/day) and rabeprazole (10mg/day) (n = 28), or rabeprazole (10mg/day) (n = 18) for a period of 4 weeks and evaluated after 4 weeks of no treatment. ACTH, cortisol, leptin and ghrelin levels were measured in all FD patients.

Results: Acotiamide and rabeprazole combination therapy significantly improved PDS-like symptoms (postprandial fullness, p = 0.018; abdominal fullness, p = 0.04; early satiety, p = 0.041), epigastric pain (p = 0.024) and STAI-state scores (p = 0.04), compared to rabeprazole monotherapy. Both acotiamide monotherapy, and acotiamide taken in combination with rabeprazole, significantly (p = 0.001 and p = 0.02, respectively) improved satisfaction with treatment, compared to rabeprazole monotherapy. Acotiamide and rabeprazole combination therapy had no significant effect on ACTH or cortisol levels in FD patients. Of interest, acotiamide monotherapy, and acotiamide and rabeprazole combination therapy, significantly ($p < 0.0001$ and p = 0.018, respectively) increased acylated ghrelin/total ghrelin ratios and significantly (p = 0.04) improved impaired gastric emptying compared to rabeprazole monotherapy.

Conclusion: Further studies are warranted to clarify how acotiamide treatment improves clinical symptoms in FD patients.

Disclosure: Nothing to disclose

P1757 ASSESMENT OF THIOL/DISUPHIDE HOMEOSTASIS IN PATIENTS WITH AUTOIMMUNE GASTRITIS

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Introduction: Autoimmune gastritis (AIG) is an organ-specific autoimmune and inflammatory disorder. It is characterized by reduction and loss of parietal cells and formation of autoantibodies against H^+/K^+-ATPase and intrinsic factor. Oxidant radicals increase secondary to inflammation in autoimmune and autoinflammatory disorders. The increase in reactive oxygen species can react with cellular macromolecules and causes in lipid peroxidation, nucleic acid damages and protein modifications. Thiols are functional sulfhydryl groups and consist of a sulfur atom and a hydrogen atom bound to a carbon atom and capable of reacting with free radicals in order to provide protection against tissue damage caused by reactive oxygen products. Thiol groups of proteins are oxidized by oxygen molecules and are reversibly converted to disulfide bonds. These disulfide bonds can be reduced to thiol groups in a condition of decreased oxidative stress. In case of oxidative stress, thiols form a number of products as a result of oxidative stress. These formed disulfide bonds can again be reduced to thiol groups, and therefore thiol-disulfide homeostasis is maintained. An abnormality in this homeostasis process may result in a variety of disorders. Since AIG is an autoimmune and inflammatory disorder, abnormal thiol/disulfide homeostasis may have a role in the pathogenesis of this condition.

Aims and Methods: Direct measurement of thiol-disulfide levels with a novel and automated method is already available. Therefore, the aim of this study was to investigate dynamic thiol/dislfide homeostasis in patients with AIG and identify possible factors associated with this oxidation. Also to determine whether thiol oxidation may have a role in the gastric emptying time in patients with AIG. Forty-nine patients with AIG and 52 healthy volunteers were enrolled in the study. Venous blood samples were collected from the subjects after overnight fasting. Serum samples were separated and stored at -80°C. Serum thiol-disulfide homeostasis was determined with a colorimetric method recently developed developed by Erel and Neselioglu (1). Native thiol and total thiol were measured directly, and disulfide level, disulfide/total thiol ratio, disulfide/native thiol ratio were obtained with calculation.

Results: Mean native thiol (330.65 ± 33.437 mmol/L *vs* 369.71 ± 21.73 mmol/L, P = 0.001) and native thiol/total thiol ratio total thiol levels (90.61 ± 98 vs 95.1 ± 26.7%, P < 0.001) were determined lower in AIG patients, compared to the control group. Mean disulphide level (21.47 ± 4.0 mmol/L *vs* 16.73 ± 2.4 mmol/L,respectively; P = 0.007), and disulphide/native thiol (5.1 ± 1.1 ± 1.2% *vs* 4.0 ± 1.2%, respectively, P < 0.001) were determined higher in AIG patients compared to the control group.

Conclusion: In this study, thiol/disulphide balance was shown to shift towards disulphide form in AIG patients, compared to the control group. According to these results, weakened thiol/disulphide equilibrium in AIG patients was thought to be associated with autoimmunity and inflammation. Determination of abnormal thiol/disulfide homeostasis in patients with AIG suggested that abnormal thiol/disulfide homeostasis may be related to the pathogenesis of AIG.

Disclosure: Nothing to disclose

Reference

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P1758 GASTRIC PH *IN VIVO* INFLUENCES LEVOTHYROXINE SODIUM TABLET REQUIREMENT IN HYPOTHYROID PATIENTS

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Introduction: In vitro studies have highlighted that the dissolution of levothyroxine sodium tablet (LT4) is inversely correlated to pH increase. An increased dose of LT4 is needed to reach therapeutic target of serum TSH in different gastric hypochlorhydric conditions as *Helicobacter pylori* infection, chronic autoimmune gastritis and chronic Proton pump inhibitors treatment. At present, a correlation between intragastric pH and required therapeutic LT4 dose is lacking.

Aims and Methods: The aim of our study was to determine *in vivo* a correlation between the pH of gastric juice and the effective dose of LT4 needed to restore euthyroidism.

Sixty-one dyspeptic hypothyroid patients (9M/52F; median age 51yrs range 26–73y) treated with LT4 were enrolled in this prospective study. In this cohort, 32 patients that required an excess of LT4 individually- tailored dose to normalize serum TSH value were screened for extraintestinal (drugs and food) and/or

gastrointestinal non-acid-related causes (celiac disease, Crohn disease, lactose intolerance, SIBO, gastric surgery) of LT4 malabsorption. All patients underwent gastroscopy with sampling of gastric acid secretion and multiple gastric biopsies to assess Sydney System-related gastritis patterns. Chronic atrophic gastritis (GCA) was defined as the presence of oxyntic glandular atrophy in fundus and corpus, pangastritis (PNG) when the active and chronic inflammation involved both the antrum and corpus, antritis (A) when inflammation was limited to the antral region. pH and [H^+] concentrations in gastric juice samples were measured by direct NaOH titration. According to the in vitro study by Pabla et al. (1), gastric pH value >2.4 was used as a cut off of established decrease of LT4 percentage dissolution in the stomach. Data are expressed as median (IQR range) and $p < 0.05$ considered statistically significant.
Results: In patients with gastric pH values ≤ 2.4, the median value of excess drug dose (+14%, IQR = 0–19) was significantly lower than that in patients with pH values >2.4 (+50%, IQR = 33–63) ($p < 0.0001$). Only 7/34 (20.6%) patients with pH values ≤ 2.4 required an excess drug dose compared with 25/27 (92.6%) patients with pH values > 2.4 ($p < 0.0001$). The increase in LT4 dose needed was differently distributed according to gastritis patterns. Indeed, 90.5% GCA patients (19/21) required an increased LT4 dose compared with 75% PNG (6/8) patients and only 22% with A or without histological alterations (7/32) (GCA vs A $p < 0.0001$, PNG vs A $p < 0.05$); these differences were strictly depended on pH value in relation to gastritis pattern (GCA median pH 6.6, IQR = 6–7.1; PNG median pH 3.1, IQR = 1.85–6.8; A or no histological alterations median pH 1.5; IQR = 1.3–1.9) (GCA vs A $p < 0.0001$, PNG vs A $p < 0.05$). The required therapeutic dose of LT4 was directly correlated with intragastric pH ($r^2 = 0.4850$; $p < 0.0001$) and inversely with gastric juice H^+ concentration ($r^2 = 0.4618$; $p < 0.0001$). Multivariate analysis including anthropometric characteristics (BMI, age, gender) of the patients revealed that gastric pH acts as independent variable in determining the dose of LT4 ($p = 0.029$).
Conclusion: *In vivo*, intragastric pH and gastritis patterns influence the required therapeutic dose of LT4. Therefore, in clinical practice, dyspeptic hypothyroid patients that need an increased LT4 dose to restore euthyroidism should be screened for any condition that impairs gastric acid secretion. The knowledge of gastritis patterns could speed up the tailoring of individual daily LT4 dose.
Disclosure: Nothing to disclose

Reference

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P1759 QUANTITATIVE PCR AS A NOVEL APPROACH TO DETERMINE INFLUENCE OF DENSITY OF BACTERIAL COLONISATION ON HEALTH AND DISEASE

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Introduction: There is increasing evidence that small intestinal bacterial overgrowth (SIBO) plays a role for the manifestation of a variety of gastrointestinal (GI) and non-GI diseases. While breath tests measuring H_2 and methane (CH_4) after ingestion of a glucose test meal are widely used to diagnose SIBO but they lack sensitivity and specificity, and are time-consuming.
Aims and Methods: To determine the mucosa-associated bacterial density in mucosal biopsies collected from the second part of duodenum. The patient groups were: i) "asymptomatic": referred for diagnostic work-up of a positive faecal occult blood test (FOBT) and/or iron deficiency anaemia (IDA) but with normal endoscopic findings; ii) patients with functional gastrointestinal disorders (FGIDs) and; iii) patients with inflammatory bowel disease (IBD). We also assessed the influence of smoking and proton pump inhibitor (PPI) intake on the bacterial densities. Biopsies were collected from 283 patients (170 female, mean age 50.5, range 17 to 78 yrs). Of these 70/283 were "asymptomatic", 94/283 with FGIDs of whom, 69 functional dyspepsia/Irritable bowel syndrome (FD/IBS) overlap, 22 FD only, 2 IBS only; 111/283 with IBD (69 UC and 42 CD); and 9/283 patients with other organic disease (OD) such as GERD. Data on demographic characteristics, type and severity of GI symptoms, psychological comorbidities and medications were assessed. During endoscopy, mucosal samples were collected utilising the Brisbane Aseptic Biopsy Forceps (MTW, Germany) to avoid the luminal and working channel contamination of tissue, and total DNA was extracted. In 98 randomly selected subjects, additional biopsies were taken with standard biopsy forceps, to allow for comparison between biopsy collection methods. Bacterial density was assessed and normalised to human DNA in each sample by qPCR, using bacteria-domain 16S rRNA gene-specific primers, and primers targeting the human beta-actin gene.
Results: Utilising the aspetically obtained biopsies, overall bacterial densities were significantly higher in patients with FGIDs (0.20 ± 0.49) compared to the controls (0.09 ± 0.29 $p < 0.02$). Bacterial density was significantly greater in patients using PPI (0.26 ± 0.61) compared to those without PPI use (0.05 ± 0.12; $P < 0.01$). However, the increased bacterial density in FGID patients compared to the asymptomatic control group was maintained, even if those patients using PPI in both groups were excluded. The bacterial densities on duodenal tissue from both UC (0.01 ± 0.02) and CD (0.02 ± 0.03) patients were significantly less relative to both FGID and the asymptomatic control group ($p < 0.05$). Smoking did not influence bacterial density ($p > 0.4$). Results from samples taken with standard biopsy forceps (and thus susceptible to cross-contamination) were only poorly correlated with the results produced from matched samples obtained with the aseptic biopsy device ($r < 0.1$; $p > 0.6$).
Conclusion: Bacterial density on duodenal tissue collected from FGID patients was significantly greater in comparison to asymptomatic controls, while the duodenal bacterial density in IBD patients was lowest of the three patient cohorts. In addition, PPI use appears to result in an increase in the bacterial density on duodenal tissue, irrespective of patient diagnosis. Measurement of both bacterial density and diversity on duodenal tissue are warranted to improve our understanding of the pathophysiology of digestive diseases and to identify patients that will respond positively to microbe-directed therapies.
Disclosure: Nothing to disclose

P1760 STW 5 IS EFFECTIVE IN 10 FUNCTIONAL DYSPEPSIA SYMPTOMS

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Introduction: Functional dyspepsia (FD) is one of the most prevalent GI diseases. It involves epigastric pain or burning, fullness and early satiety in the absence of organic systemic or metabolic diseases and it frequently overlaps with other upper gastrointestinal (UGI) symptoms (Stanghellini 2016). It recognizes a multifactorial pathohysiology and no single therapy has been shown to control all typical and overlapping symptoms.
STW 5 is a fixed herbal multicomponent preparation, that is indicated in FD with proven efficacy is several randomized controlled clinical trials (RCTs) and more than 5 decades of clinical experience.
The preparation was shown to beneficially affect different pharmacological targets associated with the pathogenesis of FD and hence is believed to improve a broad spectrum of symptoms displayed by FD patients. However, its efficacy on single symptoms was not clinically investigated until now. The current study closes this gap, as the available RCTs were specifically analyzed to investigate STW 5's effects on individual FD symptoms.
Aims and Methods: Data from previously conducted RCTs were pooled for the analysis. Of the 25 studies screened for eligibility, 6 were included [Madisch 2014; Caspary 2006; Malfertheiner 2003; Rösch 2000; Goebell 2000; Melderis 1994] which met the following: 1) 10 UGI symptoms assessed on a five-point Likert scale by the validated GIS sum score [Adam 2005], 2) Assessments of GIS items at baseline and after 28 days of treatment, 3) dosage used was 3x20 drops per day, 4) adult FD patients were included.
Results: Overall 637 patients were treated in 6 studies (STW 5: 351, placebo: 286). The full analysis set comprised 618 patients (STW 5: 346, placebo: 272). The STW 5 and placebo groups were comparable with regard to baseline characteristics, disease history, mean patient age, weight and gender distribution. Mean baseline GIS sum score was 11.8 (±4.1 SD, range: 1 to 27). Overall there were no structural differences between treatment groups with respect to baseline characteristics and length of treatment.
The mean improvement of GIS sum score from baseline observed after 28 days of treatment was 7.1 points for STW 5 and 4.9 points for placebo. The ANCOVA results (adjusted for baseline score) showed a statistically significant difference of 2.07 points between the treatments regarding improvement of GIS sum score in favor of STW 5 (95%-CI: 1.37, 2.76; $p < 0.0001$). Furthermore, the improvement of mean score for the single items comprising the GIS was consistently and significantly in favor of STW 5 for every single item.
Conclusion: In conclusion, the analysis stresses the clinically proven efficacy of STW 5 and shows that the preparation significantly improves every single FD symptom assessed in the GIS score. Theses study results substantiate STW 5's multitarget activity and ascertains its suitability for all subtypes of FD.
Disclosure: SR: Employee of Steigerwald Arzneimiittelwerk GmbH MW: None VS: None

P1761 ROUTINE OESOPHAGEAL BIOPSIES IN THE INVESTIGATION OF DYSPHAGIA: ARE THEY COST EFFECTIVE?

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Introduction: Eosinophilic oesophagitis (EO) is a chronic immunogenic-antigen mediated disease of the oesophagus, histologically defined by over 15 eosinophil counts seen in a high-power microscopic field, without gastro-oesophageal reflux disease. It causes symptoms including dysphagia, regurgitation and food bolus impaction. Oesophageal biopsies are necessary to diagnose EO. We evaluated the results of routine oesophageal biopsies to investigate patients with dysphagia.
Aims and Methods: We studied the endoscopy records and oesophageal biopsy results of 160 consecutive patients who were referred with a new diagnosis of dysphagia to the endoscopy departments of East Sussex Healthcare NHS Trust, over a 3 month period. Data collection sources included the EndoBase reporting tool and patient case notes.
Results: 23 of the 160 patients had a diagnosis at endoscopy of oesophageal cancer or Barrett's oesophagus. These did not have routine biopsies taken for assessment of EO and were excluded from analysis. Of the remaining 137 patients who had biopsies taken at different levels in the oesophagus to screen for EO, 5 were consistent with a diagnosis of EO, representing 3.6% of patients. 61.3% were normal and 35.1% showed changes of reflux related inflammation. The case notes of the patients with EO were reviewed. All revealed a history of either food bolus impaction or repeated episodes of dysphagia. Two patients had a history or family history of asthma and eczema.
Conclusion: In this series 5 of 137 patients with symptoms of dysphagia were diagnosed with EO. The cost of biopsies at two different levels in the oesophagus was £46.68 per patient. £1279 was spent to diagnose one case of EO.
A selective strategy for taking oesophageal biopsies to diagnose EO would be more cost effective. This needs evaluation but restricting biopsies to those with a history of episodic food bolus obstruction, a family or past history of asthma or atopy and endoscopic signs such as mucosal furrowing and prominent concentric rings merits further assessment.
Disclosure: Nothing to disclose

P1762 VARIATION IN THE INVESTIGATION AND DIAGNOSIS OF EOSINOPHILIC OESOPHAGITIS IN DAILY CLINICAL PRACTICE

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Introduction: Eosinophilic oesophagitis (EoE) is a recognised cause of dysphagia, with an estimated annual incidence of 6–13 cases/100,000 persons. Diagnosis can only be definitively established by endoscopic biopsy and as such, societal guidelines advocate the acquisition of six non-targeted oesophageal biopsies.
In this study, we aim to determine whether these recommendations are adhered to in routine clinical practice, and whether this practice is influenced by scope operator, patient age and referral pathway.
Aims and Methods: We performed a retrospective database review of all OGDs performed to investigate dysphagia or food bolus obstruction between 1st July 2016–31st June 2017, within three tertiary referral centres serving a total population of approximately 3.2 million people. We collected information on age, gender, endoscopy operator, referral pathway, endoscopic features and diagnosis, number of biopsies taken and histopathological diagnosis. Statistical comparisons were made using the Fisher's exact test or Chi-square test with Yates' correction to calculate odds ratios and evaluate their significance.
Results: During this time period a total of 4056 (15.9% of total) OGDs were performed as part of the investigation of dysphagia. Following exclusion criteria, 3712 (91.5%) OGDs remained eligible for our analysis. An endoscopic diagnosis for the cause of dysphagia was made in approximately one-third of cases (n = 1286; malignancy 5.1%, oesophagitis 15.7%, benign stricture 8.4%, candidiasis 2.9%, achalasia 1.1% and other 0.2%). In the remaining 2468 cases (66.5%) normal endoscopic appearances were described. Biopsies to exclude EOE were taken in 923 (37.4%) of these cases. The recommended 6 (or more) biopsies were received by histopathology in only 87 cases (9.43%).
When specifically comparing gastroenterologists to surgeons (total of 2193 normal endoscopies), we noted that gastroenterologists were 5.6 times more likely to obtain biopsies than surgeons (46.7% vs 13.6%, $p < 0.0001$, Table 1). In cases where biopsies were in fact taken, gastroenterologists were 8.6 times more likely than surgeons to obtain the recommended 6 or more biopsies (10.7% vs 1.4%, $p < 0.01$, Table 1). They were also 4.7 times more likely to consider a diagnosis of EOE at the time of endoscopy. Overall, in the 12-month period, 83 histologically confirmed cases of EOE were diagnosed of which 79 (95.2%) were made by gastroenterologists. The mean age of EOE cases was 46.2 years (range 21–85; 32.5% age > 50 years) with a M:F ratio of 2:1.

Normal Endoscopies	Total (n = 2193)	Gastroenterologists (n = 1648)	Surgeons (n = 545)	Comparison between groups
Endoscopies with biopsies taken (% of normal endoscopies)	843 (38.4%)	769 (46.7%)	74 (13.6%)	$p < 0.0001$
Endoscopies with 6 or more biopsies taken (% of endoscopies with biopsies taken)	83 (9.8%)	82 (10.7%)	1 (1.4%)	$p < 0.01$

[Table 1. Comparison of practice between gastroenterologists and surgeons]
When patient age was considered, we observed that biopsy acquisition was more than twice as likely in patients younger than 50 years old compared to older patients (52.4% vs 33.2%, $p < 0.0001$). Interestingly, we also observed that EOE was over three times more commonly diagnosed in patients referred routinely compared to those under urgent referral (5.0% vs 1.5%) although these results were possibly influenced by the proportion of patients biopsied.
Conclusion: In conclusion, our findings show that there is variable adherence to the investigation of EOE. The hospitals included serve a combined population of approximately 3.2 million, giving rise to a below average incidence of 3.32 cases per 100,000/yr. Our findings suggest that under-diagnosis may be secondary to under-investigation as a result of disparities in biopsy acquisition amongst gastroenterologists and surgeons, as well as influenced by patient age and referral pathway.
Disclosure: Prof Krish Ragunath has received research support, consultancy and educational grants from Olympus.

P1763 BRAVO WIRELESS PH MONITORING CAN SAVE TIME WHEN INVESTIGATING PATIENTS WITH EOSINOPHILIC OESOPHAGITIS

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Introduction: The incidence of eosinophilic oesophagitis (EoE) is increasing. Following diagnosis, the initial therapy is to place patients on protein pump inhibitors (PPI) and repeat oesophageal biopsies, as 30% of patients will be PPI responsive. As acid reflux is known to cause eosinophilic oesophagitis, pH impedance and manometry is also carried out to aid management. This is usually carried out as a separate hospital visit. An alternative test is wireless pH monitoring with a BRAVO device during which a pH monitoring chip is attached to the distal oesophagus at the same time as a gastroscopy. This is also an opportunity to take the repeated biopsies to assess PPI response; pH monitoring could therefore be integrated into the repeated endoscopic pathway and avoid the extra appointment for standard pH impedance. The fragile ''crêpe-paper'' mucosa of EoE has been raised as a potential source of early detachment of BRAVO capsules thereby limiting their use in this condition.
Aims and Methods: We aimed to assess whether there is any difference in the detachment day of the BRAVO capsule in patients with EoE when compared to other conditions and thereby determine its use in the pathway for the investigation of EoE patients.
The electronic records of patients with EoE who also had a BRAVO were examined retrospectively between June 2008 and January 2018 at a single centre. The total time of recording of the BRAVO capsule was noted and whether reflux was significant. In addition the number of eosinophils per high power field on the oesophageal biopsies taken prior to or at the same time as the BRAVO study was recorded.
Results: Ten patients with EoE underwent 12 BRAVO studies (M: F 1:1, age range 18–56). One study detached within one day, three after two days and eight after four days. The patient whose capsule detached early went on to have a second BRAVO study lasting 4 days. Detachment times were compared to those for non-EoE in our department for a single calendar year (December 2016-December 2017). There was no significant difference in detachment rates between these two groups ($p < 0.1$). The range of eosinophils per HPF was 20 to 71 (average 38.1, standard deviation 20.5).
Conclusion: Bravo pH manometry is a useful investigation in patients with EoE and beneficial to the patient; reducing the number of invasive procedures by allowing the attachment of the BRAVO capsule at the same time as taking post-PPI biopsies. The detachment was not significantly greater in patients with EoE although the numbers are small. There was no correlation between eosinophil count per HPF and attachment times. The only drawback is that patients are expected to stop PPI 7 days prior to the BRAVO being placed with a theoretical risk of a recrudescence of oesophageal eosinophilia in that time although the standard time for redevelopment of EoE is around 6–8 weeks.
Disclosure: Nothing to disclose

P1764 ESOPHAGEAL COMPLIANCE IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS MEASURED BY ENDOFLIP BEFORE AND AFTER TREATMENT WITH TOPICAL BUDESONIDE

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Introduction: Esophageal compliance is decreased in eosinophilic esophagitis (EoE). The reduction of compliance due to fibrosis has been shown to be a strong predictor of the risk of impaction and esophageal dilatation in patients with EoE. There is a lack of correlation between the eosinophil count and distensibility, revealing the dissociation that is sometimes observed between inflammatory and clinical activity. The reduced esophageal compliance correlates with the intensity of the endoscopic esophageal trachealization.
The functional endoluminal imaging probe (EndoFLIP®, Crospon Ltd., Galway, Ireland) for the study of esophageal distensibility and diameter uses the impedance planimetry technique and allows the analysis of volume-controlled esophageal compliance, obtaining three-dimensional images of the esophageal light.
The goal of the treatment of eosinophilic esophagitis is not only the clinical, endoscopic and histological improvement, but also the reduction in the degree of fibrosis, and therefore an improvement in esophageal compliance.
Aims and Methods: A pilot study to compare the esophageal compliance of patients diagnosed with active EEo before and after treatment with topical Budesonide.
We analyzed the esophageal compliance data of the first patients undergoing EndoFLIP at the Gastroenterology Department of the Hospital Universitario de La Princesa in Madrid. These patients presented active EoE and the esophageal compliance data were obtained before and after the treatment with Budesonide orodispersible tablets 1 mg every 12 hours for 6 weeks.
Results: Five patients were included in which clinical and histological improvement was observed (<15 eos/hpf), as well as an increase in diameter and statistically significant esophageal compliance ($p = 0.02$) after 6 weeks of treatment with topical Budesonide. The functional endoluminal imaging probe (EndoFLIP) for the study of esophageal distensibility was performed during the same endoscopic procedure, under sedation, and there were no complications associated with the procedures in any patient.
Conclusion: With topical budesonide treatment, the clinical and histological response and increased compliance in patients with EoE are achieved. More studies are needed with a greater number of patients and comparing with control subjects to know the clinical benefit of EndoFLIP in the follow-up of patients with EoE, and thus be able to establish its usefulness in the diagnostic-therapeutic algorithm of EoE.
Disclosure: Nothing to disclose

P1765 UNRESPONSIVE DYSPHAGIA TO PROTON PUMP INHIBITORS IN EOSINOPHILIC ESOPHAGITIS PATIENTS SUGGESTS TO START STEROID THERAPY WITHOUT THE NEED OF PERFORMING A SECOND UPPER ENDOSCOPY

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic immune-mediated disorder characterized by symptoms of esophageal dysfunction due to an inflammatory eosinophilic infiltrate in the esophageal lamina propria. Today the diagnostic gold standard is the histologic sampling of the esophagus and the recognition of at least 15 eosinophils for high power field (hpf). Up to 50% of patients with esophageal eosinophilia responds to a Proton Pump Inhibitor (PPI) therapy twice a day as first-line treatment. In order to confirm response to treatment, histologic sampling is necessary, and therefore according to international guidelines repeating upper endoscopy is mandatory. However, few data are available of the value of symptom reporting in predicting disease activity and response to PPI treatment.
Aims and Methods: We aimed to evaluate whether symptom remission due to PPI therapy may predict histological remission in patients with EoE responding to acid suppressive treatment. Patients with symptoms suggestive of EoE (i.e. dysphagia and bolus impaction) were prospectively enrolled in different Gastroenterology units in Italy. At baseline, an esophagogastroduodenoscopy (EGD) was performed to confirm the presence of inflammatory eosinophilic infiltrate (>15 oes/hpf) in the proximal and distal esophagus and to establish the diagnosis of EoE. Then, according to international guidelines, PPI-therapy was administered b.i.d. for eight weeks and a second EGD with biopsies was repeated to assess the endoscopic and histological remission due to acid-suppressive therapy. Esophageal symptoms including dysphagia, bolus impaction, heartburn and regurgitation were assessed before and after therapy by mean of a 4-point Likert scale, from 0 (absent symptom) to 3 (severe symptom). Histological remission was considered if esophageal samples presented less than 15 eos/hpf. A value of zero for each symptom after PPI therapy was indicative of clinical response.
Results: Thirty-one (25 Male; Age 18–68) patients with symptoms suggestive of EoE were enrolled. All of them presented dysphagia, 16 (52%) regurgitation and 19 (61%) heartburn. After 8 weeks PPI-therapy, 23 (74%) patients well responded to acid suppressive therapy and 8 (26%) subjects did not. Dysphagia disappeared in all of the subjects with a positive response to PPIs and only in 4 out of 8 refractory to PPIs. Moreover, regurgitation and heartburn resolved in 14/15 (93%) and in 16/17 (94%) of patients responding to PPIs, respectively, and in 1/1 (100%) and 1/1 (100%) of subjects refractory to PPIs, respectively. Using Fisher's test, we calculated sensitivity, specificity, positive and negative predictive values (PPV and NPV) of symptom disappearing in order to segregate PPI responders from PPI-non responders without performing an EGD. Disappearance of dysphagia presented a sensitivity of 100%, a specificity of 50%, a PPV of 80% and NPV of 100[ES1]% in detecting EoE-PPI responders ($p = 0.002$), whereas the disappearing of heartburn and regurgitation were not statistically significant ($p = 0.9$).
Conclusion: Clinical response to PPI therapy as assessed by the resolution of dysphagia is useful, but does not suffice to predict histologic response to PPI treatment. On the other hand, lack of disappearance of dysphagia after PPIs seems to justify starting steroid therapy without histological confirmation of persistent esophageal eosinophilia during upper GI endoscopy.
Disclosure: Nothing to disclose

P1766 POOR CORRELATION BETWEEN ENDOSCOPIC FINDINGS, EOSINOPHILIC INFILTRATION AND REFLUX BURDEN IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic immune-mediated disorder characterized by symptoms of esophageal dysfunction due to an inflammatory eosinophilic infiltrate in the esophageal lamina propria. Currently, the endoscopic appearance of patients with EoE is defined by using the Endoscopic Reference Score (EREFS), whereas esophageal eosinophilic infiltration is used to diagnose EoE (i.e. >15eos/ high power field) and to estimate disease severity. The relationship between EoE and gastroesophageal reflux disease (GERD) has been demonstrated, although the magnitude of it is unknown and scant data have been published to date. Moreover, no sufficient data exist about the correlation of eosinophilic infiltrate with clinical presentation, endoscopic findings and reflux burden.
Aims and Methods: We aimed to correlate eosinophilic infiltration with clinical presentation, endoscopic findings as expressed by the EREFS score and reflux burden as assessed by impedance-pH studies. Patients with symptoms suggestive of EoE (i.e. dysphagia and bolus impaction) were prospectively enrolled in different Gastroenterology units in Italy. At baseline, an esophagogastroduodenoscopy (EGD) was performed to confirm the presence and entity of inflammatory eosinophilic infiltrate (>15 oes/hpf) in the proximal and distal esophagus and to establish the diagnosis of EoE. Endoscopic findings were expressed by using the EREFS score, describing the presence of edema, rings, exudates, furrows and stricture, whereas esophageal symptoms including dysphagia, bolus impaction, heartburn and regurgitation were assessed by mean of a 4-point Likert scale, from 0 (absent symptom) to 3 (severe symptom). Moreover, each patient underwent 24-hour pH-impendance testing off-medication in order to measure reflux burden. In particular, we measured the acid exposure time (AET; abnormal if greater than 4.2%), number of total reflux episodes (TRE; abnormal if higher than 54) and post-reflux swallow-induced peristaltic wave (PSPW) index and of mean nocturnal baseline impedance (MNBI).
Results: Forty-one (34 males, mean age 38, mean BMI 24) patients with a definite diagnosis of EoE were enrolled. Patients complained of dysphagia (mean score 2, range 1–3), heartburn (mean score 1, range 0–3) and regurgitation (mean score 1, range 0–2). The mean EREFS score was 2 (range 0–4), while the mean number of eosinophils were 33 (range 15–78). Impedance-pH feature are reported in the Table. Correlation was assessed by means of linear regression analysis and no statistically significant correlation was found between pick of eosinophils or EREFS score and AET, TRE, PSPW, MNBI and symptom score ($p = ns$).

Neither a correlation between pick of eosinophils count and value of EREFS score was observed (p = ns).
Conclusion: Eosinophils pick count in the esophageal mucosa of patients with EoE does not correlate with the severity of disease in term of endoscopic findings, symptomatic presentation and reflux burden. It seems that these factors are independently associated and additional phenomena are likely to be involved in determining the entity of eosinophilic infiltration.

Acid Exposure Time (AET),%	2 (0–8)
Total Reflux Episodes (TRE), n	41 (2–92)
Acid Reflux Episodes, n	31 (1–69)
Weakly Acidic Reflux Episodes, n	9 (0–37)
Proximal Reflux Episodes, n	21 (0–65)
Bolus Exposure, sec	1 (0.1–3.6)
Median Bolus Clearance Time, sec	14 (4–35)
Post-reflux swallow-induced peristaltic wave (PSPW) index	30 (0–70)
Mean nocturnal baseline impedance (MNBI)	1001 (237–3349)

[Impedance-pH Features; data are expressed as mean (range)]
Disclosure: Nothing to disclose

P1767 COMPREHENSIVE ANALYSIS OF FACTORS DETERMINANT FOR EROSIVE REFLUX ESOPHAGITIS: SIGNIFICANCE OF DEMOGRAPHIC/LIFESTYLE FACTORS IS EMPHASIZED IN HELICOBACTER PYLORI-NONINFECTED SUBJECTS

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Introduction: The incidence of erosive reflux esophagitis has increased sharply in Japan, probably due to falling prevalence of *Helicobacter pylori* (HP) infection. HP-associated atrophic gastritis, which reduces gastric acid secretion, is known to be protective against erosive reflux esophagitis. Therefore, both gastric acid secretion level and HP infection status should be taken into consideration when analyzing the risk factors of erosive reflux esophagitis. Pepsinogen I/II ratio is reported to correlate significantly with not only gastric atrophy grade but also gastric acid secretion level. Hence, we performed comprehensive analyses of the risk factors of erosive reflux esophagitis by using pepsinogen I/II ratio as a surrogate marker of gastric acid secretion level.
Aims and Methods: A total of 959 consecutive subjects who underwent esophagogastroduodenoscopy and measurement of serum pepsinogen level at the same day were enrolled. The following subjects were excluded to avoid the influence on pepsinogen levels; 1) those who had received successful HP eradication therapy in the past, 2) those who had undergone gastrectomy, 3) those who were taking proton pump inhibitors for various reasons, and 4) those having renal failure (Creatinine > 3.0 mg/dl). HP infection status was determined by the titer of serum HP-IgG. Erosive reflux esophagitis was defined as grade M or more reflux esophagitis according to Los Angeles classification. Univariate and subsequently multivariate logistic regression analyses were performed to identify the factors of erosive reflux esophagitis. The following factors were evaluated: sex, age, body mass index (BMI), pepsinogen I/II ratio, drinking status, smoking status, and HP infection status.
Results: The 959 enrolled subjects comprised 466 males, with a mean age of 52. To neutralize an influence of HP infection status on erosive reflux esophagitis, the entire cohort was divided into 2, HP-infected (HP-IgG positive, n = 236) and HP-noninfected (HP-IgG negative, n = 723) subjects. In HP-infected subjects, univariate analysis showed that factors significantly associated with erosive reflux esophagitis were pepsinogen I/II ratio (Odds ratio (OR) 1.45, 95% confidence intervals (CI) 1.10–1.91) and BMI (OR 1.12, 95%CI 1.01–1.91). Multivariate analysis showed that pepsinogen I/II ratio was only a significant factor of erosive reflux esophagitis (OR 1.41, 95%CI 1.06–1.86). On the other hand, in HP-noninfected subjects, univariate analysis showed that male sex (OR 4.17, 95%CI 2.94–6.25), BMI (OR 1.13, 95%CI 1.07–1.19), everyday drinking (OR 3.38, 95%CI 2.16–5.31), and current smoking (OR 2.83, 95%CI 1.76–4.56) were significantly associated with erosive reflux esophagitis. Multivariate analysis showed that male sex (OR 2.70, 95%CI 1.69–4.35), BMI (OR 1.07, 95%CI 1.01–1.13), and everyday drinking (OR 1.78, 95%CI 1.07–2.96) were statistically significant.
Conclusion: The factors for erosive reflux esophagitis differ between HP-infected and HP-noninfected subjects. In HP-infected subjects, pepsinogen I/II ratio was the only significant factor. On the other hand, in HP-noninfected subjects, demographic/lifestyle factors such as male sex, BMI, and everyday drinking were significant. These results suggest that although gastric acid secretion ability is fundamentally important for erosive reflux esophagitis, demographic/lifestyle factors are more important in HP-noninfected subjects whose ability to secrete gastric acid is reserved. In the era of falling prevalence of HP infection in Japan, lifestyle modification may be promising for preventing erosive reflux esophagitis.
Disclosure: Nothing to disclose

P1768 GASTRIC BYPASS SURGERY IN THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE: A POPULATION-BASED COHORT STUDY

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Introduction: Gastric bypass (GBP) is considered an effective surgical treatment option for co-existing gastroesophageal reflux and obesity. However, previous studies examining GBP and reflux have had small sample sizes, short follow-up, and substantial loss to follow-up. This study aimed to assess how GBP influences reflux in a large study with long and complete follow-up.
Aims and Methods: This nationwide and population-based cohort study included 2,805 obese individuals with preoperative reflux who underwent GBP in Sweden in 2006–2015, with follow-up until 2016. Reflux was defined as dispensation of >6 months of antireflux medication, excluding other indications for such medication. Poisson regression was used to assess cumulative incidence and risk factors of postoperative reflux.
Results: Reflux re-occurred in 48.5% of patients within two years of GBP (48.5/100 person-years, 95% confidence interval [CI] 46.6–50.5). The re-occurrence of reflux remained stable around 50% during 3 to 10 years after GBP (yearly change in incidence rate ratio [IRR] of 1.00, 95% CI 0.99–1.02). Risk factors for postoperative reflux were high preoperative dose of antireflux medication (IRR = 1.83, 95% CI 1.67–2.01 comparing high with low dose), older age (IRR = 1.11, 95% CI 1.01–1.22 comparing age >50 with <40 years), female sex (IRR = 1.26, 95% CI 1.15–1.39), and comorbidity (IRR = 1.23, 95% CI 1.11–1.35 comparing Charlson comorbidity index ≥2 with 0).
Conclusion: Reflux re-occurs in approximately half of patients after GBP, and the rate is higher rates in individuals using high preoperative dose of antireflux medication, and in those of female sex, older age, and with comorbidities. These results suggest that the treatment effect of GBP may have been overestimated.

	Number (%)		
	Total	Women	Men
	2,805 (100.0)	2,301 (82.0)	504 (18.0)
Age (years) – mean (SD)	46.5 (9.8)	46.3 (9.8)	47.6 (9.6)
Comorbidities			
No comorbidity	1,752 (62.4)	1,486 (64.5)	266 (52.8)
1 comorbidity	762 (27.2)	604 (26.3)	158 (31.3)
≥2 comorbidities	291 (10.4)	211 (9.2)	80 (15.9)
Dose of antireflux medication prior to GBP* – mean (SD)	452.2 (240.7)	444.5 (231.8)	487.1 (275.1)
Low dose	1,227 (43.7)	1,021 (44.4)	206 (40.9)
Intermediate dose	1,256 (44.8)	1,038 (45.1)	218 (43.2)
High dose	322 (11.5)	242 (10.5)	80 (15.9)
Previous bariatric surgery	318 (11.3)	266 (11.6)	52 (10.3)
Previous antireflux surgery	35 (1.2)	31 (1.3)	4 (0.8)
Laparoscopic GBP	2,426 (86.5)	1,987 (86.3)	439 (87.1)
Post-operative infection	360 (12.8)	296 (12.9)	64 (12.7)
Re-operation	94 (3.4)	65 (2.8)	29 (5.8)
Deaths during follow-up	76 (2.7)	54 (2.3)	22 (4.4)
Follow-up time (years) – median (IQR)	4.7 (3.1–6.6)	4.8 (3.1–6.5)	4.4 (3.1–6.6)

Abbreviations: GBP – gastric bypass; IQR – interquartile range; SD – standard deviation. *Dose of antireflux medication was calculated as the sum of filled prescriptions of histamine-2 receptor antagonists and proton pump inhibitors in the year prior to GBP and presented as the standardized unit defined daily doses (DDD). DDD is defined by WHO as "the assumed average maintenance dose per day for a drug used for its main indication in adults."
[Characteristics of 2,805 obese patients with gastroesophageal reflux disease who underwent gastric bypass between 2006 and 2015 in Sweden.]
Disclosure: Nothing to disclose

P1769 WAIST CIRCUMFERENCES IS THE INDEPENDENT RISK FACTOR OF EROSIVE ESOPHAGITIS : SINGLE-CENTER STUDY ON KOREAN NATIONAL CANCER SCREENING PROGRAM

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Introduction: Decrease in the lower esophageal sphincter pressure with increased gastro-esophageal pressure gradient and the hiatal hernia have been reported to be induced by high intra-abdominal pressure due to abdominal fat accumulation and obesity are related to the high prevalence of reflux esophagitis. Moreover metabolic syndrome is diagnosed by the factors of visceral fat accumulation, dyslipidemia, hypertension, and hyperglycemia, and all 4 factors have been suggested to correlate with the occurrence of GERD.

Aims and Methods: This study was performed to clarify the association between metabolic syndrome and erosive esophagitis and to find out which one of the diagnostic criterion of the metabolic syndrome is mostly correlate with erosive esophagitis. The study subjects were an adult population who visited a National Health Insurance Ilsan hospital for Korean National Cancer Screening Program from January 2011 to December 2016. Among 101,435 screened, 9,117(8.98%) subject diagnosed with erosive esophagitis. One to one propensity score-matched 8,537 pairs of with and without esophagitis subjects were compared.

Results: Mean age was 58.8 years old. Two-third were male (70.7%). A half of the subjects were non-smokers (48.3%) and one-third were moderate alcohol consumer (32.3%, >80g of ethanol per week) based on the questionnaire. Proportion of subjects accompanied with hiatus hernia was about 8.4%. Metabolic syndrome was more prevalent in esophagitis group (45.3% vs. 53.6%; $P < 0.001$). Unadjusted odds ratio of metabolic syndrome for esophagitis tended to increase, but not statistically significant (OR = 1.512, 95% CI 0.944–2.244; $P = 0.085$). The esophagitis group showed higher rate of obese subjects defined as waist circumference, one of diagnostic criteria for metabolic syndrome (27.3% vs. 35.9%; $P < 0.001$). As waist circumference increased, the Los Angeles grade of reflux esophagitis became more severe, assessed by the trend test ($P = 0.003$). Adjusted odds ratios of waist circumferences for esophagitis was 1.355 (95% CI 1.017–1.807; $P = 0.038$).

Conclusion: Waist circumference, rather than metabolic syndrome is a reliable predictive factor for the prevalence and severity of erosive esophagitis.

Disclosure: Nothing to disclose

P1770 ALCOHOL CONSUMPTION AND THE RISK OF GASTROESOPHAGEAL REFLUX DISEASE: A META-ANALYSIS

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Introduction: Gastroesophageal reflux disease (GERD) is prevalent worldwide, which causes esophageal mucosal injury or reflux symptoms.[1] It not only affects people's health and quality of life, but also becomes a source of substantial burden and cost.[2] A variety of factors have been reported to be relevant to GERD such as body mass index (BMI), *Helicobacter pylori* infection and a certain diet.[3–5] Many studies have reported that drinking is associated to various digestive diseases.[6–8] However, there is still no comprehensive article to assess the correlation between alcohol consumption and GERD. To summarize the evidence on the effect of alcohol on GERD, we conducted a meta-analysis of observational studies. In addition, the drinking frequency and alcohol consumption were further classified and the dose response analysis was also conducted to explore the correlation.

Aims and Methods: This study aimed to investigate the association between alcohol consumption and GERD by meta-analysis. Two investigators searched for relevant studies respectively on PubMed, Cochrane and EMBASE published before December 2017. The summary odds ratios and 95% confidence intervals were calculated by random effects model to assess the association. Heterogeneity and subgroup analyses, sensitivity and publication bias analyses were also performed.

Results: Twenty-six cross-sectional studies and three case-control studies were included in the meta-analysis. Alcohol consumption was significantly associated with an increased risk of GERD in cross-sectional studies (OR, 1.55; 95%CI, 1.36–1.76; $I^2 = 89.1\%$). The case-control studies did not reveal any association between alcohol intake and GERD (OR, 1.08; 95%CI, 0.73–1.60; $I^2 = 87.2\%$). In two subtypes of GERD, the correlation between alcohol drinking and reflux esophagitis (OR, 1.78; 95%CI, 1.56–2.03; $I^2 = 87.5\%$) was stronger than that of non-erosive reflux disease (OR, 1.15; 95%CI, 1.04–1.28; $I^2 = 0.3\%$). The pooled OR for drinkers that drinking less than 3–5 times or days per week was 1.29(95%CI, 1.14–1.46; $I^2 = 35.5\%$), and 2.12(95%CI, 1.63–2.75; $I^2 = 55.1\%$) for those who drink more frequently. Dose-response analysis showed a linear association between alcohol consumption and GERD (P for nonlinearity = 0.235). The pooled OR for a 12.5g/day increment of alcohol was 1.162(95%CI, 1.065–1.268; $P = 0.001$).

Conclusion: This meta-analysis provides evidence for the association between alcohol intake and GERD. The increase in alcohol consumption and frequency showed a stronger correlation with GERD.

Disclosure: Nothing to disclose

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P1771 SMOKING AND ALCOHOL ARE ASSOCIATED WITH OESOPHAGEAL HYPOSENSITIVITY

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Introduction: Gastro-oesophageal reflux disease (GORD) is a common condition with a prevalence of up to 28%, often causing impaired quality of life [1]. Avoidance of lifestyle factors such as tobacco and alcohol is often recommended in GORD management; mostly based on tradition and only to some degree on epidemiological findings. Hence, smoking is associated with an up to two-fold increased risk of GORD as well as Barrett's oesophagus (BO), whereas the effects of alcohol are less well known [1]. Physiologically, lower oesophageal sphincter pressure (LOSP) decreases during tobacco smoking and after alcohol intake [1]. Correspondingly, smoking cessation has been shown to improve reflux symptoms, but only in normal-weight GORD patients, whereas the effect on acid exposure is less clear [1]. For alcohol, any immediate effect on oesophageal function in regard to reflux symptoms and/or reflux monitoring is doubtful [1]. In the long-term however, alcohol may lead to neuropathy [2] and possibly even have positive effects on chronic pain [3]. Only one study has addressed the association between smoking and oesophageal sensitivity, finding no relation, likely due to the inclusion of only three smokers.

Aims and Methods: We aimed to characterize the impact of alcohol and tobacco consumption on experimental oesophageal sensitivity, and hypothesized that both of these are associated with hyposensitivity. Twenty-three patients with BO (mean age: 64.2 ± 7.8 years) and 12 healthy controls (mean age: 54.9 ± 10.8 years) were included. At baseline, all subjects reported consumption of alcohol (standard drinks per week) and tobacco (accumulated pack years). At a later visit, experimental oesophageal pain sensitivity was assessed by placing a multimodal stimulation probe in the lower oesophagus. The probe was then used to apply mechanical distension, thermal stimulation, electrical stimulation, and acid perfusion with 0.1 M hydrochloric acid (a Bernstein test). All stimulations were stopped when the subject felt moderate pain.

Results: Tolerated acid volume (hyposensitivity) increased with greater tobacco exposure and alcohol consumption in healthy controls (tobacco: $P < 0.001$, alcohol: $P = 0.001$), but not in patients with BO (all $P > 0.3$). Concerning mechanical stimulation, a greater tolerated bag volume was associated with greater tobacco exposure only in patients with BO ($P = 0.02$). For healthy controls in relation to tobacco smoking and for alcohol use in both groups, no significant associations with sensation to mechanical stimulation were found (all $P > 0.6$). For electrical and thermal stimulation, neither alcohol nor tobacco use showed any significant associations in any of the groups (all $P > 0.1$).

Conclusion: Oesophageal sensitivity decreased with greater reported consumption of alcohol and tobacco. Previous findings of a strong association to smoking in asymptomatic patients with oesophagitis support this [4]. Hyposensitivity in smokers could be due to a direct nociceptive effect of nicotine [5], whereas other factors might explain hyposensitivity related to alcohol. Further evidence is needed to support these findings.

Disclosure: Nothing to disclose

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P1772 ASTHMA UNDER CONTROL IS INVERSELY RELATED WITH EROSIVE ESOPHAGITIS AMONG HEALTHY ADULTS

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Introduction: Some recent studies suggested that reflux esophagitis is positively correlated with asthma. However, there are debates on this issue.
Aims and Methods: The aim of this study is to clarify the true association between reflux esophagitis and asthma in a large population. Medical records of subjects who received health surveillance checkup between January 2005 and December 2011 were reviewed. There endoscopic finding, medical history, body mass index, smoking history were analyzed. Reflux esophagitis was defined as endoscopically detected mucosal break at the Z-line irrespective of reflux symptom. Information about patients' history of asthma was obtained from their questionnaire and medical records.
Results: Out of the total 15,999 patients, 986 had reflux esophagitis and 376 had asthma. In this population, reflux esophagitis was inversely related with asthma in univariabe analysis (OR, 0.586; 95% CI, 0.342–1.003, $p = 0.049$). In multivariable analysis, asthma was demonstrated as an independent negative risk factor for reflux esophagitis (OR, 0.472; 95% CI, 0.257–0.869, $p = 0.016$), under adjustment with age (OR, 0.472; 95% CI, 0.257–0.869, $p = 0.016$), male sex (OR, 2.092; 95% CI, 1.683–2.601, $p < 0.001$), body mass index (OR, 1.115; 95% CI, 1.090–1.141, $p < 0.001$), smoking (OR, 1.584; 95% CI, 1.318–1.902, $p < 0.001$), and urban residence (OR, 1.363; 95% CI, 1.149–1.616, $p < 0.001$). Likewise, reflux esophagitis was shown to be an independent negative risk factor for asthma (OR, 0.558; 95% CI, 0.324–0.960, $p = 0.035$) under adjustment with age (OR, 1.025; 95% CI, 1.015–1.034, $p < 0.001$), male sex (OR, 0.861; 95% CI, 0.691–1.074, $p = 0.185$), BMI (OR, 1.067; 95% CI, 1.030–1.106, $p < 0.001$) in multivariable analysis.
Conclusion: Contrary to previous studies, this large-scale data showed inverse association between reflux esophagitis and asthma. Further studies investigating the clear mechanism of this phenomenon are warranted.
Disclosure: Nothing to disclose

P1773 CLINICAL CHARACTERISTICS OF GASTROESOPHAGEAL REFLUX DISEASE IN SUBJECTS WITH SLEEP-DISORDERED BREATHING

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Introduction: There is insufficient evidence for a relationship between gastroesophageal reflux disease (GERD) and obstructive sleep apnea (OSA). The purpose of this study was to determine whether OSA patients proven by polysomnography would be related to GERD.
Aims and Methods: A total of 424 subjects was evaluated in St. Paul's Hospital, Catholic Medical Center, Korea, between September 2009 and September 2015. Nocturnal polysomnography was performed and a GERD questionnaire was asked. The apnea-hypopnea index < 5 was defined as non-OSA subjects. Subjects with heartburn or acid regurgitation at least once a week were classified as having GERD.
Results: Among 424 subjects who underwent polysomnography, 320 were OSA and 104 were non-OSA. There was no difference in the prevalence of GERD between OSA and non-OSA (10.6% vs 13.1%, P = 0.609). There was no relationship between the percentage of subjects with GERD and the severity of OSA (Non-OSA: 11, mild OSA:8, moderate OSA:12, severe: 22, P = 0.549). Subjects with GERD had the higher scores in Stanford sleepiness scale (SSS) (P = 0.001), Epworth sleepiness scale (ESS) (P = 0.003), and depression (P < 0.001) than non-GERD subjects. GERD subjects had higher waist-to-height ratio and waist circumference to height index than non-GERD. The multiple logistic regression showed that SSS, ESS, and depression were independent factors associated with GERD.
Conclusion: There may not be little relationship between GERD and OSA. SSS, ESS, and depression are associated with GERD in subjects with sleep-disordered breathing.
Disclosure: Nothing to disclose

P1774 MONITORING RISK FACTORS FOR THE ONSET OF ESOPHAGITIS IN A LONG 15-YEARS FOLLOW-UP

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Introduction: Gastroesophageal reflux disease (GERD) is a disease determined by several concomitant factors. The pathophysiology is particularly linked to obesity, smoking habits and the secretive activity of the stomach; the variability of endoscopic findings depends on different resistance and sensitivity of the individual patient's mucosa.
Aims and Methods: Aim of this study was to evaluate the influence of epidemiological risk factors (age, sex, obesity, smoking habits) and gastric acid secretion status in the development of esophagitis in a *H.pylori*-negative population.A group of 320 patients (M = 234, F = 86, mean age = 42.7 ± 11.6 range = 18.80) with symptoms of the upper GI tract was recruited. They underwent gastroscopy in order to assess the presence of esophagitis: 150 had esophagitis (Group A) in comparison with 170 without lesions (Group B). All patients underwent to gastric acid aspiration test for measuring basal acid output (B.A.O.) and maximal acid output (M.A.O.) after stimulation with pentagastrin (i.m., 6 μg/kg). All of them underwent a blood sampling for serum pepsinogen I and G17 determination. Statistical analysis were performed by means of Mann-Whitney test for the comparison of demographic characteristics and endoscopic diagnoses. An univariate analysis was used to evaluate risk factors such as age, sex, smoking habit, BMI, M.A.O., PGI, G17. All patients underwent a 15-years follow-up using gastroscopy when symptoms occurred to assess the onset of a feature of esophagitis.
Results: Univariate analysis demonstrated a significant association between the feature of esophagitis, lasting the follow-up, and M.A.O. (p = 0.0001), PGI (p = 0.0001), G17 (p = 0.0001), BMI (p = 0.014), while no association was found with age, gender nor smoking habit.
Conclusion: Our study demonstrated a positive association between high gastric secretion (M.A.O., PGI and G17) as well as BMI and the onset of esophagitis in an H.p. negative population lasting a long 15-years follow-up.
Disclosure: Nothing to disclose

P1775 LARYNGEAL MUCOSAL IMPEDANCE VALUES; A NEW DIAGNOSTIC TOOL FOR LARYNGOPHARYNGEAL REFLUX DISEASE

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Introduction: There are great difficulties for the diagnosis of laryngopharyngeal reflux disease (LPR). Reflux finding score (RFS) and reflux symptom index (RSI) were proposed for the diagnosis however their value is questionable. We propose a new diagnostic tool with the measurement mucosal impedance in different areas of larynx and pharynx in patients with LPR and controls.
Aims and Methods: The objective of the study was to assess the relation of laryngeal mocusal impedance values with LPR. In total 78 patients (38 female) were included who were operated for different ENT pathologies other than laryngeal diseases. Exclusion criteria; previous upper gastrointestinal or laryngeal surgery, on-going proton pump inhibitor treatment, other laryngeal disorders, previous radiotherapy in the head and neck, laryngeal carcinoma. Patients were divided into four groups according to RSI, RFS (Table). Normal values were accepted < 13 for RSI and < 7 for RFS. After the general anesthesia and intubation, the mucosal impedance measurements of band ventricle, arytenoid, vallecula, posterior comissure, endolaryngeal surface of epiglottis and buccal area (as control) were recorded using Ohmega (Laborie) MII-pH equipment with an impedance catheter (Unisensor). A mean value from a stabile measurement was taken from each area.
Results: It was possible to achieve stabile and reliable values from all measured areas. Mean mucosal impedance values of the band ventricle, arytenoid, posterior comissure, endolaryngeal surface of epiglottis, vallecula and buccal area were given in the table. A statistically significant difference was found for band ventricle, arytenoid, vallecula and endolaryngeal surface of epiglottis ($p < 0.05$) within all groups but especially between groups I (both RFS & RSI pathologic) and IV (both normal). 51 non-smokers exhibited higher but insignificant

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Table 1: Mean impedance values of the laryngeal areas and buccal area (ohms) (* $p < 0.05$; comparison of four groups).

Groups	Band ventricle*	Arytenoid*	Posterior commissure	Endolaryngeal surface of epiglottis*	Valleculae*	Buccal area
I (n = 30) (RFS+/RSI+)	835 ± 270	793 ± 302	1153 ± 300	566 ± 147	1520 ± 346	2268 ± 369
II (n = 8) (RFS-/RSI+)	1047 ± 385	1293 ± 308	1302 ± 208	733 ± 214	1843 ± 421	2192 ± 553
III (n = 11) (RFS+/RSI-)	1182 ± 125	1043 ± 153	1304 ± 165	727 ± 95	1651 ± 246	2145 ± 341
IV (n = 29) (RFS-/RSI-)	1203 ± 325	1191 ± 317	1278 ± 374	740 ± 253	1850 ± 241	2484 ± 406

measurements compared to 27 smoker patients in all measured areas except band ventricle (1183 vs 779 ohms). Binary logistic regression analysis revealed that a model using measurements from ventricular fold (OR 0.995, 95%CI 0.991–0.999), arytenoid (OR 0.991, 95%CI 0.984–0.998) and endolaryngeal surface of epiglottis (OR 0.993, 95%CI 0.988–0.999) was able to distinguish especially between group I and group IV with a sensitivity of 93% and a specificity of 83%.
Conclusion: Mucosal impedance measurement of the larynx and pharynx can be used as a promising diagnostic tool. Smoking, as a possible strong confounding factor, has very limited impact on measurements. When our findings were evaluated with the parameters of RFS, posterior commissure hypertrophy should not be taken into consideration however ventricular obliteration should be more emphasize. Considering the results of logistic regression more attention should be paid also to the arytenoids and endolaryngeal surface of epiglottis. It is possible to create a new diagnostic scoring system with this more objective technology. Outcome data and thinner catheters are needed for office-based measurements.
Disclosure: Nothing to disclose

P1776 ON-THERAPY PARAMETERS RATHER THAN OFF-THERAPY IMPEDANCE-PH FEATURES BETTER IDENTIFY PATIENTS WITH NON-EROSIVE REFLUX DISEASE RESPONDING TO PROTON PUMP INHIBITOR THERAPY

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Introduction: Impedance-pH monitoring, providing a comprehensive assessment of reflux independently of the pH of refluxate, allows to reliably distinguish non-erosive reflux disease (NERD) from functional heartburn, and thus represents a valuable test for investigating proton pump inhibitor (PPI)-refractory patients.
Aims and Methods: We aimed to investigate whether impedance-pH off- or on-therapy may better identify patients with NERD responding to PPI treatment. In this prospective, multicenter study, 64 patients complaining of heartburn and with a negative upper endoscopy, underwent impedance-pH testing off-therapy. Then, patients with proven NERD based on traditional parameters (i.e. abnormal AET and/or positive symptom association analysis) were treated with PPI for 8 weeks and repeated the impedance-pH testing on-therapy. Tracings were blindly and manually reviewed and we measured conventional reflux testing parameters, such as esophageal acid exposure time (AET), number of reflux episodes and symptoms association analysis (symptom index, SI, and symptom association probability, SAP), and novel impedance-detected features, including the post-reflux swallow-induced peristaltic wave (PSPW) index and mean nocturnal baseline impedance (MNBI).
Results: Thirty-two individuals (16 male, mean age 48) had PPI-refractory heartburn (i.e. < 50% of symptom relief after 8-week high-dosage PPI therapy), and thirty-two (18 male, mean age 56) had PPI-responsive heartburn. Demographic and clinical characteristics were not different between the two groups at baseline (p = ns). At off-therapy impedance-pH monitoring, no differences were found between PPI-refractory and PPI-responsive patients in terms of median AET, number of reflux episodes, symptoms association analysis, PSPW and MNBI, as illustrated in the Table. At on-therapy reflux testing, median esophageal AET and symptom association analysis did not differ between the two groups. However, the total number of refluxes, weakly acidic refluxes and bolus exposure were significantly higher, while PSPW index and MNBI were significantly lower in PPI-refractory cases ($p < 0.05$), as shown in the Table.

Impedance-pH Features	PPI-refractory N = 32	PPI-responsive N = 32	P Value
Off-Therapy			
Mean AET,%	6.2 (4.2–9.9)	5.0 (3.3–8.9)	0.471
PSPW index (%)	24 (19–31)	29 (20–32)	0.378
Mean MNBI, Ohms	1321 (889–1861)	1127 (741–1655)	0.214
Total Refluxes, n	53 (39–77)	42 (31–68)	0.053
Total Refluxes, n	46 (33–63)	41 (26–50)	0.076
Weakly Acidic Refluxes, n	7 (4–13)	3 (1–13)	0.087
Mean Bolus Exposure Time (%)	2.3 (2.0–3.2)	1.4 (0.8–2)	0.568
On-Therapy			
Mean AET (%)	0.4 (0.1–1.9)	0.1 (0.0–0.8)	0.190
PSPW index (%)	26 (19–37)	46 (35–51)	<0.001
Mean MNBI, Ohms	2129 (1615–2742)	2779 (2199–3122)	0.012
Total Refluxes, n	53 (35–81)	29 (14–47)	0.002
Acid Refluxes, n	9 (3–16)	4 (1–9)	0.061
Weakly Acidic Refluxes, n	34 (17–64)	23 (8–37)	0.018
Mean Bolus Exposure Time (%)	2.3 (1.2–5.0)	0.9 (0.4–1.9)	0.008

[Baseline off- and on-therapy impedance-pH features of 32 patients with PPI-refractory and 32 patients with PPI-responsive heartburn]
Conclusion: Our data showed that only on-therapy impedance-pH monitoring is able to differentiate patients with NERD who are responding to PPI therapy from those who are refractory to acid-suppressive treatment. In particular, impedance-detected characteristics (i.e. total number of refluxes, bolus exposure, PSPW index and MNBI) seem to better correlate with response to PPI therapy. This study provides additional evidence on the value of impedance-pH testing as compared to pH-metry alone in investigating reflux disease patients and evaluating therapeutic outcome
Disclosure: Nothing to disclose

P1777 MULTICHANNEL IMPEDANCE MONITORING FOR DISTINGUISHING NON-EROSIVE OESOPHAGITIS WITH MINOR CHANGES ON ENDOSCOPY

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Introduction: There are reports about the relationship between baseline impedance level and oesophageal mucosal integrity by endoscopic findings such as erosive and non-erosive reflux oesophagitis. However, many children with symptoms of GORD have normal findings or minor changes on oesophagogastroduodenoscopy (OGD). We would like to examine whether trivial changes in OGD study can be evaluated by multichannel Impedance monitoring as an alternative measure.
Aims and Methods: Patients (ages 0–18 years) with symptoms related to GOR who underwent OGD and pH-MII monitoring in Women's and Children's Hospital in Adelaide, Australia, between 2014 and 2016 were retrospectively studied and the following data were collected: demographics (age, gender), pH-MII data (acid exposure (pH), included reflux index (acid exposure time), mean acid clearance time, longest episode of acid exposure). Impedance data included: the number of acid and non-acid reflux events, and baseline impedance (distal channels; 5,6 was objectively calculated using software created using Matlab (MathWorks, Natick, MA)). Endoscopic findings were classified by modified Los Angeles grading, LA-N as normal, LA-M as with a minimal change such as the reddish or whitish mucosa, or friability in the mucosa. Patients on proton pump inhibitors were excluded. Other exclusions were the presence of esophageal anatomical anomaly, eosinophilic esophagitis, and previous anti-reflux surgery.
Results: Seventy patients (43 boys 61%) were enrolled with a mean of age of 7.9 years (range 10 months to 17 years) in this study. Fifty-one patients (72.9%) were allocated to LA-N, while LA-M evident in 19 patients (27.1%). Statistical differences were observed in four parameters: frequency of acid ($p = 0.034$) and non-acid reflux ($p = 0.022$), baseline impedance in channel 5 ($p = 0.024$) and 6 ($p = 0.005$). The mean values ± SE of the data were LA-N: 22.16 ± 2.94 episodes,

21.86 ± 2.26 episodes, 2574.8 ± 97.60 Ω, 2491.1 ± 109.3 Ω, In LA-M: 32.68 ± 3.84 episodes, 40.4 ± 7.21 episodes, 2163.2 ± 130.7 Ω, 1897.3 ± 169.2 Ω.
Conclusion: In children with GOR Minor oesophageal endoscopic findings were associated with lower baseline impedance. It is therefore reasonable to relate the number of acid and non-acid reflux episodes to minor changes in the distal oesophagus.
Disclosure: Nothing to disclose

P1778 THE CONSISTENCY OF LOS ANGELES CLASSIFICATION OF GASTROESOPHAGEAL REFLUX DISEASE ACCORDING TO THE INSERTION/WITHDRAWAL PHASES OF ESOPHAGOGASTRODUODENOSCOPY

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Introduction: During esophagogastroduodenoscopy (EGD), patients often belch and retch. Gastroesophageal junction (GEJ) is a narrow area easily affected by endoscopic manipulation and belching or retching of patients during endoscopy. But there is no consensus on optimal timing of grading esophagitis during EGD, and no study was performed to assess the effect of these factors on the Los Angeles (LA) classification of reflux oesophagitis.
Aims and Methods: We performed prospective observational study to investigate the effect of endoscopic movement and patients' belching/retching during EGD on the GEJ appearance. Still images of GEJ were captured during both insertion and withdrawal phases of EGD and analyzed separately. All the image sets of GEJ (each subject has two image sets, one during insertion and the other during withdrawal) were mixed randomly, and reviewed by two expert endoscopists (who had performed more than 3000 upper gastrointestinal endoscopy), who are unaware of the relationship of mixed image sets. LA classification was recorded as normal, minimal change, A, B, C, and D. Simplified working definition of minimal change lesion (i.e., white turbid discoloration and Z-line blurring) was adopted in this study [1]. LA classifications determined by two reviewers were compared. For incongruent results, final grading was made by mutual agreement after discussion. During EGD, patients' belching and retching were scored by endoscopist as follows: none, mild (no significant but presence of any event), moderate (able to complete examination but difficult and prolonged examination due to the event), and severe (cannot evaluate completely due to the event).
Results: We prospectively enrolled 369 consecutive subjects, and 11 subjects were excluded due to unclear GEJ image for LA classification. Finally, 358 subjects (183 males and 175 females, mean age 59.6 years, range 17–87 years) were analyzed in this study. Belching occurred in more than 70% of subjects (none: 29.7%, mild: 52.1%, moderate: 15.7%, severe: 2.5%). Retching occurred in 7.5% of subjects (none: 92.4%, mild: 3.4%, moderate: 4.2%, severe: 0%). LA classifications graded from image sets during withdrawal phase were upgraded significantly compared to classifications graded from image sets during insertion phase ($p < 0.001$; Wilcoxon signed ranks test). Totally, LA classification change was occurred in 49 subjects (13.7%). The most common change between insertion and withdrawal phase was from 'normal' to 'minimal change' (Table 1). Even though LA classification was not affected, there were several cases developing mucosal erosions and minor bleeding on GEJ during withdrawal phase (N = 12, 3.4%). Belching and retching was not significantly associated with LA classification change ($p = 0.075$ and $p = 0.128$ for each; Linear by linear association).

		Withdrawal phase				
	normal	minimal	LA-A	LA-B	Total	
Insertion phase	normal	159	38	4	0	201
	minimal	5	81	2	0	88
	LA-A	0	0	62	0	62
	LA-B	0	0	0	7	7
	Total	164	119	68	7	358

[Relationship of LA classifications between insertion and withdrawal phase]
Conclusion: LA classification of gastroesophageal reflux disease can be affected by endoscopic manipulation during EGD. We suggest taking pictures of GEJ during insertion phase rather than withdrawal phase for exact classification of reflux esophagitis.
Disclosure: Nothing to disclose

Reference

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P1779 SYMPTOMS AND CLINICAL PRESENTATION ARE NOT PREDICTIVE OF ESOPHAGEAL REFLUX BURDEN IN OBESE PATIENTS EVALUATED FOR BARIATRIC SURGERY

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Introduction: The spectrum of esophageal motor function, and reflux burden within obese subjects is not fully known. We compared esophageal questionnaire data, esophageal motor function and reflux metrics on pH-impedance monitoring among symptomatic and asymptomatic obese subjects presenting for bariatric surgery.
Aims and Methods: Our aim was to describe esophageal motor function and esophageal reflux metrics in symptomatic and asymptomatic obese subjects (BMI > 30). Patients undergoing esophageal function testing (HRM, pH-impedance monitoring off medications) over 1.5 years prior to bariatric surgery were eligible for inclusion. Prior foregut surgery, lack of symptom data and incomplete esophageal tests were exclusion criteria. Patients completed standardized questionnaires evaluating reflux symptoms (GERDQ). HRM studies were evaluated using Chicago Classification 3.0 and GERD classification metrics; acid exposure time (AET, physiologic < 4%, pathologic > 6%), numbers of reflux episodes and mean nocturnal baseline impedance (MNBI, normal > 2292 ohms) recorded 5 cm proximal to the lower esophageal sphincter (LES), and post-reflux swallow-induced peristaltic wave index (PSPW index) were extracted from pH-impedance monitoring. Data were analyzed to determine the discriminative value of esophageal physiologic testing in identifying patients with pathologic esophageal acid exposure in obese patients.
Results: 34 obese patients (43.0 ± 2.3 yr, 85%F, BMI 49.6 ± 2.7) fulfilled study inclusion criteria; 28 (82.4%) reported heartburn or regurgitation on questionnaires, and 17 had a positive GERDQ (≥8). Demographics, esophageal motor diagnoses and esophageal pH-impedance metrics were similar regardless of symptom status. Using AET > 6% and MNBI < 2292 as indicative of pathologic reflux, the two metrics were concordant in 21/34 (61.8%), discordant in 11/34 (32.4%); AET was borderline (4–6%) in 2 patients. Compared to AET < 4%, patients with AET≥4% had higher numbers of reflux episodes (43.5 ± 4.0 vs. 66.3 ± 10.3 respectively, $p = 0.02$), and lower mean MNBI (2184 ± 219 vs. 1128 ± 206 respectively, $p = 0.003$) and a trend toward a higher proportion with low MNBI (84.5% vs. 52.4%, $p = 0.06$), but similar BMI, symptom burden and motor characteristics. When the study cohort was segregated by MNBI, those with low MNBI (<2292 ohms) had lower BMI, higher total AET, supine AET, and a lower PSPW index compared to patients with normal MNBI ($p \leq 0.04$ for each comparison, Table). In the normal MNBI cohort, there was 1 patient (8.3%) with AET > 4 and no patients with AET > 6%, compared to 10 patients (45.5%) with AET > 4 and > 6 when MNBI was low ($p = 0.005$). Symptom assessment (GERDQ, MDQ), EGJ morphology and barrier function, esophageal body contraction vigor, and esophageal motor diagnoses could not differentiate AET-based or MNBI-based cohorts.

	Low MNBI (<2292 ohms)	Normal MNBI
Body mass index	46.5 ± 1.61	55.4 ± 3.37*
Ineffective esophageal motility	23%	25%
Number of reflux episodes	51.8 ± 6.01	53.0 ± 4.6
Total AET	4.93 ± 0.91	2.27 ± 0.47*
Supine AET	4.22 ± 1.09	0.64 ± 0.32*
AET > 6%	45.5%	0%
PSPW index	17.4 ± 2.3%	30.1 ± 3.1%*

[$p < 0.05$ compared to normal MNBI]*
Conclusion: Symptom questionnaires, HRM EGJ findings, and esophageal body motor function are unable to identify abnormal reflux metrics in obese patients, implying that ambulatory reflux monitoring is necessary to define reflux burden in this population. MNBI recorded 5 cm above the LES is able to segregate patients with abnormal AET from those with borderline and physiologic AET.
Disclosure: Nothing to disclose

P1780 HIGH PREVALENCE OF GERD IN PATIENTS SYMPTOMATIC ON PPI: RESULTS OF THE BRAZILIAN LOST PATIENT (LOPA) STUDY

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Introduction: Randomized controlled trials report ~30% of GERD patients complain of bothersome residual symptoms (heartburn/regurgitation) despite PPI. Some patients' symptoms are caused by functional disease, however only a minority undergo anti-reflux surgery or formal evaluation. The LOPA (Lost Patients) studies of GERD patients in Germany revealed 46% of patients

experienced residual symptoms ≥2 days per week despite PPI but < 10% received specific GERD diagnostics or were recommended treatment alternatives.
Aims and Methods: The LOPA Brazil study is a prospective, multicenter, observational study conducted in 17 reflux specialty centers with 21 physicians (9 gastroenterologists, 12 surgeons). "Lost Patients" – with chronic GERD, on PPI therapy ≥1 year, and not satisfied with their treatment, were asked to complete a questionnaire. The physician was then asked to complete the patient's physiological information and treatment recommendation following the visit.
Results: Responses were collected from 511 patients (42% male, mean age 46.7). Mean duration of GERD was 7.2 years; patients were prescribed PPI therapy on average 5.2 years.
Overall, 77% (n = 393) experienced heartburn and/or regurgitation ≥2 days per week (39% 4–7 days). More than half (54%) of patients were dissatisfied with their GERD condition (score 1–2 on an Likert scale 1–5). Reasons for dissatisfaction included breakthrough symptoms (88%), fear of risks associated with long-term medication (49%), inconvenience of daily medication (48%), and side effects from medication (5%).
However, 62% of dissatisfied patients (166/265) and 66% overall (331/499) had never visited a surgeon for their GERD; 49% of patients said their doctor advised them against surgery.
pH or pH-impedance results were available for 56% (n = 288) of patients. In the GI and surgeon groups, 51% (46/84) and 56% (113/206) had pathological 24-h pH (time pH < 4.0 > 6.0%), respectively, and 65% (54/84) and 69% (143/206) with pathological DeMeester score (> 14.7), respectively.
Despite similar patient-reported symptoms and physiological results, differences were seen in how patients were consulted. GIs recommended 18% of patients to surgical consult, 79% to continue PPI therapy, 8% to try different reflux medication, and 7% to seek treatment for a non-GERD condition. Surgeons recommended 63% for surgical consult, 20% to continue PPI therapy, 1% to try different reflux medication, and 9% to seek treatment for a non-GERD condition.
Conclusion: "Lost Patients" with bothersome GERD symptoms are frequently seen in practice in Brazil. A screening tool could help identify and consult these patients, and raise awareness in general practice of patients who could benefit from additional investigation and specialized treatment.
Disclosure: All authors have worked as medical consultants for Endostim.

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P1781 GERD PATIENTS ACROSS CULTURES HAVE SIMILAR CONCERNS: A COMPARISON OF "LOST" GERD PATIENTS IN GERMANY AND BRAZIL

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Introduction: The LOPA (Lost Patients) I Study in Germany revealed 46% of patients experienced heartburn and/or regurgitation symptoms at least twice per week despite PPI; 20% were dissatisfied with their treatment. Few patients had received specific GERD diagnostics or recommended treatment alternatives (< 10%) despite breakthrough symptoms.
Aims and Methods: Follow-up studies to explore the perceptions of these GERD "Lost Patients" were conducted in Germany and Brazil. Patients with chronic GERD, taking PPI therapy for at least 1 year, and not satisfied with their treatment were asked to complete a questionnaire including satisfaction with their current condition, reasons for dissatisfaction, and perceptions about anti-reflux interventions. In Germany, the study was conducted in 17 general practice clinics; in Brazil, the study was conducted in 17 reflux specialty centers (21 physicians).
Results: Responses were collected from 641 patients in Germany and 511 patients in Brazil. The German patients suffered from GERD on average 9.4 years and were on PPI therapy for an average of 7.8 years; 72% were dissatisfied with their current treatment (score 1–2 on a Likert scale 1–5). The Brazilian patients suffered from GERD on average 7.2 years and were on PPI therapy for an average of 5.2 years; 54% were dissatisfied. In the German group, 82% reported heartburn or regurgitation symptoms at least 2 days in the prior week (50% 4–7 days). In the Brazilian group, 77% reported symptoms at least 2 days in the prior week (39% 4–7 days). 51% of the German group vs. 32% of the Brazil group reported using additional medication other than their prescribed PPI at least 2 days per week (35% vs. 14% 4–7 days).
Reasons for dissatisfaction included breakthrough symptoms (87% Germany; 88% Brazil), fear of risks associated with long-term medication (33% Germany; 49% Brazil), burden of daily medication (29% Germany; 48% Brazil), and side effects from medication (7% Germany; 5% Brazil).
Reasons why dissatisfied patients had not undergone anti-reflux surgery included being unaware of surgical options for reflux (47% Germany; 18% Brazil), concern about possible complications (26% Germany; 31% Brazil), feeling their condition was not serious enough (17% Germany; 49% Brazil); and a recommendation against anti-reflux surgery from their doctor (6% Germany; 38% Brazil).
Conclusion: Despite different healthcare systems, chronic GERD patients dissatisfied with long-term PPI therapy are frequently seen in routine care in both Germany and Brazil. Most patients experience breakthrough symptoms despite PPI, but also share concerns about the long-term risk of medications and burden of taking daily medication. Specialized reflux centers and new less invasive anti-reflux interventions could benefit these patients.
Disclosure: All authors have worked as medical consultants for Endostim.

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P1782 ENDOSCOPIC TRANSORAL FUNDOPLICATION WITH MUSE FOR GASTROESOPHAGEAL REFLUX DISEASE: RESULTS OF A SINGLE-CENTER STUDY

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Introduction: Proton pump inhibitors (PPI) are the treatment of choice of gastroesophageal reflux disease (GERD), but adverse events associated with long-term therapy are emerging. Anti-reflux surgery can control GERD symptoms, however patients are usually reluctant to undergo surgery. Endoscopic Transoral Fundoplication with MUSE system (Medigus Ultrasonic Surgical Endostapler) can offer an effective therapy for GERD, less invasive than surgery.
Aims and Methods: This retrospective, chart review of prospectively collected data evaluates the clinical outcomes of patients who were treated with MUSE in a single center.
All patients who underwent MUSE at our endoscopy center between May 2015 and December 2017 were retrospectively identified from a prospective database, collected and analyzed. The procedure was offered to patients with GERD, diagnosed by EGD and pH-monitoring study, who required and responded to pharmacological therapy. Symptoms were evaluated with a validated clinical score – GERD Health-Related Quality of Life (HRQL) score – and by monitoring the use and dosage of PPI. Objective parameters including findings at esophagogastroduodenoscopy (EGD) and esophageal pH-monitoring study were assessed before the procedure, after 6 months and every year. Clinical success was defined by ≥50% reduction of the dosage of PPI and by the GERD HRQL score (≥50% reduction compared to baseline or normalization [< 10] of the score).
Results: A total of 20 patients underwent MUSE during the study period (mean age 50.4 [± SD14.6], 65% males). The last 5 patients did not complete the minimum 6-month follow-up and were excluded from this analysis. One patient was lost to follow-up immediately after treatment. Mean symptoms duration before MUSE was 63 months (30–240). A median follow-up of 14.1 (6–36) months was available for 14 patients. At the date of the last visit, clinical success was achieved in 78.6% of patients (9 patients [64%] discontinued PPI and 2 patients [14%] take < 50% of the initial dosage). Three patients (21.4%) did not change the dosage of PPI after the procedure, because of enduring symptoms. All the clinical failures were diagnosed at the 6-month follow-up visit.
GERD-HRQL score was normalized or improved by ≥50% compared to baseline in 11 patients (78.6%) (table 1). The post-operative DeMeester score was significantly reduced compared to baseline ($p < 0.05$). De Meester score was normal in 6/10 patients (60%) with post-operative pH-monitoring study, and considerably reduced in an additional 10% of patients.

14 patients	Baseline 14 patients with f/u	Last follow-up (mean 14 months) 14 patients	p value
GERD-HQRL (mean, SD)	30.4 (±7.4)	13.3 (±10.8)	< 0.005
%TRT (mean, SD)	13.8% (±10.5)	3.75% (±16.6)	0.0677
DeMeester Score (mean, SD)	48 (±47.7)	48 (±47.7)	< 0.005
Esophagitis (%)	35.7	21	0.065

[Table 1]
Postoperative EGD revealed grade A esophagitis in 3 patients, and normal findings in 11 patients.
No adverse events occurred during the procedure and follow-up.
Conclusion: Our study confirms the safety and efficacy of the MUSE procedure for the treatment of GERD. Studies on large cohorts of patients, and with a longer follow-up, are needed to consolidate the role of MUSE in the treatment of GERD.
Disclosure: Nothing to disclose

P1783 ALGINATE AS ADD-ON FOR GORD WITH INSUFFICIENT PPI EFFECT: THE LOPA III TRIAL

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Introduction: Chronic reflux patients with long-term PPI therapy frequently have persistent symptoms. At least 20% of the patients are unhappy with their therapy. Therapy options are limited. A critical source of the persistent acid reflux is the *acid pocket*, which can be treated effectively by the non-systemic reflux suppressing action of alginates.
Aims and Methods: Chronic GERD patients with at least one year of PPI long-term therapy, who were dissatisfied with their therapy, were treated over a period of 14 days with alginate as add-on and when required (up to 4 times daily) in a prospective, multi-centre observational study in GP practices. The frequency of symptoms in the week before treatment was recorded, as well as in the second week of the study phase and the consumption of alginate. The validated GERD Q score was also applied. The patients assessed satisfaction with the therapy on a five-point Likert scale (very unhappy – happy) before the beginning and at the end of the study. The primary endpoint of the study was improvement in satisfaction with the therapy by ≥ 1 point.
Results: 155 patients (53% women, median age 57 (18–85) years) entered the study. Six patients had to be excluded from the final efficacy analysis (no intake of study drug, lost to follow-up). The median duration of GORD was 8 (1–50) years and the median time on PPI therapy was 6 years. On average the patients took 3 sachets of alginate per day. The alginate therapy led to an improvement by at least 1 point on the Likert scale in 72% of patients (1 step $n=45$, 2 steps $n=41$, 3 steps $n=16$, 4 steps $n=5$). Patients with a Gerd Q score > 8 had a higher response rate at 81%. There was improvement in all typical reflux symptoms and sleep disorders. The treatment was generally well-tolerated.
Conclusion: In chronic GORD patients on long-term PPI therapy who are dissatisfied because of remaining troublesome symptoms an alginate as add-on and taken on demand is a new and effective option to improve patients satisfaction. Typical reflux symptoms are a valuable predictor of treatment success.
Disclosure: J. Labenz received speakers honoraria, consulting fees and an unrestricted grant from Reckitt Benckiser G. Labenz received speakers honoraria from Reckitt Benckiser

P1784 EFFECTS OF DEXRABEPRAZOLE ON INTRAGASTRIC AND INTRAESOPHAGEAL ACIDITY IN GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Gastroesophageal reflux disease (GERD) is a prevalent disease worldwide. The prevalence of GERD was found to be 22.8% in Turkey. The treatment of GERD is still based on acid suppression therapy and accordingly proton pump inhibitors (PPIs) are the most frequently preferred agents. Complications related to long-term PPI consumption are always worrying.
Aims and Methods: To evaluate efficacy and safety of dexrabeprazole 10 mg on intragastric and intraesophageal acidity in gastroesophageal reflux disease (GERD) patients.
This open-label, single-arm efficacy and safety study included patients aged between 18 and 65 years who were diagnosed with GERD. During the screening visit, the symptoms of the patients were recorded. The patients were prescribed to receive dexrabeprazole 10 mg tablet daily for 7 days. Physical examination, laboratory analysis for safety, upper gastrointestinal endoscopy and 24-hour intragastric and intraesophageal impedance-pH measurements were performed. In addition, the Reflux Symptom Score was calculated by applying a validated questionnaire both before and after the treatment.
Results: Among 14 patients included, 2 were unable to complete the study (one due to biliary colic and the other due to missing visits). The analyses were performed in 12 patients (7 males, 5 females). After one-week treatment period, significant decreases were observed in the percentage of time for 24-hour intragastric $pH<4$ (from 84.15 ± 26.51 to 50.59 ± 18.32; $p=0.0269$) and $pH<2$ (from 35.03 ± 41.48 to 11.68 ± 14.88; $p=0.0125$) and in the area under the curve (from 18714 ± 25739 to 6078 ± 12898, $p=0.0236$ for $pH\leq4$ and from 1562.4 ± 2777.1 to 23.550 ± 46.191, $p=0.0156$ for $pH\leq2$). The percentage of time for 24-hour intraesophageal $pH<4$ decreased after treatment (4.48 ± 3.08) as compared with the pre-treatment value (24.68 ± 28.38; $p=0.0253$). A significant change was also observed in the nocturnal measurement (from 45.24 ± 24.41 to 54.49 ± 17.63; $p=0.0001$). Significant decreases were observed after treatment in DeMeester score (from 44.74 ± 25.92 to 16.36 ± 10.45; $p=0.0036$) and acid reflux (from 70.3 ± 21.7 to 19.1 ± 14.2; $p < 0.0001$). The heartburn and regurgitation scores significantly decreased from the first day of treatment. No serious safety event was determined.
Conclusion: Dexrabeprazole evaluated in this study is the R(+) enantiomer of rabeprazole. The standard dose of rabeprazole is 20 mg; however, R enantiomer is recommended to be used at a dose of 10 mg. It has been demonstrated that R(+) rabeprazole is more effective than racemic rabeprazole and S(-) rabeprazole in preventing acid-induced gastric lesions. In conclusion, dexrabeprazole 10 mg was considered an effective and safe option for GERD treatment.
Disclosure: Nothing to disclose

P1785 PROSPECTIVE, RANDOMIZED EX VIVO TRIAL TO ASSESS THE ANTI-REFLUX EFFECT OF ANTI-REFLUX MUCOSECTOMY IN PORCINE MODEL

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Introduction: Both long-term proton pump inhibitor (PPI) use and surgical fundoplication have potential drawbacks as treatments for chronic gastroesophageal reflux disease (GERD).
Aims and Methods: Our aim was to investigate the safe and efficacy of anti-reflux mucosectomy (ARMS) in porcine and determine the optimal circumference of resection in relation to gastroesophageal junction (GEJ). Nine swine were allocated into the following 3 groups by computerized randomization: Group A: control, Group B: 1/3 circumference of esophagus, Group C: 2/3 circumference of esophagus. We performed mucosectomy with a crescentic mucosal resection at 3cm above GEJ and 1cm below GEJ. The animals were kept on a liquid diet for 24 h prior to endoscopy. At 6 weeks, animals underwent esophagoscopy, X-ray barium meal, gastric yield pressure (GYP) and gastric yield volume (GYV) determination, and sacrifice for histopathologic to evaluate the cardia wall thickness and collagen deposition.
Results: The weight of swine were no significant difference, and swine had maintained their weight in three groups after the procedure. We both found scar formation at the GEJ in group B and C. Acute inflammatory cells and fibrous tissue were found in study groups. Compared with group A and group B, group C produced significantly higher GYP (24.23 ± 3.42mmHg, $p=0.009$) and significantly smaller GYV (2200.0 mL ± 238.96, $p=0.039$) after 6 weeks. Barium meal X-ray showed that the width of cardia was narrower (13.06 ± 2.10mm, $p=0.018$) and the time of wave was longer (2.88 ± 0.28s, $p=0.032$) in group C after the procedure, compared group A and B.
Conclusion: Our study demonstrated the potential anti-reflux effect and safety of ARMS. We also recommend the 2/3 circumference resection of esophagus at 3 cm distance from the GEJ.
Disclosure: Nothing to disclose

P1786 ACUTE ADMINISTRATION OF FRUCTANS INCREASES THE NUMBER OF TRANSIENT LOWER ESOPHAGEAL SPHINCTER RELAXATIONS IN HEALTH

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Introduction: Dietary measures such as avoiding high-fat meals, sweets, alcoholic and carbonated beverages, are often advised to patients with gastro-esophageal reflux disease (GERD). Fermentable Oligo-, Di-, Mono-saccharides and Polyols (FODMAPs) induce lower gastrointestinal symptoms through their effects on intestinal function. However, the effect of FODMAPs on upper gastrointestinal physiology, including the occurrence of transient lower esophageal sphincter relaxations (TLESRs), reflux events and GERD symptom induction is unknown.
Aims and Methods: We aimed to investigate the effect of acute administration of two key FODMAPs, fructose and fructans, on the number of TLESRS, reflux episodes and symptom perception in healthy volunteers (HV). After an overnight fast, 20 HV (10 males, 30 y [21–56]) underwent a high-resolution impedance manometry. The number of TLESRs and reflux episodes were quantified 5 hours after consumption of a high-caloric meal (mashed potatoes and meatloaf; 740 kcal) enriched with 40g of either fructose, fructans or glucose (placebo). The HV undertook all 3 challenges in a single-blind randomized fashion with at least 1 week washout. Results were analyzed using mixed models.
Results: Overall, there was a significant difference in the number of TLESRs between the three conditions ($p=0.006$, Table 1). Post hoc analysis showed a significantly higher number of TLESRs in the fructan condition compared to placebo (corrected p-value, $p=0.005$) and a trend for fructose versus placebo ($p=0.05$, Table 1), which did not survive Bonferroni correction. The total number of reflux events was not affected by either FODMAP condition. The number of gas and mixed reflux events tended to be higher in the fructan condition, but this did not reach statistical significance (Table 1). LES pressures dropped significantly in the first postprandial hour in all 3 conditions to recover slowly back to baseline values ($p < 0.0001$), without any difference in LES pressure between the three conditions.
Conclusion: Ingestion of fructans increased the number of TLESRs compared to placebo. This increase was not seen after ingestion of fructose. Fructans are rich in FODMAPs, however fructose is only a FODMAP when present in excess of glucose. The absorption of fructose is probably enhanced because of the presence of other sugars including glucose in the meal. Ingestion of either FODMAP did not alter the number of reflux episodes in the HVs, but GERD patients have a higher incidence of reflux during TLESRs. Therefore, the effect of FODMAPs such as fructans or a low FODMAP diet on reflux parameters in GERD patients remains to be investigated.

	Glucose (placebo)	Fructose	Fructans	p-value of the main effect
TLESRs	25.2 ± 6.7	27.0 ± 8.7	28.4 ± 7.4	**0.006**
Reflux	16.6 ± 8.0	15.9 ± 9.6	18.7 ± 8.3	0.16
Mixed + Gas	6.7 ± 5.9	7.1 ± 5.7	8.8 ± 7.1	0.12

[The number of TLESRs and reflux episodes in the three different conditions (mean ± SD).]

Disclosure: Nothing to disclose

P1787 RISK FACTORS FOR PATHOLOGICAL UPGRADING OF ESOPHAGEAL LOW-GRADE INTRAEPITHELIAL NEOPLASIA DIAGNOSED WITH ENDOSCOPIC FORCEPS BIOPSY

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Introduction: Several studies have reported changes of the pathologic analysis before and after endoscopic resection (ER) for esophageal intraepithelial neoplasia. We aimed to explore the risk factors for pathological upgrading after ER for lesions diagnosed as low-grade intraepithelial neoplasia (LGIN) with preoperative biopsy.

Aims and Methods: A total of 70 lesions which were initially diagnosed as esophageal LGIN by forceps biopsy and later underwent ER from November 2013 to July 2017 were included. They were divided into two groups according to pathological grading after ER. The risk factors for post-operation pathological upgrading were analyzed.

Results: The study enrolled 70 patients. The change of post–operation pathological diagnosis occurred in 30 (42.9%) patients (upgrade 28 (40.0%); downgrade 2 (2.9%)). In the upgrading group, ER upstaged it to high-grade intraepithelial neoplasia (HGIN) for 20 (28.6%) lesions and to early esophageal cancer for 8(11.4%) lesions. Univariate analysis showed that lesions≥1/2 esophageal circumference (P = 0.006), maximal longitudinal-diameter≥3cm (P = 0.005), submucosal infiltration in endoscopic ultrasonography (P = 0.037), lesions based on depressed type (0-IIa+IIc, 0-IIc, 0-IIc+IIa)(P = 0.005) and reddish surface (P = 0.019) were factors for pathological upgrading compared with preoperative biopsy. Multi-factor analysis indicated maximal longitudinal-diameter≥3cm (P = 0.008) and reddish surface (P = 0.013) were independent factors for pathological upgrading compared with preoperative biopsy.

Conclusion: Pathological upgrading of LGIN after ER was common, especially in large lesions with reddish surface. Endoscopic resection may be recommended for these lesions instead of follow-up observation.

Disclosure: Nothing to disclose

P1788 PLANNED SEMI-CIRCULAR ENDOSCOPIC SUBMUCOSAL DISSECTION FOR WIDESPREAD SUPERFICIAL ESOPHAGEAL CANCER

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Introduction: Although endoscopic submucosal dissection, which makes it possible to perform *en bloc* resection with tumor-free lateral and vertical margins, has been accepted as the standard treatment of superficial esophageal cancer, the incidence of stricture formation caused by ESD for widespread lesions is high. Some studies have reported that the use of oral steroids and local steroid injection are useful for preventing such stricture formation. We perform "planned ESD" to prevent severe stricture at our institution. When we resect widespread lesions that involve three-quarters or more of the circumference of the esophageal lumen, semi-circular ESD is performed. Small portions of the intraepithelial neoplasm are left. After reviewing the histopathological findings, we attempt a second endoscopic treatment (ESD, endoscopic mucosal resection, or argon plasma coagulation) to manage the remaining parts.

Aims and Methods: The aim of this study was to evaluate the usefulness of planned ESD for widespread superficial esophageal cancer in controlling post-procedural esophageal stricture. Between September 2005 and April 2015, 204 superficial esophageal neoplasms were treated with ESD in 192 patients. We evaluated clinical outcomes of ESD for the tumors in 22 patients (males: 20, females: 2, mean age: 68.5 years old) that involved three-quarters or more of the circumference of the esophageal lumen.

Results: The involved esophageal circumference was three-quarters in 13, four-fifths in 4, and whole in 5. Seventeen lesions were resected with positive tumor-lateral margins, and five had unknown margins, Twenty lesions underwent semi-circular resection, and two circular resection. Six patients received local steroid injection, 6 received systemic steroid treatment, and 10 received systemic steroid treatment combined with local steroid injection. The median number of endoscopic balloon dilatations was 1 session, 9 patients (41%) did not require any endoscopic balloon dilatation, but 4 (18%) required more than 20 sessions. The major complications were two cases of perforation. The median postoperative hospital stay was 5 days (range 3∼29 days). The depth of invasion was as follows, mucosal in 18 lesions, and submucosal invasion in 4 lesions. The mean tumor size was 51mm (range 42–90mm), and microvascular permeation was observed in two cases. Five cases of remnants were retreated endoscopically, and two required esophagectomy. Three patients developed local recurrence, and all cases were able to be retreated endoscopically. During the median follow-up period of 60 months (range 36-148), all the cases are still alive.

Conclusion: Planned semi-circular ESD for widespread superficial esophageal neoplasm may be an efficient strategy for preventing severe stricture formation.

Disclosure: Nothing to disclose

P1789 THE MID-TERM OUTCOMES OF ENDOSCOPIC TREATMENT FOR SUPERFICIAL CERVICAL ESOPHAGEAL CANCER

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Introduction: Cervical esophageal cancer (CEC) is a less common form of cancer. The survival rates of CEC patients remain poor because it is often locally advanced at the time of its diagnosis. With advances in endoscopy, more cases of superficial CEC are being found.

Aims and Methods: Endoscopic treatment was performed for 72 lesions of superficial CEC in 61 patients (male, n = 49; female, n = 19; median age, 68 years; range, 40–88 years) from April 2005 to December 2016. We divided the patients into 3 groups according to the location within the cervical esophagus: Group A (with invasion to the hypopharynx), Group B (proximal margin within 2 cm from the orifice of the esophagus), and Group C (proximal margin >2 cm from the orifice of the esophagus). Multiple esophageal cancers were observed in 50 patients (81.9%). CEC coexisted with primary head and neck cancer in 42 patients (68.8%). The aim of this retrospective study was to clarify the clinical outcomes of endoscopic treatment in patients with superficial CEC.

Results: Nineteen lesions (hypopharynx-dominant, 14 lesions; cervical esophagus-dominant, 5 lesions) were enrolled as Group A, 21 lesions were classified into Group B, and 32 lesions as were classified into C. Five lesions of Group A and One lesion of Group B were treated by neoadjuvant chemotherapy with the aim of preserving the larynx. Endoscopic treatment was performed under general anesthesia in Groups A and B, while 20 lesions (62.5%) in Group C were treated under intravenous anesthesia.

The procedures performed in Group A included transoral surgery (TOS) with endoscopic submucosal dissection (ESD; 12 lesions), TOS (3 lesions), endoscopic mucosal resection (EMR; 3 lesions), and ESD (1 lesion). The procedures performed in Group B included ESD (15 lesions), and EMR (6 lesions). The procedures performed in Group C included EMR (24 lesions), and ESD (8 lesions). Regarding the depth of tumor invasion, 5 lesions in Group A (cervical esophagus-dominant) were carcinoma *in situ* or showed micro-invasion, while 14 lesions (hypopharynx-dominant) showed subepithelial invasion.

The median size of the tumors was 29 mm (range, 8–52 mm), 3 lesions showed vascular invasion, all lesions were followed with no additional therapy.

Nineteen lesions in Group B were diagnosed as mucosal cancer, and 2 lesions invaded the submucosa. The median tumor size was 18 mm (range, 6–50mm), 2 lesions showed vascular invasion, and one lesion was treated with additional chemoradiotherapy.

Twenty-seven lesions in Group C were diagnosed as mucosal cancer; 5 lesions invaded the submucosa. The median tumor size was 11 mm (range, 2–25 mm), 3 lesions showed vascular invasion, and one lesion was treated with additional chemoradiotherapy.

Regarding complications, 4 patients experienced laryngeal edema and 4 developed esophageal stricture; however, there were no severe complications. The median hospital stay was 4 days (range, 2–10 days). There was one case of local recurrence in Group B; endoscopic retreatment was successful in this case. Lymphadenectomy were performed for three patients with lymph node metastasis occurred in Group A. During the median follow-up period of 48 months (range, 16–153 months), 6 patients died from other cancer and 2 died from other disease. There were no esophageal cancer-related deaths. Laryngectomy was performed in one case due to another hypopharyngeal cancer; the larynx was preserved in the other cases (98.3%). The cause-specific survival rate at 3 years was 100%.

Conclusion: Endoscopic treatment is less invasive and effective for improving the prognosis of patients with CEC.

Disclosure: Nothing to disclose

P1790 SURVIVAL RATES FOR PATIENTS WITH BARRETT'S HIGH-GRADE DYSPLASIA AND OESOPHAGEAL ADENOCARCINOMA WITH OR WITHOUT HUMAN PAPILLOMAVIRUS

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Introduction: High-risk (hr)-human papillomavirus (HPV) has been associated with Barrett's dysplasia and oesophageal adenocarcinoma (OAC). Nevertheless, the prognostic significance of oesophageal tumour HPV status is unknown.
Aims and Methods: We hypothesized that HPV associated oesophageal tumours would show a favourable prognosis (as in viral positive head and neck cancers). Thus, we studied the association between HPV and related biomarkers of high-grade dysplasia (HGD)/OAC and survival. Pre-treatment biopsies were used for HPV DNA determination via PCR, in-situ hybridization for E6/E7mRNA and immunohistochemistry for p16INK4A and p53. Sequencing of TP53 was also undertaken.
Results: Amongst 142 HGD/OAC patients [M:F, 126 (88.7%): 16 (11.3%)] with a mean age of 66.0, SD+/− 12.1, 37 were HPV+ and 105 HPV-. HPV+ patients were mostly p16ink4a$_{high}$, p53$_{low}$ and wild-type TP53. There were more Tis/T1/T2 tumours in HPV+ subjects as compared with HPV- patients (75.7% versus 54.3%, p = 0.02). Mean disease-free survival was superior in the HPV+ group (40.3 months versus 24.1 months, p = 0.003) as was overall survival [43.7 months versus 29.8 months, p = 0.009]. Recurrence/progression was much reduced in the HPV+ cohort (24.3% vs 58.1%, p = 0.0004) as was distant metastasis (8.1% vs 27.6%, p = 0.015) and death from EAC (13.5% versus 36.2%, p = 0.01). HPV and transcriptionally active virus positivity were both associated with a superior DFS (HR = 0.33; 95%CI: 0.16–0.67, p = 0.002) and (HR = 0.44; 95%CI: 0.22–0.88, p = 0.02) respectively (log-rank test). E6/E7 mRNA positivity had borderline significance for improved DFS (HR = 0.50; 95%CI: 0.24–1.05, p = 0.069) but not p16INK4A$_{high}$ or p53$_{low}$. On multivariate analysis, superior DFS was demonstrated for HPV (HR = 0.39, 95%CI; 0.18–0.85, p = 0.02) biologically active virus (HR = 0.36, 95%CI: 0.15–0.86, p = 0.02), E6/E7mRNA (HR = 0.36, 95%CI: 0.14–0.96, p = 0.04) and p16$_{high}$ (HR = 0.49, 95%CI: 0.27–0.89, p = 0.02).
Conclusion: HPV+ HGD/OAC is a distinct biological entity with a favourable prognosis as compared with viral negative oesophageal tumours. If these findings are confirmed in larger cohorts with more advanced disease, it presents an opportunity for treatment de-escalation in the hope of reducing toxicity without deleteriously affecting survival.
Disclosure: Nothing to disclose

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P1791 THE MODIFIED GLASGOW PROGNOSTIC SCORE (MGPS) HAVE A PROGNOSTIC ROLE IN ESOPHAGEAL CANCER. (COMPARISON WITH PLASMA FIBRINOGEN AND SERUM ALBUMIN LEVELS (FA SCORE) AND NEUTROPHIL TO LYMPHOCYTE RATIO (NLR))

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Introduction: Although the outcome of treatment of esophageal cancer has been improved, esophageal cancer still has poor prognosis. More accurate and convenient prognostic predictions are desired. It is reported that modified Glasgow Prognostic Score (mGPS) using albumin and CRP levels reflects long-term prognosis of solid cancer. We investigated the reliability of mGPS for prediction of long-term recurrence and survival.
Aims and Methods: One hundred and twenty-seven patients who underwent curative esophagectomy for esophageal cancer between February 2011 and January 2016 were enrolled. We investigated the reliability of mGPS for the prediction of OS and DFS. Furthermore, the comparison with FA score and NLR was conducted.
Results: The patients were105 males and 22 females. The average age was 63.9 ± 8.7 years old (35–81 years old). 57, 24, 37 and 9 patients were diagnosed with clinical stage I, II, III and IV. 64 patients received chemotherapy and 6 patients received chemoradiotherapy as a preoperative treatment. Thoracoscopic esophagectomy was performed in 108 patients and transthoratic esophagectomy was performed in 19 patients. Overall survival (OS) for 3 years was 71.0% and disease-free survival for 3 years (DFS) was 58.0%. This analysis included 104 patients with mGPS 0 (low-mGPS group) and 23 patients with mGPS 1 or 2 (high-mGPS group). OS and DFS in the high-mGPS group were significantly shorter (OS; p = 0.00008, DFS; p = 0.0002). In multivariate analysis, high levels of mGPS were independent risk factors on OS and DFS, such as ages and clinical stages (OS; HR 2.70, 95% CI: 1.08–6.76, p = 0.034. DFS; HR 2.16, 95% CI: 1.01–4.63, p = 0.046). The FA score and the NLR were not significant risk factors in multivariate analysis.
Conclusion: High levels of mGPS were significantly prognostic factors in patients who had undergone esophagectomy for esophageal cancer. More patients for analysis are needed.
Disclosure: Nothing to disclose

P1792 OUTCOMES OF ESOPHAGECTOMY FOR PATIENTS AFTER NON-CURATIVE ENDOSCOPIC RESECTION OF EARLY ESOPHAGEAL CANCER

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Introduction: ESGE guidelines advise surgery in case of non-curative endoscopic resection in the esophagus considering the risk of lymph node metastasis. To our knowledge, no study had examined the outcomes of this surgery.
Aims and Methods: A retrospective review from 2012 to 2017 was performed in the department of digestive endoscopy of four French tertiary referral center. All patients had a non-curative endoscopic resection, defined by deep mural invasion, vertical positive margins, or poor histopronostic features, followed by esophagectomy after a multidisciplinary meeting decision. Outcomes measurements were the histological outcomes of surgical resection vs endoscopic resection, the rate of postoperative complications, overall, disease-free, and cancer specific survival and the evaluation of the post-operative complications.
Results: Twenty-one patients (10 with squamous cell carcinoma and 11 with Barrett's carcinoma) with a median age of 66 years were included. Tumors are localized in the mid and the lower esophagus for 11 and 10 patients respectively. The reasons of non-curative resection were: positive vertical margins (n = 6), SCC invading the muscularis mucosae (n = 5) and lesion invading the submucosal layer (n = 13), poorly differentiated cancers (n = 11) and presence of lymphovascular invasion (n = 5). Surgical techniques were Ivor-Lewis and transhiatal esohagectomies. Only two patients, with deep submucosal infiltration (500 for a squamous cell carcinoma, and 1200 µm for a Barrett's carcinoma) and poor differentiation had a lymph node involvement on the surgical specimen. We diagnosed 2 relapses (mediastinal lymph nodes, lung metastases) during a median follow-up of 16 months. The patient with lung metastases only had lymph node involvement on the surgical specimen. There were 4 deaths during the follow-up: one postoperative mortality (90-day), one death related to

aspiration pneumonia due to post-operative esophageal stricture, and two non-cancer related deaths. Forty-two percent of the patients (9/21) had a severe post-operative morbidity according to the Clavien-Dindo classification: IIIa (n = 2), IIIb (n = 3), IVa (n = 3) and V (n = 1). At the end of the follow-up, overall, disease-free and cancer specific-survival were 81%, 91%, and 91% respectively.
Conclusion: Esophagectomy after non-curative endoscopic resection of esophageal cancers allowed to resect lymph node metastases in two out 21, at the cost of 42% severe morbidity and 5% perioperative morbidity. Esophagectomy in this setting has comparable morbidity and mortality to that of esophagectomy for larger tumors, and the risk of lymph node involvement of early esophageal cancer, as well as the possibility of chemoradiation therapy or close follow-up need to be assessed in multidisciplinary meetings before indicating esophagectomy after endoscopic resection.
Disclosure: Nothing to disclose

P1793 ACCURACY OF ENDOSCOPIC TUMOR DEPTH PREDICTION IN SUPERFICIAL ESOPHAGEAL SQUAMOUS CARCINOMA

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Introduction: Even though the accurate prediction of tumor depth (T staging) for superficial esophageal squamous carcinoma (SESC) is essential for making the proper decision on treatment strategy, there are not enough studies about standard endoscopic criteria. In this study, we tried to know the diagnostic accuracy of conventional endoscopy for T staging in SESC and to make the conventional endoscopic criteria for classifying mucosal and submucosal esophageal cancer.
Aims and Methods: For first step, new endoscopic criteria of mucosal (T1m) and submucosal cancer (T1sm) were created by 2 experienced endoscopists with 60 randomly selected cases of pathologically proven SESC. For second step, endoscopic findings of total 292 cases, which were treated by surgical or endoscopic resection for SESCs between 1991 and 2010, were reviewed according to the new endoscopic criteria to predict the tumor depth.
Results: The overall accuracy of new endoscopic criteria was 79.5% (232/292). The sensitivity, specificity, and positive and negative predictive values of mucosal cancers were 78.4%, 81.0%, 85.4%, and 72.6%, and those for submucosal cancers were 81.0%, 78.4%, 72.6%, and 85.4%. The prediction rate of mucosal cancers was high (95.9%) when the lesions were shown as flat or slightly elevated/depressed with smooth/even surface regardless of size. And those of submucosal cancers were high (85.6%) when the lesions were irregular/nodular protrusion regardless of size. In multivariate analysis, tumor size less than 3cm (odd ratio 0.450, p = 0.014) was found as independent affect for the accuracy of endoscopic criteria.
Conclusion: The accuracy of endoscopic prediction for estimating T staging is acceptable in SESC. Careful endoscopic examination with new endoscopic criteria in SESC can provide more information and help to decided treatment methods between surgery and endoscopic resection.
Disclosure: Nothing to disclose

P1794 ARTIFICIAL INTELLIGENCE FOR AUTOMATED DETECTION OF EARLY OESOPHAGEAL SQUAMOUS CELL NEOPLASIA THROUGH CLASSIFICATION OF INTRAPAPILLARY CAPILLARY LOOPS

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Introduction: Intrapapillary capillary loop (IPCL) patterns provide an endoscopically visible marker of early squamous cell neoplasia (ESCN). Narrow-band imaging with magnification endoscopy (ME-NBI) allows detailed assessment of these microvascular patterns. The Japanese Endoscopy Society (JES) **AB** classification describes ESCN and predicts invasion depth based on the intrapapillary capillary loop (IPCL) pattern. Early lesions are amenable to endoscopic therapy (EET) so the prompt characterisation and identification of mucosal lesions is vital. Endoscopists, particularly those in areas with low ESCN prevalence, may not be familiar with the characterisation of ESCN. We have designed a novel deep convolutional network (CNN) able to classify IPCL patterns as normal (A) or abnormal (B1/B2/B3), in order to alert endoscopists to abnormal areas in ESCN during lesion assessment.
Aims and Methods: 17 patients were recruited at a referral centre in Taiwan. Endoscopies were performed using ME-NBI (Olympus). IPCLs were classified for each video by 2 experts as normal (type A), or abnormal (type B1/B2/ B3), using the JES classification. Matched tissue was obtained by ESD for histologic evaluation of invasion depth. Images were quality controlled to remove uninformative (blurred) images. Our dataset consisted of 7046 images. A CNN was developed with five-fold cross validation. On average, each fold used 3962 images for training, and 1637 unseen images (846 normal and 791 abnormal) for testing. Class activation maps were generated to provide a clinically interpretable network output. Accuracy, F1 scores, sensitivity and specificity for abnormal IPCL detection were calculated.
Results: 17 patients were included (10 had early neoplasia [1 high-grade intraepithelial neoplasia (HGIN) 4 carcinoma in situ (CIS) invading to the lamina propria, 4 to the muscularis mucosa and 1 to the submucosa] and 7 were normal). Our algorithm operates at video rate and had an accuracy for differentiating abnormal IPCL patterns (type B1, B2, B3) from normal (type A) of 93.69%. The average F1 score for identifying abnormal areas of ESCN based on IPCL classification was similarly high at 92.2%. Our network also achieved a sensitivity and specificity for abnormal IPCL detection of 89.3% and 98% respectively.
Conclusion: We introduce a novel application of deep learning by developing a real-time CNN, with promising results in classifying squamous mucosa as normal or neoplastic based on the JES IPCL classification. Our system demonstrates a high accuracy, sensitivity and specificity for differentiating type A from type B1/2/3 IPCLs. Importantly for potential clinical applications our CNN operates in real-time. eCAMs demonstrate a novel and clinically interpretable network output – allowing clinicians to visualise which areas of IPCL patterns were classified as abnormal by the CNN. Further work is underway to develop a multiclass classifier, using a larger dataset, to distinguish between the subtypes of IPCL patterns. Such a validated system could be used in vivo to alert endoscopists to the presence of ESCN and direct planning of appropriate EET.
Disclosure: Nothing to disclose

P1795 CHARACTERISTICS OF SYNCHRONOUS LESIONS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC EPITHELIAL NEOPLASIA

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Introduction: Since endoscopic submucosal dissection (ESD) has been accepted as the treatment of choice for early gastric cancer (EGC) without lymph node metastasis, synchronous gastric epithelial neoplasia is no longer rare in the clinical practice. Knowledge about the characteristics associated with synchronous gastric epithelial neoplasia is of great importance to prevent delayed diagnosis.
Aims and Methods: Between November 2008 and December 2014, a retrospective study was conducted in a single tertiary referral hospital. Patients who underwent ESD due to EGC or high-grade dysplasia were analyzed to evaluate the incidence of synchronous gastric epithelial neoplasia and the factors associated to synchronous and overlooked synchronous lesions.
Results: A total of 488 patients were analyzed in this study. Synchronous lesions were found in 59 patients (12.1%) during the mean 37.7 months of follow-up. Among 77 synchronous lesions, 25 lesions (32.4%) were overlooked at the time of initial ESD. Age of $\geq$ 65 years, moderate to severe endoscopic atrophic gastritis, and elevated morphology of primary lesions were associated with synchronous gastric epithelial neoplasia. An important factor associated with overlooked lesions is the non-elevated morphology of lesions.
Conclusion: Careful endoscopic examination of the whole stomach is necessary in patients who are older and who have moderate to severe atrophic gastritis and elevated morphology of lesions to prevent delayed diagnosis of synchronous gastric epithelial neoplasia, especially non-elevated lesions. These factors may be considered as to selecting candidates for ESD.
Disclosure: Nothing to disclose

P1796 TYPE AND TUMOR SIZE AFFECT CLINICAL OUTCOME IN GASTRIC NEUROENDOCRINE NEOPLASMS: A MULTICENTRE RETROSPECTIVE STUDY

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Introduction: Gastric neuroendocrine neoplasms (gNENs) are classified into three categories: type I associated with atrophic body gastritis, type II related to multi-endocrine neoplasia type I, and type III when no background pathology is

identified. Type I gNENs are indolent diseases, mostly with low proliferative index (Ki67 ≤ 2%), and extremely low metastatic risk (<5%). Tumors > 1 cm are usually considered at higher risk of malignancy deserving more aggressive management, although data supporting this recommendation are scanty. Conversely, type III are malignant diseases with extremely high risk of dissemination and mortality. However, beyond the above-mentioned clinical classification, little is known on additional factors potentially related with poor clinical outcome in gNENs.

Aims and Methods: Retrospective analysis of type I and type III gNENs collected in four referral centers. Risk factor analysis was performed by logistic regression model. A composite negative endpoint was defined to identify patients with poor clinical outcome, and was considered to have occurred if tumor-related death, presence of metastases, or presence of angioinvasion at histology was observed. ROC curve analysis was used to identify the cutoff level variables as predictors of presence of negative endpoint. Survival probabilities were calculated by the Kaplan-Meier method. The distribution of continuous variables was reported as median and interquartile range (IQR; 25th to 75th percentiles). Mann-Whitney U test was used to compare the continuous variables.

Results: 161 patients included, with a total of 195 tumors: 171 type I (87.7%), and 24 type III (12.3%). Compared with type III, type I gNENs were smaller (median size 5 mm and 15 mm, respectively. $P < 0.0001$) and with lower Ki67 (2% and 5.5%, respectively. $P < 0.0001$). Negative endpoint occurred in 16 pts (9.9%), specifically in 14 type III (58.3%) and 2 type I (1.1%). In this subgroup, median Ki67 was 10% (3% – 41%), and median size was 20 mm (14 mm – 25 mm). Among patients with type I gNENs without features supporting negative endpoint (no tumor related death, no metastases, no angioinvasion), 20.3% had Ki67> 2%. When ROC analysis was performed to detect tumor size cut-off level able to predict negative endpoint, the value > 11 mm was identified (AUC 0.921, $p < 0.001$). Overall, 12.3% type I and 70.8% type III gNENS were > 11 mm, respectively ($p < 0.0001$). Regarding proliferative activity, 21.6% type I and 62.5% type III had Ki67 > 2%. When multivariate logistic regression was performed, tumor type and size were associated with negative poor clinical outcome (type III vs type I: OR = 9.2, $p = 0.005$; size: OR 1.12 for each increasing mm, $p = 0.0006$), whereas Ki67 did not maintain statistical significance (OR 1.03 for each increasing unit, $p = 0.149$). Overall, 5-yr survival probability was 100% and 60.5% in type I and type III gNENs, respectively ($p < 0.0001$).

Conclusion: In addition to tumor type, size was the strongest negative prognostic factor, which independently predicted negative outcome in gNENs. Ki67 > 2% was observed in a relevant proportion (20.3%) of type I gNENs with indolent clinical course. Compared with NENs rising from other digestive sites, Ki67 seems to have a minor prognostic role in these tumors. When facing patients with gNENs, tumor type and size should be considered as major factors affecting clinical outcome.

Disclosure: Nothing to disclose

P1797 CLINICAL OUTCOMES OF CASES DIAGNOSED AS NON-CURATIVE ENDOSCOPIC RESECTION OF EARLY GASTRIC CANCER AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: In the 5th edition of gastric cancer treatment guidelines published by Japanese Gastric Cancer Association, the curability of endoscopic resection is classified by two factors: the degree of local resection and the possibility of lymph node metastasis. We examined cases diagnosed as non-curative endoscopic resection; endoscopic curability C (eCuraC).

Aims and Methods: Of 759 patients who underwent ESD for gastric tumors at our hospital from September 2005 to December 2017, 74 patients with eCuraC were retrospectively analyzed. They were classified into two groups, 30 patients who were adapted the expanded criteria for ESD but pathologically diagnosed only positive horizontal margin after ESD (eCuraC-1 group) and 44 patients didn't meet the curative criteria except for eCuraC-1(eCuraC-2 group). Patients who underwent additional surgical resection were examined pathologically for risk factors of lymph node metastasis.

Results: The sex (male / female) was 23/7, 36/8, average age was 71.1/72.2 years old, respectively. The pathological type (differentiated/undifferentiated) was 30/0, 36/8 ($p = 0.0134$), respectively. The operation time was 167.8 ± 112.6 minutes, 131.8 ± 98.1 minutes, the post-bleeding was 13.3%, 15.9%, the perforation was 3.3%, 11.4%, respectively, there were no differences. In eCuraC-1 group, 3 patients underwent additional ESD, 1 patient did argon-plasma coagulation, and 1 patient accepted surgical resection one year after ESD (no lymph node metastasis). 25 patients were followed without additional treatment (no recurrence). In eCuraC-2 group, 23 patients underwent surgical resection and 21 patients didn't receive treatment. The patients who underwent surgical resection were significantly younger than those who didn't receive treatment (67.0 ± 9.1 vs 77.8 ± 7.1 years; $p < 0.0001$). Among 21 patients, tumor was located in the upper third of the stomach more than those who underwent surgical resection (47.6% vs 8.7%; $p = 0.0128$). There was no gastric cancer death and 2 patients died of other cancers (cholangiocarcinoma, lung cancer). In surgical cases, risk factor for lymph node metastasis was histological lymph infiltration ($p = 0.0431$). There was no gastric cancer death and one patient died of lung cancer.

Conclusion: In eCuraC-1 group, risk of lymph node metastasis was low. In eCuraC-2 group, risk of lymph node metastasis was pathological lymph infiltration. Because elderly patients tend not to undergo surgical resection, it is necessary to observe them diagnosed with pathological lymph infiltration closely.

Disclosure: Nothing to disclose

P1799 DECREASE OF SIGNET RING CELL GASTRIC CANCER IN JAPAN; A SINGLE-INSTITUTE EXPERIENCE

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Introduction: It had been shown that while gastric cancer (GC) was decreasing, signet ring cell carcinoma (SRC) had increased. However, the majority of the studies were performed more than 10 years ago. Recent trends of the tumor occurrence was not fully elucidated. In Japan, nation-wide registry started in 2006 in major cancer institutes and hospitals by the government support. In our institution, this registry enrolled 20,231 cancers for the most recent 10 years from 2007 to 2017 including 2,344 gastric cancers. It is particular interest to see SRC is still showing a tendency to increase in the era of *H. pylori* eradication.

Aims and Methods: Since January 2007 to December, 2017, there were 205 patients (8.7%) of SRC in 2,346 patients with gastric cancer registered in our hospital. We compared the period of earlier 6 years (2007–2012) and recent 5 years (2013–2017) and compared the characteristics and trends of SRC. Age, gender, clinical data of patients were obtained from the databases of in-hospital cancer registry.

Results: There was little difference between the characteristics of SRC and Non SRC (NSRC). The number of all GC in earlier 6 years was 1,354 (average 225.7/year, range 204–263), whereas in recent 5 years 992 (average 198,4, range 183–220).

We then compared the relative occurrence of SRC in GC. It was shown that in earlier 6 years (2007 to 2012), the range varied from 9.1 to13.8%, whereas the range was 4.6 to 9.6% in recent 5 years (2013 to 2017). The difference is statistically significant ($p = 0.0086$)

Conclusion: Reduction of SRC seems more rapid than that of all GC. Speculation could even be expanded the direct relation between *H. pylori* eradication and occurrence of SRC.

Disclosure: Nothing to disclose

P1800 DIAGNOSIS OF EARLY GASTRIC CANCER: A 17 YEARS SURVEY BASED ON SURGICAL SPECIMEN IN PARMA AREA

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Introduction: In 2012 the reported incidence of gastric cancer (GC) in both sexes was 12.3/100,000 but the mortality was still high (8.7/100,000), early detection being strictly related to a better survival. Parma is considered a medium-low incidence area for GC. For early diagnosis, the detection of a precancerous condition like chronic atrophic gastritis (CAG) seems crucial, but the majority of such patients is asymptomatic and the diagnosis by means of non-invasive tests (serum Pepsinogens and Gastrin 17), as suggested in Kyoto and Maastricht V Guidelines, is up to now limited in clinical practice.

Aims and Methods: The aim of the study was to establish the burden of incidence of GC in a 17 years survey, focusing on the detection of Early GC. A 17-years interval (from January 2000 to December 2017) was considered in order to state the incidence of GC as reported in the archives of the Pathology Department of Parma University. Gastric cancers were classified as Early, following the Kodama classification, and Advanced. Furthermore the incidence per year throughout the considered interval was analyzed. Only the surgically removed cases were taken into account. A picture of CAG nearby the neoplasia was assessed according to O.L.G.A staging system. In both Early and Advanced cancers the node status was investigated.

Results: Overall, 1,674 (M = 969, F = 705) cases of GC were detected in the 17 years considered interval, representing 2 cases/week and 98 cases/year. Only 1,214 out of 1,674 (M = 707, F = 506, mean age: 82yrs, range: 26–108yrs) were surgical specimens, therefore analyzed. The diagnosis of Early gastric cancer was made in 128/1214 (10.54%) (M = 81, F = 79 mean age: 80yrs, range: 49–104yrs). The diagnosis of Advanced gastric cancer was established in 1086 pts (89.46%)

(M = 641, F = 445, mean age: 82.5yrs, range: 36–108yrs). A picture of CAG was found in more than 95% of the cases, both in Early and Advanced ones. Early cancers showed node metastasis in 20% of the cases compared with 80% in Advanced ones. Concerning the number of involved nodes, in early presentation of neoplasia pN1 staging was assessed in 30.76% (M = 21.21%; F = 40.32%) of the cases whereas in the advanced one the pN1 cases were only 14.73%, being N3 the most reported node status.
Conclusion: Early gastric cancer diagnosis is confirmed to be a very infrequent finding and this could account for the high mortality rate of the gastric neoplasia. The search for precancerous conditions like chronic atrophic gastritis is therefore mandatory. The incidence of GC in the Parma area is higher in male patients and seems to be permanent through the considered interval.
Disclosure: Nothing to disclose

P1801 EFFECTIVE DIAGNOSTIC STRATEGY FOR GASTROINTESTINAL MALT LYMPHOMA FOCUSING ON TREE-LIKE APPEARANCE

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Introduction: Gastrointestinal malignant lymphoma has diverse endoscopic findings; therefore, it is difficult to diagnose in many cases. Since a long time, multiple erosions and cobblestone-like mucosa have been considered as characteristic endoscopic findings of MALT lymphoma. However, tumour advancement-induced submucosal vascular changes that show an irregular, tortuous microvasculature [tree-like appearance (TLA)] have been recently reported. In this study, we retrospectively investigated the characteristic endoscopic findings of gastrointestinal lymphomas, including MALT lymphoma.
Aims and Methods: Fifty patients who were histopathologically diagnosed with gastrointestinal malignant lymphoma (MALT lymphoma, 20; non-MALT lymphoma, 30) at our institute after 2010 were included in the study. The sensitivity and specificity of TLA using magnifying narrow-band imaging (NBI) and general endoscopy (based on Sano's classification and the findings of Akamatsu et al.) were determined. Patients with treatment-resistant MALT lymphoma were followed up for these findings.
Results: Among patients who were observed using magnifying NBI, TLA frequency in patients with MALT lymphomas was 72.7% (8/11), which was significantly higher than that in patients with non-MALT lymphoma (1/10, P = 0.008). Using a conventional light microscope, the frequencies of flat depression (11/20; 55%) and cobblestone-like mucosa (12/20; 60%) in the MALT lymphoma group were also observed to be significantly higher than those in the non-MALT lymphoma group (P = 0.005, 0.002); however, the sensitivity and specificity were lesser than those of TLA. No significant difference was noted in the presence or absence of colour change, white coat or multiple lesions. A correlation between the treatment effect and TLA finding was noted in treatment-resistant MALT lymphoma cases.
Conclusion: For MALT lymphoma with low epithelial invasiveness, morphological diagnosis using endoscopy is crucial to accurately determine the biopsy site. This study clarified that TLA is a specific finding of MALT lymphoma compared with all other gastrointestinal lymphomas showing a diverse morphology. In addition to a detailed observation using magnifying NBI, the presence of flat depression and cobblestone-like mucosa following conventional observation may facilitate an efficient endoscopic diagnosis of MALT lymphoma.
Disclosure: Nothing to disclose

P1802 ENDOSCOPIC MANAGEMENT OF EARLY FOREGUT NEUROENDOCRINE TUMORS

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Introduction: Neuroendocrine tumors (NETs) are defined as epithelial neoplasms with predominant neuroendocrine differentiation. Depending on the point of origin, gastrointestinal neuroendocrine tumors (NETs) can be classified as a tumor of the foregut (esophagus, stomach and duodenum), midgut (distal duodenum to proximal colon), or hindgut (distal colon and rectum). Foregut NETs are considered rare, and the reported incidence is 10%-30% of all gastrointestinal NETs, but their incidence has been increasing in most countries over last 50 years[1]. The treatment of choice for NET is usually surgery. Early foregut NETs limited to mucosa/submucosa demonstrate low frequency of lymph node and distant metastasis, and thus have been managed with local excision (including endoscopic treatment) which offers improved quality of life compared with surgery[2]. We report our single-center experience of endoscopic resection (ER) for early foregut NET.
Aims and Methods: Patients with NET confirmed on histology were identified from a prospectively maintained endoscopic database over 5 years (2013–2017). All patients underwent pre-procedure radial endosonography (EUS) and abdominal CT scan. EMR, ESD or EFTR was performed in all patients under general anesthesia. High-definition gastroscope (GIF-HQ-190, Olympus Corporation, Japan) with distal transparent attachment was used. EMR was performed using diathermy snare. ESD and EFTR was performed using either Dualknife™ (Olympus) or Hybrid knife™ (ERBE GmBH, Germany). Hemostasis was achieved using Coagrasper™ (Olympus). For EFTR, closure was achieved using hemoclips (Olympus), PadlockTM clip (Aponos Medical, USA) or Overstitch™ (Apollo Endosurgicals, USA). Foregut NETs were graded as G1, G2, or G3 on basis of proliferative activity by mitotic count. All patients underwent regular follow-up to evaluate for any local recurrence or distant metastasis.
Results: Foregut NET managed by ER include 23 patients (25 lesions). Location – Stomach – 1, duodenal bulb – 17, descending duodenum – 7. Males-16. Mean age- 60.7 years. All lesions found incidentally during routine EGD for other indications; no patients reported symptoms of carcinoid syndrome. All tumors resected en bloc. Mean cross sectional area – 18.3 mm (range: 5–50); mean procedure time – 98.6 min (range: 20–135). EMR in 7 (30%), ESD in 13 (57%) & EFTR in 3 (13%). EFTR defect closed using omental patch & hemoclips in 1; full-thickness clip in two patients. According to WHO 2010 classification, histology – NET-G1–19; NET-G2–4. No intra procedural adverse events noted. Two delayed adverse events (11%) – delayed hemorrhage – 1, delayed perforation – 1. No mortality. Histology – clear margins in all. Follow up EGD at 4–6 weeks - complete healing in all. Median follow up was 12 months (3–72). No recurrence noted. One patient developed new lesion during follow up; ESD performed.
Conclusion: Endoscopic resection of foregut NET's is safe and effective. ER is safe and effective to provide high histologically complete resection rate, accurate histopathological evaluation, and a low complication rate.
Disclosure: Nothing to disclose

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P1803 ENDOSCOPIC AND HISTOPATHOLOGICAL FINDINGS OF PATIENTS WITH GASTROINTESTINAL TRACT 18-FDG ACCUMULATION OF INCIDENTALLY FOUND ON PET/CT

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Introduction: Positron emission tomography/computed tomography (PET-CT) is an important imaging modality in the diagnosis, staging and monitoring the treatment response in oncology departments. As a result of the increased availability of PET-CT imaging, unexpected FDG uptake has been identified in a variety of sites in the gastrointestinal (GI) tract. Although incidental lesions of the GI tract on PET-CT scans are found only in about 3% cases, they are associated with a substantial risk of an underlying cancerous or precancerous lesion.
Aims and Methods: The aim of this study was to investigate whether incidental FDG uptake and has any clinical and histopathological importance detected in patients with non-GI malignancies. We particularly sought a suv-max value in predicting malign lesions of the GI tract. Between February 2011 and November 2016, 12530 patients had undergone PET/CT scan. Patients with GI malignancies, patients without Suv-max value on PET/CT and patients without endoscopic and histopathological examinations were excluded from the study. Patients with FDG uptake were stratified as follows: according to localization (esophageal, gastric and colonic) and histopathological findings (benign and malign). Receiver operating characteristic (ROC) curves were used and optimal cut-off points were calculated to describe the ability of suv-max value to predict the presence of a malign process.
Results: 157 out of 12530 patients with GI tract FDG uptake and endoscopic/histopathological results were included into the study. 40 patients had abnormal esophageal FDG uptake, 66 patients had gastric and 51 patients had incidental focal colorectal uptake. One patient had malign mesenchymal tumor and 39 patients had benign conditions (37.5% esophagitis) at esophagus. 12 patients had lymphoma, 1 plasmocytoma involvement and 2 patients had a newly diagnosed carcinoma of the stomach at gastroscopy. As for benign conditions, 37 had gastritis, 6 had benign ulcers, 5 had submucosal lesions and 2 patients had hyperplastic polyps of the stomach. A total of 27 patients had premalign/malign conditions of the colon. The histological results are as follows: adenomatous polyps (n = 15), colon cancer (n = 5), dysplasia (n = 4), insitu cancer (n = 2) and malign melanoma involvement (n = 1). The results of the benign condition of the colon are as follows: infectious colitis (n =), diverticular disease (n =), anastomotic line (n = 1), non-specific ulcer (n = 1) and no finding (n = 12). The cut-off values of Suv-Max for discriminating benign and malign conditions of the stomach and colon were 15.9 [AUROC;89.2, sensitivity% (95%CI) 78(52–92), specificity% (95%CI) 92(81–96)] and 9.7 [AUROC;71.6, sensitivity% (95%CI) 81(63–91), specificity% (95%CI) 62(42–78)].
Conclusion: Incidental focal gastric and colorectal FDG uptake is associated with a substantial risk of underlying premalign/malign conditions but not for esophagus. Gastroscopy and colonoscopy should be recommended due to incidental

focal FDG uptake, early identification of these lesions may change management of these patients.
Disclosure: Nothing to disclose

P1804 PREVALENCE AND PROGNOSIS OF MISMATCH REPAIR DEFICIENCY IN OESOGASTRIC ADENOCARCINOMA

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Introduction: In oesogastric cancer (OGC), recent studies have shown a prevalence of mismatch repair deficiency (dMMR) from 8 to 23% with heterogeneous data between European and Asian studies. Questions have been raised about the prognostic impact of dMMR.
The aim of our study was to determine dMMR prevalence in a cohort of OGC, to determinate associated BRAF mutation and to evaluate the prognostic value of dMMR.
Aims and Methods: We have performed a retrospective multicenter study that has enrolled all consecutive patients from 2010 to 2015 with junction or gastric adenocarcinoma for which tumor sample (biopsies or surgical samples) and clinical data with follow up were available.
dMMR was determined by genotyping with PCR of 5 monomorphic mononucleotide repeats. In case of dMMR tumor, BRAF V600E mutation screening and immunohistochemistry (IHC) of MMR proteins were performed.
Overall survival (OS) was estimated by Kaplan Meier method and compared between groups by log rank test. Recurrence cumulative incidence were estimated and compared according to MMR status by Gray test.
Results: Two hundred and twenty-three tumors were analyzed, among them 180 (80%) were mismatch repair proficient (pMMR), 31 (14%) were dMMR and 12 tumors were undetermined. Patients with dMMR tumors were older than patients with pMMR tumors (median age 70.5 versus 60.8 years, $p = 0.003$). dMMR prevalence was 26% in patients ≥ 70 versus 12% in patients < 70 years. dMMR tumors were located in junction, fundus and antrum in 7.1%/25%/67.9% respectively versus 33.6%/27%/33.6% and 5.8% unknown for pMMR tumors ($p = 0.02$). There was no significant difference regarding gender (male 53.6% in dMMR versus 67.2% in pMMR), localized or metastatic stage (85.7%/14.3% in dMMR versus 81.6/18.4% in pMMR), histologic type (diffuse/intestinal/indeterminate type respectively 22.7%/ 45.5%/22.7% in dMMR and 29.7%/42.3%/18% in pMMR), tumor with signet-ring cells (47% of dMMR tumor versus 52% of pMMR tumor) or HER2 surexpression (11.1% in dMMR versus 9% in pMMR). We observed a trend for less lymph node metastasis (LNM) in dMMR tumor (N0: 60.9% in dMMR versus 32.1% in pMMR, $p = 0.056$). R0 surgery was obtained in 82% of cases in both groups. A trend for less neoadjuvant chemotherapy was observed in dMMR compare to pMMR (39.1% versus 58.4%, $p = 0.11$).
All the tumors that were determined dMMR by PCR presented a loss of expression of one of the MMR proteins (all MLH1 except 1 MSH6). For 12 tumors with equivocal status by PCR, none presented MMR proteins loss of expression. None of the 22 dMMR tumors had the V600E mutation of *BRAF*.
The median OS for all stages was 32.8 months in dMMR versus 25.2 months in pMMR ($p = 0,94$). In the subgroup of 136 patients who had surgery for localized cancer, cumulative incidence of recurrence at 3 years was 21% in dMMR versus 52% in pMMR group ($p = 0.03$).
Conclusion: In this cohort, dMMR prevalence in OGC was 14%, mostly associated with antral localization and aged patients. dMMR was associated with a lower risk of LNM and a lower cumulative incidence of recurrence. dMMR status determined by PCR was confirmed by IHC in all cases, with loss of MLH1 in nearly all cases. None of the dMMR tumor presented a *BRAF* mutation.
Disclosure: Nothing to disclose

P1805 ACCURACY OF A SERUM BIOMARKER TEST (GASTROPANEL®) FOR THE DIAGNOSIS OF MODERATE TO SEVERE ATROPHIC GASTRITIS IN PATIENTS WITH UNINVESTIGATED DYSPEPSIA

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Introduction: Atrophic gastritis (AG) is the most important known risk factor for the development of non-cardial gastric cancer (GC), mainly in cases of extensive or advanced (moderate-severe) atrophy. Serological biomarkers (pepsinogen-I (PG-I), pepsinogen-II (PG-II), gastrin-17 (G-17), anti-H. pylori antibodies - HpAb-), provide non-invasive information about the morphological and functional integrity of the stomach, and they could be an useful tool for selecting patients at risk.
Aims and Methods: The aim of this study is to assess the diagnostic accuracy of a serological biomarker panel, GastroPanel® (GP) to predict the presence of moderate-severe AG in the corpus (CAG2+) and/or antrum (AAG2+) in patients with uninvestigated dyspepsia.
Methods: A prospective observational study was conducted. Inclusion criteria: patients > 50 years, with univestigated dispepsia, submitted to our Endoscopic Unit for upper GI endoscopy. PPIs were discontinued 4 weeks before fasting levels of PG-I, PG-II, G-17 and HpAb were determined by ELISA method. Five gastric biopsies were obtained (2 antrum, 2 body and 1 incisura) during endoscopy, that were independently evaluated by two pathologists blinded to the GP result. In case of discrepancy, histologic slides were reviewed by a third external pathologist. Updated Sydney System (USS) was used to graduate the presence of AG: 0 (absent), 1 (mild), 2 (moderate) or 3 (severe). Concordance between GP and histology was assessed using the kappa index. The accuracy and area under the ROC curve (CI95%) of PG-I < 30 µg/l and PG-I/PG-II ratio < 3 for the diagnosis of CAG2+ and of G-17 < 1 pmol/l for the diagnosis of AAG2+ were calculated.
Results: 131 consecutive patients were included (median 63 years (range 48–86), 60.3% women, 49.6% *H.pylori* positive). According to GP results, 16 patients (12.2%) presented AG: 13 CAG and 3 AAG, while AG was observed in histological analysis in 34 cases (25.9%): 16 CAG (8 CAG2+), 12 AAG (8 AAG2+) and 6 multifocal AG (4 CAG2+, 1 AAG2+). The overall agreement between histology and GP was 75.6% (99/131), kappa index: 0.63. For the diagnosis of CAG2+, the overall efficacy of PG-I < 30 µg/l and PG-I/PG-II ratio < 3 was respectively 96.2% (CI95%: 91.4–98.4) and 95.4% (CI95%: 90.4–97.9), with AUC-ROC 0.963 (CI95%: 0.923–1) for PG-I and 0.967 (CI95%: 0.928–0.997) for PG-I/PG-II ratio. For the diagnosis of AAG2+, the overall efficacy of G-17 < 1 pmol/l was 81.7% (CI95%: 74.2–87.4) with AUC-ROC 0.745 (CI95%: 0.611–0.878).
Conclusion: The serological biomarker panel GastroPanel® is an effective tool for the non-invasive screening of patients with uninvestigated dyspepsia, that allows detecting those patients at the highest risk of developing GC (basically, moderate-severe CAG).
Disclosure: Nothing to disclose

P1806 USEFULNESS OF UNDERWATER EMR FOR NON-AMPULLARY DUODENAL TUMOR

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Introduction: Complication rate of endoscopic submucosal dissection (ESD) for superficial non-ampullary duodenal epithelial tumors (SNADET) is higher than that of other organ, because of thin muscle layer. Recently a new method, underwater EMR (UWEMR) has reported. However, the usefulness is not well known.
Aims and Methods: The aim of this study is to investigate the outcome of UWEMR for SNADET.
One hundred seven lesions of SNADET were treated from Feb. 2016 to Feb. 2018. Lesions less than 15mm in size were indicated for UWEMR. Large lesions were indicated for ESD or laparoscopy endoscopy collaboration surgery (LECS). Two, thirty-one and eight lesions were treated by EMR with injection, ESD and LECS, respectively. And the residual sixty six lesions undergone to UWEMR.
The procedure was changed from UWEMR to EMR or ESD, when the snaring was impossible. Four and 4 lesions were treated by EMR and ESD, respectively. Finally, fifty-eight lesions were treated by UWEMR. UWEMR was performed with a 10-mm or 15-mm snare (SnareMaster; SD-210L-10, SD-210L-15, Olympus, Tokyo).
Median age was 66 (43–87) years old. Macroscopic type; 0-I, 0-IIa and 0-IIc were 8, 26 and 24, respectively. Location; bulbs, 2nd portion and 3rd portion were 4, 42 and 12, respectively.
Artificial ulcer was closed by endo clips (EZ clip; HX-610-090L, Olympus, Tokyo) to prevent delayed perforation and bleeding. Intravenous PPI were used from just before UWEMR for two days, and followed by per-oral PPI

for one month. The patients were allowed to eat loose meal from two days after UWEMR.
Results: 1. The median diameter of tumor and specimen was 7 (2–25) and 12 (4–25) mm, respectively.
2. En-bloc resection rate was 91% (53/58). R0 and Rx rate was 69% (40/58) and 31% (18/58), respectively. When the final section contains neoplasia, lateral margin (LM) was diagnosed as LMx (N = 13). And, piecemeal resected cases were diagnosed as LMx (N = 5), too. The median diameter of tumor in R0 was 6 (3–18) mm. In contrast, that in LMx was 11 (2–25) mm. There was significant difference between diameter of tumor of R0 and that of RX (p = 0.0032). The rate of R0 was 87% (13/15) in 1–5mm, 77% (20/26) in 6–10mm, 60% (6/10) in 11–15mm, 20% (1/5) in 16–20mm and 0% (0/2) in 21–25mm. There was significant difference (p = 0.0095). The R0 rate for SNADET 10mm or less was excellent. However, it wasn't satisfactory for large lesion 16mm or bigger.
3. The rate of local recurrence was 0%.
4. Closing method; The mean number of clips was 5 (1–8). A second look EGD was performed 2 day after UWEMR. And some clips were dropped in 4 of 58 cases. However, the artificial ulcer was closed by the remaining clips. All of the clips were remained in 93% (54/58). Therefore, second look EGD to check closure of ESD is unnecessary.
5. Complications; Perforation during UWEMR was 0% (0/58). The rate of delayed perforation and bleeding was 0% and 0%, respectively.
Conclusion: UWEMR is a safe treatment for SNADET. And, R0 rate in 10 mm or less was excellent.
Clip closure after UWEMR was effective to prevent delayed bleeding and perforation.
Second look EGD is unnecessary to check the closure of artificial ulcer.
References: None
Disclosure: Nothing to disclose

P1807 OUTCOME OF ESD FOR ESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA

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Introduction: The incidence of Esophago-gastric junctional adenocarcinoma (EGJAC) is lower than that of esophageal or gastric cancer. Therefore, the outcome of ESD for EGJAC is still unknown.
Aims and Methods: The aim of this study is to investigate the outcome of ESD for EGJAC.
One hundred eight patients (90 males and 18 females) with one hundred eleven EGJAC treated by ESD from Jan. 2000 to Mar. 2015 were enrolled to this retrospective study. EGJAC was defined as adenocarcinoma located between 1cm oral and 2cm anal from EGJ.
The median age was 74 (32–91). Follow-up period was 82 (1–211) months. Protuberant, flat and depressed type were 52, 3 and 56 lesions, respectively. T1b was sub-classified into T1bSM1 (500 micrometer or less) and T1bSM2 (501 micrometer or deeper). T1aM, T1bSM1 and T1bSM2 were 82, 15 and 14, respectively. Differentiated (DA) and poorly differentiated adenocarcinoma (PDA), were 106 and 5 lesions, respectively.
T1aM and T1bSM1 were followed up without an additional therapy (AT). And, AT was recommended for T1bSM2, and when lymph vascular involvement was positive.
Results: 1. The median diameter of tumor and specimen were 18 (2–61) and 40 (22–82) mm, respectively.
2. Complete resection and R0 rate was 100% and 99% (110/111), respectively.
3. Local recurrence rate was 0%.
4. Complications: The bleeding during ESD and delayed bleeding required blood transfusion was 0% and 0.9% (1/111). The perforation during ESD and delayed perforation was 0.9% (1/92) and 0%.
5. Prognosis
a) T1a-M (N = 82) and T1b-SM1 (N = 15)
All patients were followed up. No patients had metastasis, and died of EAC.
b) T1b-SM2 (N = 14)
Surgery was performed for eight patients (57%). No patient had lymph node metastasis (LNM). Five patients are alive without metastasis 3 patients were died of other disease without metastasis.
One was treated by radiation, and died of EGJAC 16 months after ESD.
Five patients were followed up without additional therapy. Three patients are alive without recurrence. One patient was died of EGJAC 70 months after ESD. One patient was died of other disease.
6. The risk factors of LNM (Univariate analysis)
a. Invasion depth; The rate of LNM in T1aM, T1bSM1 and T1bSM2 were 0% (0/82), 0% (0/15) and 7% (1/14), respectively (p = 0.0303).
b. Histological type; The rate of LNM in DA and PDA were 0% (0/106) and 20% (1/5), respectively (p = 0.0450).
c. Lymphatic involvement (LI); The rate of LNM of LI(+) and (-) were 33% (1/3) and 0% (0/108), respectively (p = 0.027).
7. The risk factors of LNM (Multivariate analysis)
Lymphatic involvement was the independent risk factor of LNM (p = 0.0339).
8. Prediction value of eCura system[1] for EGJAC
Twenty two patients were diagnosed as out of indication. Sixteen, four and 2 patients were classified to low, intermediate and high-risk groups. And the LNM rate were 0% (0/16), 0% (0/4) and 50% (1/2). The eCura system was compatible for not only gastric adenocarcinoma but also EGJAC.
Conclusion: ESD was a safe and useful treatment for superficial EGJAC.
The eCura system is an useful method to predict prognosis, for out of indication cases of EGJAC.
Disclosure: Nothing to disclose

Reference

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P1808 COMPARISON BETWEEN REDO ENDOSCOPIC TREATMENT AND SURGERY IN PATIENTS WITH RECURRENT GASTRIC NEOPLASMS

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Introduction: Treatment of locally recurrent gastric neoplasms after endoscopic resection remains challenging. We investigated the efficacy and safety of treatment options for recurrent gastric neoplasms localized to the scar of previous endoscopic submucosal dissection (ESD).
Aims and Methods: The clinicopathological characteristics and treatment outcomes of patients who underwent endoscopic treatment or surgery for recurrent gastric neoplasms between June 2010 and May 2017 were retrospectively reviewed.
Results: Of the 92 patients included, 74 underwent endoscopic treatment (54 redo ESD, 23 argon plasma coagulation [APC] ablation) and 18 underwent surgery. The redo ESD procedure time was significantly longer than that of the primary ESD (31.0 versus 22.0 minutes, $p = 0.018$). Overall, adverse events occurred in 11 patients (12.0%), with the incidence being significantly higher in the surgery group (27.8% versus 8.1% in the endoscopic treatment group, $p = 0.036$). Local recurrence-free survival rates were 81.1% for the endoscopic treatment group (86.3% and 69.6% for redo ESD and APC groups, respectively) and 100% for the surgery group (log rank $p = 0.033$). Logistic regression analysis showed that tumor size > 15 mm (odds ratio [OR]: 7.52, 95% confidence interval [CI]: 1.65–45.3, $p = 0.014$) and tumors located in the upper two thirds of the stomach (OR: 6.10, 95% CI: 1.32–37.1, $p = 0.029$) were associated with non-curative resection after redo ESD.
Conclusion: Endoscopic treatment could be an effective and safe alternative to surgery for selected patients with gastric neoplasms recurring at the site of previous ESD.
Disclosure: Nothing to disclose

P1809 EVALUATION OF GASTRIC POLYPS DETECTED BY ENDOSCOPY: WHAT IS THE CLINICAL SIGNIFICANCE?

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Introduction: Found in 6% of upper endoscopies, gastric polyps are a heterogeneous group of lesions that can vary in histology, neoplastic potential, and management. Currently, there are no clear guidelines for the management of these lesions.
Aims and Methods: The aim of this study was to evaluate gastric polyps, detected by upper endoscopy in our institution, with respect to their frequency, size, anatomic location, presence of dysplasia, histopathologic features and clinical outcomes. Clinical records from patients who underwent upper endoscopy with polypectomy between January 2012 and December 2017 were reviewed retrospectively.
Results: A total of 405 patients with a median age of 66 years (interquartile range 55–74 years) were included; 66.2% were female; 26.9% had *Helicobacter pylori* infection; 62.2% were taking proton pump inhibitors; 8.9% were diagnosed with hereditary polyposis or non-polyposis syndromes; 4.3% had a positive family history for gastric cancer. A total of 463 upper endoscopies with polypectomy were performed. Most polyps detected by endoscopy were solitary (56.8%). Of all gastric polyps, 40.2% measured between 0–5mm, 27.0% between 6–9mm and 32.8% ≥ 10mm. Gastric polyps were found most commonly in the corpus/fundus (58.8%), followed by antrum (33.5%), cardia (5.6%) and a minority (2.2%) in the antrum-body transitional zone or anastomotic site. Histopathologically, the most common polyp type was hyperplastic (60.5%), followed by fundic gland (14.5%), nonspecific/foveolar polypoid hyperplasia (14.3%), inflammatory fibroid (4.5%), adenomatous (3.9%), neuroendocrine (1.5%) and hamartomatous (0.9%). Among adenomatous polyps, 11 were low-grade dysplasia, 6 high-grade dysplasia and 1 had features of adenocarcinoma. Additionally, 3 hyperplastic polyps had dysplastic foci; all of these were ≥ 10mm. Dysplasia was shown to be significantly associated with polyp size ≥ 10mm (p = 0.018), and Familial Adenomatous Polyposis (FAP) (p = 0.009). During a median follow-up period of 12 months (data available in 96 cases), 45.3% of gastric polyps recurred, the large majority (78.9%) with the same histological type.
Conclusion: Most polyps detected by endoscopy were solitary, smaller than 1 cm, and found in the corpus/fundus. The most common type was hyperplastic polyp. Dysplasia was shown to be significantly associated with polyp size ≥ 10mm and

Familial Adenomatous Polyposis (FAP), which underlines the importance of endoscopic excision in these situations.
Disclosure: Nothing to disclose

P1810 IMPACT OF PRE-NEOPLASTIC LESIONS AND TUMORS OF GI TRACT IN AFRICAN POPULATION IN PARMA AREA BASED ON PATHOLOGY RECORDS: RELATIONSHIP WITH RISK FACTORS AND HELICOBACTER PYLORI STATUS

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Introduction: In Italy, in recent years African population is increasing, in particular in some regions like Emilia-Romagna where in 2017 Africans were 11.9% out of resident population. The life style of African immigrants is different from the Italian population, in particular as regards the consumption of meat, use of spices, alcohol consumption and smoking habit. The distribution of GI lesions both in Upper and in Lower tract is matter of interest for the public health in order to investigate risk factors, epidemiological data and burden of expenses in particular related with neoplastic diseases.
Aims and Methods: The aim of this study was to investigate the distribution of GI lesions in this two populations and to establish possible relationship with life style and epidemiological data. Based on records from Parma's Department of Anatomo-Pathology a Database was performed collecting biopsies coming from Upper and Lower GI endoscopy from 01/01/2007 to 30/12/2017. In particular, 25,763 biopsies have been examined from Upper GI endoscopy and divided in 24,683 diagnosis of Chronic Atrophic Gastritis (CAG) and 1,080 of Gastric Cancer (GC); while 40,673 biopsies from Lower GI endoscopy have been analysed and were divided in 36,988 polyps and 3,685 diagnosis of Colo-Rectal Cancer (CRC).
The records of Database allowed to set apart two different groups: Group A standing for non-African population inhabiting in Parma and Group B for African population resident in Parma.
Moreover, 321 consecutive African subjects resident in Parma (M/F 186/135), were enrolled to fill out a structured questionnaire about their feeding and life habits.
Results: Respectively 23,559 out of 24,683 CAG diagnosis (95.4%) and 1,076 out of 1,080 GC diagnosis (99.6%) were from Group A against 1,124 (4.5%) and 4 (0.4%) in Group B. However, *Helicobacter pylori* status was investigated in these pts and the data obtained showed 39% H.p.+ in Group A and 68% in Group B. In Group A, 41% of CAG diagnosis (mean age 63.5 yrs) were associated with intestinal metaplasia (IM), about 3 times higher than in Group B (95 pts, m.a. 52 yrs); within African population IM was more common in people coming from Sub-Saharan Africa (59 pts, 14%) than people from North Africa (36 pts, 10%). Concerning Lower GI biopsies, 36,899 out of 36,988 (99.8%) colonic polyps diagnosis were observed in 19,356 pts (M/F 12,368/6,988) from Group A, showing an higher rate than in Group B in which colonic polyps were detected in just 89 biopsies (0.2%) from 78 pts (M/F 36/42). Furthermore no CCR was diagnosed in Group B.
Records obtained by the questionnaire showed that 60% of sample eat foods from their country, less refined and fiber richer, with a lower consumption of red meat; 88% use spices, 65% don't drink alcohol and 92% don't smoke. In addition, 49.6% don't rely on conventional drugs, only 50.4% admit to follow medical prescriptions and, 27% try as first approach drugs coming from their country.
Conclusion: The results obtained in the study show discrepancy between diagnosis of CAG and GC in non-African Parma population in comparison with African one. This data is opposite to the trend of H.p. status in the two populations, as well as for the distribution of intestinal metaplasia. As regards Lower GI features, African people is affected by very little number of lesions (both colonic polyps and CCR). The results from questionnaire also demonstrated peculiar pattern of eating, smoking and drinking from African subjects, searching for original country products.
Disclosure: Nothing to disclose

P1811 ACCURACY OF LINEAR-ARRAY EUS FOR PREOPERATIVE STAGING OF GASTRIC CANCER

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Introduction: The incidence of gastric cancer is declining worldwide. However, it still remains the second most common cause of cancer-related death in the world. Endoscopic ultrasound (EUS) is used for preoperative staging of gastric cancer due to its potential ability to assess both depth of local tumor infiltration and regional lymph node involvement. The indication and accuracy of linear EUS, however, are still controversial.
The aim of this retrospective multicenter trial was to determine the accuracy of linear EUS compared with the contrast enhanced computed tomography (CECT) and with final pathologic specimen with regard to tumor depth and nodal status.
Aims and Methods: We retrospectively enrolled 132 cases of gastric cancer who underwent surgical resection between 2015 and April 2018 from two hospitals of Northen Italy, preoperatively evaluated for depth of invasion of tumor and lymph nodes stations involvement with linear EUS and classified according with TNM classification (UICC).
Results: Of 132 patients, 56 were localized in corpus, 45 in antrum, 20 in the gastric angulus, 8 in fundus, 2 in cardia and in one case the tumor was in the pylorus. Mean age of patients was 65 (+/−10) and mean tumor size was 45 mm (+/−15) ranging from 15 to 80 mm maximum. The overall diagnostic accuracy of EUS in preoperative determination of cancer depth of invasion was 66.7% (4/6) and 62% (18/29), 65% (41/63), 76% (26/34), for T1 (T1b), T2, T3, and T4, respectively. The diagnostic accuracy of metastatic lymph node involvement or N staging of EUS was 68% (46/67) for N0 and 67% (50/65) for N+.
The performance of T staging with CT scanners was not high: 66.7% for T1, 62% for T2, 61% for T3, 8% for T4. For lymph node involvement, the sensitivity value for CECT was significantly lower than that for EUS: 47% for N1, 0% for N2.
Conclusion: Our data indicates that EUS may be superior to CECT in preoperative locally N staging. Additionally, EUS accuracy in T staging is still suboptimal and probably more than one single diagnostic procedure should be used.
Disclosure: Nothing to disclose

P1812 CORRESPONDENCE BETWEEN GASTRIC FUNCTION MARKERS AND SEVERITY OF HISTOLOGICALLY ASSESSED GASTRIC INJURY: A PROSPECTIVE STUDY IN 144 CONSECUTIVE PATIENTS

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Introduction: Diagnosis of autoimmune diseases warrants exclusion of concomitant autoimmune disorders, as the coexistence in the single individual is frequent. The diagnosis of autoimmune gastritis (AG), a condition in which auto-antibodies targeted against components of the oxyntic epithelium progressively destroy the mucosa of gastric body (C) and fundus, is established histologically, with the presence of mucosal atrophy. Although the Operative Link on Gastritis Assessment (O.L.G.A.) is a widespread staging system for gastric atrophy, it does not provide information on the severity of disease in terms of the degree of gastric function impairment.
Aims and Methods: The aim of the present study was to establish the usefulness of pepsinogen I (PGI) and gastrin-17 (G-17) in the evaluation of gastric atrophy severity, assessed by the O.L.G.A. staging system.
Patients with autoimmune gastritis, diagnosed by APCA positivity and histological assessment, according with O.L.G.A. staging, were consecutively enrolled in the study. Serological determination of PGI and G-17 was performed in all. Patients on therapy with acid suppressants were excluded, as these drugs cause an alteration in serum levels of PGI and G-17. Accordingly to literature, patients were considered affected by gastric atrophy when PGI < 30 μg/l and G-17 > 7 pmol/l.

Abstract No: P1812
Table 1: Concordance between PGI, G-17 and O.L.G.A. staging

	STAGE 0	STAGE I		STAGE II		STAGE III	
	A0C0 *(n = 33)*	A0C1 *(n = 7)*	A1C1 *(n = 3)*	A0C2 *(n = 12)*	A1C2 *(n = 8)*	A0C3 *(n = 35)*	A1C3 *(n = 25)*
PG I: Medium value ± SD	110.0 ± 85.7	25.6 ± 25.3	23.20 ± 31.3	16.42 ± 16.6	13.5 ± 11.5	7.87 ± 4.56	10.8 ± 9.74
G-17: Medium value ± SD	8.09 ± 17.8	24.6 ± 29.6	44.2 ± 34.9	118.6 ± 136.4	144.1 ± 92.8	122.8 ± 133.4	108.3 ± 78.4

Results: A total of 144 patients (124 F, mean age 58.3 ± 13.6) were included in the study; 21 patients with antral (A) atrophy only were excluded from the analysis. PGI levels showed a progressive reduction that paralleled the increasing O.L.G.A. stage, shown in the table below. The concordance between the mean values of PGI and atrophy severity was statistically significant ($p < 0.0001$). A similar, but opposite, statistically significant ($p < 0.0001$) result was observed for G-17, which levels show a progressive increase with worsening of gastric atrophy.
Conclusion: In our study, the concordance between PGI, G-17 and the prognostic O.L.G.A. staging permits to consider the non-invasive test as a first level cost-effective exam for the evaluation of gastric function. Furthermore, G-17 levels showed a significant increase moving from stage I to stage II, a stage that corresponds to a different risk of developing gastric adenocarcinoma, so the serological markers resulted able to correlate to the severity of lesions, assessed by O.L.G.A. staging.
Disclosure: Nothing to disclose

P1813 HYPERTHERMIA REGULATES BOTH SLC22A16 EXPRESSION AND ABCG2 EXPRESSION VIA ROS PRODUCTION TO ENHANCE THE CYTOTOXICITY OF DOXORUBICIN

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Introduction: Hyperthermia (HT) is a non-invasive cancer therapy. Treatment temperature between 41 to 44°C has no cytotoxic damage in normal cells, while the temperature does in cancer cells because of the underdeveloped vascular system. HT often used with other cancer therapy such as radiation-therapy and chemotherapy. However mechanisms of synergistic effects among these therapies remains unclear. The 42°C environment is a cellular mild heat stress generating O_2^- from mitochondrial electron transport chain. We have previously reported that the expression of ATP-binding cassette sub-family G member 2 (ABCG2), which is known as breast cancer resistant protein (BCRP), was suppressed by increasing mitochondrial ROS to induce cancer specific porphyrin accumulations.
Aims and Methods: Since ABCG2 is a transporter of doxorubicin (DOX), we hypothesized that synergistic effect of HT and chemotherapy may be induced by down-regulation of ABCG2 expression via intracellular ROS increase. In this study, we elucidated whether HT with intracellular ROS increase by HT can enhance the cytotoxic effect of DOX for gastric epithelial cells. The gastric epithelial cellular cancerous mutant, RGK1 was incubated at 37 or 42°C for 1h. Intracellular ROS generation was detected by electron spin resonance (ESR). Cytotoxicity of DOX was measured using the Cell Counting Kit 8. ABCG2 expression was analyzed by Western blotting.
Results: ESR signal peak with HT treatment became high as compared to without HT treatment, indicating intracellular ROS level was increased by HT treatment. Cell viability and ABCG2 expression were decreased by DOX exposure and by HT treatment.
Conclusion: Thus we conclude that the enhancement of HT treatment effect by DOX is considered to be result of down-regulation of BCRP expression by ROS.
Disclosure: Nothing to disclose

P1814 HOXB9 FUNCTIONS AS A POTENTIAL ONCOGENE AND IS NEGATIVELY REGULATED BY MIR-28-5P IN GASTRIC CARCINOGENESIS

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Introduction: Homeobox (HOX) genes encode a family of homeodomain-containing transcription factors that bind with specific DNA strands. HOXB9 is a member of the HOX family and is classified into B cluster. The function of HOXB9 has been extensively investigated in lung and breast carcinomas. However, knowledge about its function and regulation mechanism in gastric cancer (GC) is still quite limited.
Aims and Methods: This study aims to comprehensively investigate the expression and functional role of HOXB9 and elucidate its regulatory mechanisms in gastric carcinogenesis. HOXB9 were screened out by expression microarray of GC cell lines. The clinical relevance of HOXB9 in GC was analyzed from both online datasets and immunohistochemistry of tissue microarray. siRNA-mediated HOXB9 knockdown were applied in the functional assays such as cell proliferation, monolayer colony formation, cell invasion, cell-cycle distribution analysis, and anti-tumor drug sensitivity test. The miRNA that potentially binds to the 3'UTR of HOXB9 was predicted by miRDB and TargetScan. The regulation of HOXB9 by putative miRNA was confirmed by qRT-PCR, Western blot, and dual luciferase activity assays. The *in vivo* functional roles of HOXB9 and miRNA were revealed by xenograft formation assay.
Results: HOXB9 showed higher mRNA expression compared with other HOX members in GC cell lines. The relative mRNA expression of HOXB9 was upregulated in GC cells compared with immortalized gastric epithelium cell GES-1. Its overexpression was associated with poorer outcome in GC patients. Knocking down HOXB9 led to suppression of cell proliferation, monolayer colony formation, and cell invasion ability. In addition, siHOXB9 induced G1 phase cell cycle arrest and increased anti-cancer drug such as Fluorouracil and Cisplatin sensitivity. HOXB9 was further confirmed to be a direct target of tumor suppressor miRNA, miR-28-5p. Their expressions exhibited negative correlation in primary GC samples. Re-overexpression of HOXB9 partly reversed the tumor-suppressive effect of miR-28-5p.
Conclusion: HOXB9 is over-expressed and plays oncogenic role in gastric carcinogenesis. The activation of HOXB9 in GC is partly due to the silence of a tumor-suppressive miRNA, miR-28-5p. These findings not only elucidated a novel oncogenic transcription factor HOXB9 in gastric carcinogenesis but also enriched its regulatory mechanism by miRNA.
Disclosure: Nothing to disclose

P1815 *FUSOBACTERIUM NUCLEATUM* IS FREQUENTLY DETECTED IN GASTRIC MUCOSA AND IS ASSOCIATED WITH WORSE PROGNOSIS IN DIFFUSE-TYPE GASTRIC CANCER PATIENTS

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Introduction: There is an increasing evidence that microbiota may substantially contribute to carcinogenesis. *Fusobacterium* species (*Fusobacterium* spp.), in particular *Fusobacteria nucleatum* (*F. nucleatum*), are frequently found in colorectal cancer (CRC), and prognostic role in CRC has been suggested. Gastric cancer (GC) is strongly related to *H. pylori* infection; however, the data on microbiota and in particular *F. nucleatum* are limited to microbiome profiling studies and clinical relevance not elucidated.
Aims and Methods: The aim of the study was to evaluate the presence of *Fusobacterium spp.* and *F. nucleatum* in GC, chronic gastritis with or without atrophy/intestinal metaplasia, and to correlate the positivity to clinicopathological characteristics and prognosis of GC patients. For this purpose, *Fusobacterium* spp. and *F. nucleatum* were measured in several biopsies, including CRC tissues (n = 27, T-CRC), matching non-tumoral colon tissues (n = 26, N-CRC), GC tissues (n = 81, T-GC), matching non-tumoral gastric tissues (n = 78, N-GC), gastritis (n = 26) and controls (n = 18). Probe-based qPCR with internal normalization to PGT was used for quantification. Expression data were further analyzed for clinicopathological characteristics and survival (up to 2500 days) and correlated with global (LINE-1) and gene-specific miR-137 methylation.
Results: *Fusobacterium spp.* and *F. nucleatum* were present more frequently in T-CRC with 92.6% and 74.0% in comparison to N-CRC with 80.8% and 53.9%, respectively. In comparison, *Fusobacterium* spp. were detected in N-GC in 65.4% and in T-GC in 77.8%, while *F. nucleatum* was present in N-GC in 23.1% and in T-GC in 28.8% of the gastric samples. The comparison of normalized Ct-values of T-GC and T-CRC revealed a significantly higher bacterial content in CRC for both *Fusobacterium* spp. ($p = 0.0003$) and *F. nucleatum* ($p = 0.007$). Overall, there was a significant correlation between *Fusobacterium* spp. and *F. nucleatum* in T-GC ($p < 0.0001$) as well as of *F. nucleatum* between N-GC and T-GC ($p < 0.0001$). Furthermore, we observed no significant difference between controls, chronic gastritis with and without atrophy/intestinal metaplasia, N-GC and T-GC. Clinicopathological analysis between *F. nucleatum*-positive and -negative subgroups revealed no difference in regard to gender, *H. pylori*-status, tumor stage and tumor localization. There was a positive correlation between *F.nucleatum* and age. Overall survival analysis of GC patients revealed a trend towards the worse survival in *F. nucleatum* positive subjects ($p = 0.13$). However, we observed a significantly worse overall survival only in Lauren's diffuse (positive 244.5 day vs. negative 1229.5 days, $p = 0.009$), but not in intestinal type (median 1406.5 days vs. 1323 days, $p = 0.64$) GC. *F. nucleatum* showed no correlation to global DNA methylation marker LINE-1 or miR-137 methylation.
Conclusion: *F. nucleatum* is frequently present in GC tumoral and non-tumoral tissues although less frequently as in CRC. *F. nucleatum* positivity showed strong association with overall survival in Laurenńs diffuse, but not in intestinal type of GC. Further data are needed to explore the possible functional role of *F. nucleatum* in diffuse type GC patients and interaction with gastric microbiota.
Disclosure: Nothing to disclose

P1816 GASTRIC CANCER IN YOUNG ADULT: IT'S TIME TO SOUND THE ALARM!

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Introduction: Although gastric cancer is considered as a disease of middle-aged and elderly, 2%-15% of patients with gastric cancer are young. Only a few studies with small samples have been conducted. The purpose of our study is to review the epidemiological characteristics, evaluate the survival and prognostic factors of gastric cancer in young subjects.
Aims and Methods: This is a retrospective study including patients admitted in our department for gastric adenocarcinoma between January 2007 and June 2017. Our study included a descriptive component of the epidemiological and clinical characteristics of gastric cancer in patients under 45 and a univariate analytical component of clinical differences with older subjects, survival analysis (Kaplan Meier) and prognostic factors in multivariate.
Results: 265 patients were included during this period. Patients under 45 accounted for 30.6% (n = 81). The average age of our patients was 36 ± 6.10. We observed a male predominance with a sex ratio H / F of 1.25. The familial forms remain infrequent (1.2%) The distal site of the tumor represented 27.2%. Histologically, the linitic form (24.7%, $p = 0.009$) and the poorly differentiated ADK were significantly more frequent. 93.9% of patients had a significantly advanced or metastatic disease (p 0.002). Survival at 5 years in young subjects was 7%, in multivariate analysis only vascular invasion, advanced stage and linitic or poorly differentiated forms were prognostic factors.
Conclusion: In our study, gastric cancer remains frequent and aggressive in young subjects compared to western series. Survival remains low in the literature values.
Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 09:00–14:00
H. Pylori III – Hall X1

P1817 EVALUATION OF *EPIYA* PATTERN IN HELICOBACTER PYLORI *CAGA* AND ITS POSSIBLE RELATION WITH PEPTIC ULCER DISEASE AND GASTRIC CANCER IN EGYPTIAN PATIENTS

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Introduction: Cytotoxin associated gene A protein *(CagA)* of *Helicobacter pylori (HP)* is a major virulence factor that plays a crucial role in gastroduodenal pathologies [1]. *CagA* gene contains the Glu-Pro-Ile-Tyr-Ala *(EPIYA)* segments in its variable region. Polymorphisms of *EPIYA* motifs results in variations of behavior and aggressiveness between *HP* strains [2]. According to *EPIYA* motifs, *HP CagA* gene is subcategorized as East Asian (more aggressive) or Western (less aggressive) types. Western strains contain only *EPIYA motifs A, B and C*. On the other side, East Asian strains contain *EPIYA motifs A, B and D* without *EPIYA-C*. The *EPIYA* pattern and its correlation with the various gastroduodenal disorders differ geographically. Understanding the role of *EPIYA* pattern could be used regionally as individual risk stratification tool for *PUD* and gastric cancer [3].
Aims and Methods: The aim of our work is to define the *EPIYA* pattern of the *HP* isolates in Egyptian patients and to evaluate any possible correlation with *PUD* and gastric cancer. One hundred and twenty-one patients were recruited in Cairo university Endscopy unit. After signature of the informed consent, multiple biopsies were taken endoscopically from antrum and body of the stomach for molecular detection of *HP* and histopathological assessment. Fifty-eight *HP* isolates were detected by PCR. Out of them, 33 isolates contain *CagA* gene. After endoscopic and histopathological assessment, patients were divided to 3 groups (chronic non atrophic gastritis, PUD and gastric cancer). After that, the *EPIYA* motif genotyping was determined then patients were sub-grouped to 2 groups (No more than *EPIYA-C* motif and multiple *EPIYA-C* motifs). Finally, statistical analysis was done to determine any possible correlations with *PUD* or gastric cancer.
Results: Out of the 33 *CagA* positive strains, *EPIYA-ABC* was the most presented pattern in 23 isolates (69.7%) and the least common pattern was *EPIYA-ABCCC*, which was positive only in two cases (6.1%). Both *EPIYA-AB* and *EPIYA-ABCC* were presented in 4 strains for each (12.1% for each). There were significant statistical correlations between presence of *CagA* gene and *PUD*, beside the correlation between no more than one *EPIYA-C* motif group and chronic non-atrophic gastritis. No significant correlation was found between the increase in *EPIYA-C* motifs number and *PUD* or gastric cancer despite the fact that all patients with gastric cancer (4 isolates) had multiple *EPIYA-C* motifs.
Conclusion: In Egypt, the *CagA* gene is Western type with a variable number of *EPIYA-C* and no *EPIYA-D* motifs. Furthermore, a significant statistical association is confirmed between the *CagA* gene and *PUD*. Regarding *EPIYA* pattern, a significant relation is found between the decrease in *EPIYA -C* motifs and chronic non atrophic gastritis (less aggressive behavior). But, no significant association is confirmed between the increase in number of *EPIYA-C* motifs and *PUD* or gastric cancer.
Disclosure: Nothing to disclose

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P1818 PRIMARY RESISTANCE OF *H. PYLORI* TO ANTIMICROBIALS AGENTS IN A NORTHERN ITALIAN REGION: RESULTS FROM A PROSPECTIVE 5-YEARS STUDY

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Introduction: Therapies for *H. pylori* are based on antimicrobial agents also used for other infectious diseases. Since antibiotic resistance develops continuously, it is mandatory to perform periodic prevalence assessment to guide clinicians in selecting the most appropriate therapy in their setting.
Aims and Methods: The aim of this study was to evaluate trends in the prevalence of primary resistance to clarithromycin, metronidazole and levofloxacin over a 5-year period. Consecutive 1325 naïve *H. pylori*-positive patients were studied between 2010 and 2015, and resistances assessed by E-test using the MICs clinical breakpoints recommended by the EUCAST- (>0.5 mg/L, >8 mg/L and >1 mg/L for clarithromycin, metronidazole and levofloxacin, respectively). A univariate and multivariate logistic regression analysis was conducted to examine whether age, sex, BMI, smoking, alcohol consumption, familiarity for gastric cancer, education, country of birth, endoscopic findings, and year of enrolment in the study were potentially involved in bacterial resistance.
Results: When all the 3 antimicrobial agents were considered together, only 39.1% (95% CI: 36.4 to 41.7) of patients were susceptible to all the drugs tested. In the remaining 60.9% (95% CI: 58.3 to 63.5), resistance to one, two or all three agents was present. However, 12.5% (95% CI: 10.9 to 14.4) of patients were resistant to all the antimicrobial agents. When clarithromycin and metronidazole were considered, 45.0% (95% CI: 42.3 to 47.7) of strains were susceptible to both agents. In the remaining 55% (95% CI: 52.3 to 57.7), resistance to one or two agents was present. However, 22.6% (95% CI: 20.5 to 25.0) of patients were resistant to both antimicrobials. Considering clarithromycin, 59.2% (95% CI: 56.6 to 61.9) of the strains were susceptible, and 36.1% (95%CI: 30.4 to 41.9) were resistant. Considering metronidazole, 61.4% (95% CI: 58.7 to 63.9) of the strains were susceptible, and 38.6% (95%CI: 36.1 to 41.3) were resistant. Finally, considering levofloxacin, 61.4% (95% CI: 58.7 to 63.9) of the strains were susceptible, and 38.6% (95%CI: 36.1 to 41.3) were resistant. The multivariate analysis showed that the risk of carrying resistant strains increased significantly and independently over the years (OR: 1.15; 95% CI: 1.08 to 1.23; $p < 0.0001$; OR: 1.11; 95% CI: 1.04 to 1.19; $p = 0.002$; OR: 1.16; 95% CI: 1.08 to 1.25; $p < 0.0001$, for clarithromycin, metronidazole, and levofloxacin respectively).
Conclusion: The prevalence of primary resistances to the antimicrobial agents tested in our region was high and increased significantly between 2010 and 2015. Regional health authorities should consider to set up regular monitoring of primary resistance for *H. pylori*. If strategies to reduce and to improve the use of antibiotics are nor put in place, it will be increasingly difficult to eradicate *H. pylori* infection in future years.
Disclosure: Nothing to disclose

P1819 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): BACTERIAL RESISTANCE OF 2,684 H. PYLORI ISOLATES

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Introduction: Antibacterial resistance is the major cause of failed eradication attempts in the management of *Helicobacter pylori*.
Aims and Methods: Our aim was to evaluate the *H. pylori* resistance rates encountered by European Gastroenterologists in their routine clinical practice. A Local Coordinator was selected from each country with more than 10 *H. pylori* references in PubMed. Each Coordinator selected a representative group of recruiting investigators from his/her country. An e-CRF was created on AEG-REDCap to systematically register all adult patients infected with *H. pylori*. Variables included: *H. pylori* diagnostic test used, use of culture and susceptibility testing, or molecular tests for the evaluation of antibiotic resistance.
Results: Data regarding resistance to antibiotics was available in 12% (2,684) of cases (21,300 patients). In naïve patients, there was no resistance in 44% of strains. Resistance to the most common antibiotics in naïve patients was: 22% to clarithromycin, 31% to nitroimidazoles, and 18% to quinolones; and dual resistance to clarithromycin and nitroimidazole in 13% of the cases. Resistance rates increased after each failed eradication attempt. Table shows antibiotic resistance per line.
Conclusion: The mean rate of *H. pylori* clarithromycin resistance (22%) in European treatment-naïve patients discourages the empirical use of standard triple therapy. Furthermore, concomitant treatment may be soon limited by the increasing dual resistance to clarithromycin and metronidazole (13%). There is a strong acquisition of antibiotic resistance after failed treatments.

Resistance	Line of treatment					
	Overall	First (naïve)	Second	Third	Fourth	Fifth
No resistance	35%	44% (40–48)	13% (4–25)	9% (0–23)	9% (0–37)	16% (0–63)
Clarithromycin	35%	22% (18–27)	60% (54–67)	73% (67–79	78% (64–92)	79% (54–100)
Metronidazole	39%	31% (27–35)	52% (44–59)	65% (58–73)	64% (48–80)	64% (33–96)
Levofloxacin	24%	18% (14–23)	29% (21–40)	46% (40–52)	47% (27–67)	32% (0–76)
Dual (C+M)	23%	13% (8–18)	41% (32–50)	56% (47–65)	55% (37–73)	58% (24–92)

C – clarithromycin, M – metronidazole; the parenthesis includes the 95% confidence interval
[Table 1]
Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions and is an advisor of Mayoly.

P1820 *HELICOBACTER PYLORI* HTRA IS NOT ASSOCIATED WITH CLINICOPATHOLOGICAL GASTRITIS PHENOTYPE OR VACA VIRULENCE FACTOR POLYMORPHISMS

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Introduction: Virulence factors of *Helicobacter pylori* (*H.pylori*) affect the immunopathological gastritis pattern. The serine protease HtrA is a newly identified virulence factor that disrupts intercellular adhesion and contributes to the intercellular entry of *H.pylori in vitro*.
Aims and Methods: Aim of the study was to evaluate the phenotype of gastritis and HtrA expression of *H.pylori* isolates in relation to CagA and VacA virulence factors. In a prospective study with focus on the relationship of *H. pylori* virulence and gastritis phenotypes, we cultivated 157 *H.pylori* strains from antrum and corpus from 89 patients with chronic gastritis (CNAG), atrophic gastritis (AG), peptic ulcer diseases (PUD) and gastric cancer (GC). *H.pylori cagA*, *vacA* s/m genotype and HtrA and GlmM mRNA expression were determined by PCR. Anti-*H.pylori* and anti-CagA-IgG status was evaluated using commercially available ELISA. Histological gastritis phenotype was characterized based on the updated Sydney score.
Results: All *H.pylori* isolates expressed HtrA, which was similar between isolates from antrum and corpus within each individual patient. HtrA expression was independent from *cagA* positivity or *vacA* s/m genotypes. There was no association between HtrA expression and anti-*H.pylori*-IgG or anti-CagA-IgG systemic immune response. Histopathological analysis revealed similar HtrA expression between patients with CNAG, AG, PUD or GC, which was not correlated with gastritis activity and chronicity scores. No correlation was found between HtrA expression and intestinal metaplasia or degree of atrophy. PPI intake had no effect on the HtrA expression.
Conclusion: HtrA is constantly expressed in all *H. pylori* strains. However, HtrA expression showed no association with gastritis phenotypes nor with *cagA*, *vacA* status or *H.pylori*-serology. The functional role of HtrA remains uncertain.
Disclosure: Nothing to disclose

P1821 A QUICK FLOW CYTOMETRY PROTOCOL TO ASSESS *HELICOBACTER PYLORI* VIABILITY AND DENSITY

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Introduction: Culture methods have been traditionally used to evaluate the efficacy of *Helicobacter pylori* eradication assays. Nevertheless, they are material and time consuming so a quicker and easier methods are needed.

Aims and Methods: We aimed to design a protocol to assess *H. pylori* viability using flow cytometry (FC). Strain TIGR-26695 was cultured in Columbia Agar medium supplemented with blood (COS). Growing bacteria were suspended in 0.9% NaCl (3 McFarland of turbidity). Colony counting was performed by 1:10 dilution, plating 10µl in COS and 5-days incubation in a CO_2 incubator. Aliquots of bacterial suspension were killed by heat, 70% isopropanol, or 0.5% bleach. Live-dead mixed suspensions were performed, ranging from 0–100% in intervals of 10% of live. Live/Dead BacLight™ Kit was used to stain bacteria for FC analyses using FACS-CantoII cytometer. The%live bacteria added to each mix was compared to the % live estimated by FC. Counting beads (CB) were used to estimate the microbial density using FC.
Results: The optimized protocol involved addition of 1.5µl Syto9 and 0.2µl propidium-iodide to a 1:100 dilution of the bacteria in 979µl NaCl (15 minutes, dark); 10µl CB were added immediately before FC acquisition. A good correlation between the % live and the FC-estimations were obtained for the heat-killed ($R^2 > 0.99$) and the isopropanol models ($R^2 > 0.97$). Bleach treatment caused the fragmentation of bacteria, and could not be properly detected using FC. Bacterial density estimations were comparable between FC and culture.
Conclusion: FC is a fast, accurate and reproducible method to assess *H. pylori* density and viability.
Disclosure: Nothing to disclose

P1822 EFFICACY OF PYLERA VERSUS STANDARD THERAPY WITH ESOMEPRAZOLE AS THE FIRST LINE OF TREATMENT IN THE ERADICATION OF HELICOBACTER PYLORI. REAL-LIFE STUDY

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Introduction: Due to the high rates of resistance to clarithromycin, triple therapy with PPI, amoxicillin, and clarithromycin is inadequate when the local clarithromycin resistance rates exceed 20%. Quadruple therapy with bismuth subcitrate, metronidazole and tetracycline administered in conjunction with a PPI has shown eradication rates greater than 80–90% in randomized controlled trials as primary therapy and appears to be highly effective even in strains that are resistant to metronidazole.
Aims and Methods: The purpose of this study is to evaluate the efficacy of quadruple therapy with a combination formula containing in a capsule 140 mg of bismuth potassium subcitrate (equivalent to 40 mg of bismuth oxide), 125 mg of metronidazole and 125 mg of hydrochloride of tetracycline (Pylera®, Aptalis Pharma, Bridgewater, NJ, USA) administered four times a day, associated with omeprazole twice daily compared to classical first-line therapy based on clarithromycin 500 mg, amoxicillin 1 g and esomeprazole 40 mg administered twice daily, who have never received treatment prior to eradicating *H. pylori* infection. We did a retrospective unicentric observational study in conditions of usual clinical practice, comparing the efficacy of 10 days of quadruple therapy with omeprazole plus a single three-in-one capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline (quadruple therapy) versus 10 days of esomeprazole, amoxicillin, and clarithromycin (standard therapy) in adults with recorded *H. pylori* infection. The eradication rates of both groups were identified as intention-to-treat (ITT) and per-protocol (PP) analyses. *H. pylori* eradication was confirmed by a 13C-urea breath test at least 4 weeks after the completion of eradication therapy.
Results: A total of 221 patients (114 and 107 patients in the standard therapy and quadruple therapy, respectively) were analyzed. There were 82 male and 139 female patients. ITT eradication rates were 86.92% (93/107; 95% confidence interval (CI), 84.4%-93.3%) in the 10-day bismuth-based quadruple therapy group and 78.07% (89/114; 95% CI, 70.3%-85.7%) in the 10-day standard therapy group ($P = 0.08$). And, PP eradication rates were 91.18% (93/102; 95% CI, 85.6%-96.7%) in the 10-day bismuth-based quadruple therapy group and 82.41% (89/108; 95% CI: 75.1%-89.6%) in the 10-day standard therapy group ($P = 0.06$). There were no significant differences in both treatment groups according to both ITT and PP analyses.
Conclusion: Despite there being no significant differences between the two groups, the eradication rate 10-day bismuth-based quadruple therapy is more higher for treatment of *H. pylori* infection than 10-day standard therapy with esomeprazole.
Disclosure: Nothing to disclose

P1823 SHORT-TERM AND LONG-TERM CHANGES OF GUT MICROBIOTA AND METABOLIC PARAMETERS AFTER *HELICOBACTER PYLORI* ERADICATION

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Introduction: Little is known about the long impact of *Helicobacter pylori (H. pylori)* eradication therapies on the gut microbiota and metabolic parameters.
Aims and Methods: We aimed to assess the changes in the gut microbiota and metabolic parameters before and 2 weeks, 2 month, and 1 year after first-line treatment of *H. pylori* infection. Adult patients with documented *H. pylori* infection ($n = 1620$) were randomized in this multicenter, open-label trial to receive concomitant therapy for 10 days (CT10) or bismuth quadruple therapy for 10 days (BQ10) or triple therapy for 14 days (TT14). The long-term outcomes included the reinfection rate, the changes in the gut microbiota, body weight, glucose, insulin resistance, and lipid profiles. Fecal samples were collected before and 2 weeks, 2 months, and at least 1 year after eradication therapy in a subgroup of patients (National Taiwan University Hospital and its Yun-Lin Branch). Amplification of the V3 and V4 hypervariable regions of the 16S rRNA was done followed by high throughput sequencing (Illumina miseq). Weighted-unifrac method was used to analyze the β-diversity.
Results: Of the 1155 successfully treated patients, reinfection/recrudescence was observed in 3.3% (13/390), 2.6% (10/388), and 3.4% (13/377) of patients treated with TT14, CT10, and BQ10 after 1.55 years, respectively ($p = 0.751$) in our preliminary results. 16S rRNA was sequenced and analyzed in a total of 782 fecal DNA samples. Compared to baseline ($N = 83$), the species-richness (α-diversity) was significantly reduced at 2 weeks ($N = 57$, $p = 0.000078$), but the richness gradually returned at 2 month ($N = 70$, $p = 0.11$) and 1 year ($N = 79$, $p = 0.83$) after TT14 treatment. Compared to baseline ($N = 76$), α-diversity was significantly reduced at 2 weeks ($N = 40$, $p = 6.3 \times 10^{-15}$), at 2 month ($N = 62$, $p = 0.00015$), and 1 year ($N = 65$, $p = 0.017$) after CT10 treatment. Compared to baseline ($N = 83$), the α-diversity was significantly reduced at 2 weeks ($N = 32$, $p = 9.1 \times 10^{-13}$), at 2 month ($N = 72$, $p = 3.3 \times 10^{-8}$), and 1 year ($N = 63$, $p = 0.0024$) after BQ10 treatment. Compared to baseline, there was significant

Abstract No: P1822
Table 1: Univariate analysis showing factors affecting *Helicobacter pylori* eradication rates in the ITT and PP populations

	ITT		PP	
	Pylera	EAC	Pylera	EAC
Gender – Male – Female	37/43 (86.0%) 56/64 (87.5%)	34/39 (87.1%) 55/75 (73.3%)	37/41 (90.2%) 56/61 (91.8%)	34/38 (89.4%) 55/70 (78.5%)
Age, y (18-<40) (40–60) (≥60)	20/22 (90.9%) 51/60 (85.0%) 22/25 (88.0%)	14/16 (87.5%) 43/53 (81.1%) 32/45 (71.1%)	20/21 (95.2%) 51/57 (89.4%) 22/24 (91.6%)	14/15 (93.3%) 43/52 (82.6%) 32/41 (78.0%)
Arterial Hypertension – Yes – No	21/25 (84.0%) 72/82 (87,8%)	19/27 (70,3%) 70/87 (80,4%)	21/24 (87.5%) 72/78 (92.3%)	19/23 (82.6%) 70/85 (82.3%)
Cigarette smoking – Yes – No	08/10 (80.0%) 54/64 (84.3%)	10/11 (90.9%) 58/74 (78.3%)	08/09 (88.8%) 54/61 (88.5%)	10/11 (90.9%) 58/70 (82.8%)
Alcohol consumption – Yes – No	12/14 (85.7%) 48/58 (82.7%)	08/12 (66.6%) 57/70 (81.4%)	12/13 (92.3%) 48/55 (87.2%)	08/12 (66.6%) 57/66 (86.3%)
Diabetes Mellitus – Yes – No	02/06 (33.3%)* 91/101 (90.1%)*	04/06 (66.6%) 85/108 (78.7%)	02/04 (50.0%) 91/98 (92.8%)	04/05 (80.0%) 85/103 (82.5%)
NSAIDs consumption – Yes – No	13/15 (86.6%) 80/92 (86.9%)	11/16 (68.7%) 78/97 (80.4%)	13/14 (92.8%) 80/88 (90.9%)	11/15 (73.3%) 78/93 (83.8%)
Dyspepsia – Non-ulcer – Ulcer	58/71 (81,6%) 19/20 (95%)	55/70 (78,5%) 16/19 (84,2%)	58/67 (86.5%) 19/19 (100%)	55/66 (83.3%) 16/19 (84.2%)
Endoscopic findings – Gastritis – Peptic ulcer	78/90 (86,6%) 04/04 (100%)	70/91 (76,9%) 04/06 (66,6%)	78/86 (90.7%) 04/04 (100%)	70/86 (81.4%) 04/06 (66.6%)

* $p < 0.005$

differences in the fecal microbiota structure (β-diversity) at 2 weeks ($p = 0.0005$) and at 2 month ($p = 0.0427$) after TT14, but the difference was not significant at 1 year ($p = 0.085$). There was significant difference in the β-diversity at 2 weeks ($p = 0.0001$) and at 1 year ($p = 0.038$) after CT10. There was significant differences in the β-diversity at 2 weeks ($p = 0.0001$), 2 month ($p = 0.0002$), and 1 year ($p = 0.0074$) after BQ10. We observed mild increase in the body weight (64.3 vs. 65 kg, $p < 0.001$), body mass index (24.38 vs. 24.59, $p < 0.001$), high-density lipoprotein (54.9 vs. 58.4 mg/dL, $p < 0.001$), and total cholesterol (194.6 vs. 197.8 mg/dL, $p = 0.009$) 1.55 year after eradication therapy. However, there were no significant changes in the insulin resistance (HOMA-IR) and low-density lipoprotein levels.
Conclusion: The abundance and diversity of gut microbiota changed significantly immediately after *H. pylori* eradication therapy. The microbiota appeared to be restored with time but the speed and extent of restoration varied according to the eradication regimens. (Funded by National Taiwan University Hospital and Ministry of Science and Technology of Taiwan; ClinicalTrials.gov, NCT01906879)
Disclosure: Nothing to disclose

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P1824 EFFECTIVENESS OF PYLERA AS FIRST-LINE ERRADICATION THERAPY FOR *H. PYLORI* INFECTIONS

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Introduction: Pylera associated with a proton pump inhibitor (PPI) for 10 days is, according to actual statements, a therapeutic option as first line eradication therapy, after proving a satisfactory efficacy (more than 90%). Our working group recommends that *H.pylori* eradication treatments should be validated in each geographical area before they can be recommended as a first-line therapy.
Aims and Methods: Unicenter, observational, prospective, non-controlled study. A total of 125 consecutive patients with *Helicobacter pylori* infection were included from 2016–2018. The average age is 54-year-old (18–81), 57% women, 41.6% with non-investigated dyspepsia, 25.6% with functional dyspepsia, 19.2% peptic ulcer disease and 13.6% with other diagnoses. All patients received a first-line therapy with Pylera for 10 days, 3 capsules four times a day with a PPI (68% omeprazole 40 mg) at breakfast and dinner. In each patient was studied the compliance, adverse effects by telephone contact as well as and the efficacy. The treatment was considered effective when the urea breath test (UBT) was negative 4 weeks after finishing treatment. All cases are included in *H.pylori* European Register (HP-EuReg) and monitored through AEG-REDCap platform.
Results: 119 patients (95.2%) completed the treatment (>90% of the dose). 5 of the 6 patients that discontinued treatment were due to adverse events. 35% of patients (28%) reported some side effect, being serious adverse event in only just 1 patient (*C.difficile* colitis). *H.pylori* eradication rates were 94.9% (IC 95% 90.9–98.9) of patients (113/119) per protocol analysis; and 92% (IC 95% 87.1–96.8) of patients (115/125) for the intention to treat analysis.
Conclusion: Therapy with Pylera for 10 days has, according to our experience, high efficacy, high compliance (>90%) and acceptable security, being a recommended therapeutic option as first-line eradication therapy.
Disclosure: Nothing to disclose

P1825 EFFICACY OF ORAL N-ACETYL CYSTEINE ON *HELICOBACTER PYLORI* ERADICATION IN ADDITION TO QUADRUPLE THERAPY REGIMEN

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Introduction: N-acetyl cysteine (NAC) has mucolytic, antioxidant, and antimicrobial effects which has been suggested recently as an adjuvant to the eradication of *Helicobacter pylori (H. pylori)* infection. This study was aimed to determine the effectiveness of NAC in addition to standard quadruple therapy on Eradication of *Helicobacter Pylori.*
Aims and Methods: In this double-blinded controlled clinical trial (IRCT201605201155N24), 92 patients with the diagnosis of *H. pylori* infection in gastric biopsies were randomly allocated into intervention and control groups. Both groups received a 14-day regimen of quadruple therapy comprising amoxicillin, clarithromycin, pantoprazole and bismuth subcitrate. In addition to quadruple therapy regimen with similar timing, the intervention and control groups received NAC and placebo, respectively. The urea breath test (UBT) was performed to confirm the eradication of *H. pylori* eight weeks after the end of treatment.
Results: The percentage of *H. pylori* eradication in the intervention and control groups was 78.3% (CI 95%: 66.38–90.21) and 71.7% (CI 95%: 59.57–84.49%), respectively ($p = 0.804$) which were not statistically significant. Eradication rate was significantly higher in smokers who were treated with NAC.
Conclusion: Although the *H. pylori* eradication rate was higher in patients who received NAC as an adjunctive drug, it was not statistically significant. This study showed that the rate of *H. pylori* eradication significantly increased in smokers who received NAC.
Disclosure: Nothing to disclose

P1826 EFFECTS OF PROBIOTICS OR BROCCOLI SUPPLEMENTATION ON *HELICOBACTER PYLORI* ERADICATION WITH STANDARD CLARITHROMYCIN-BASED TRIPLE THERAPY

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Introduction: The eradication failure of standard triple therapy (proton pump inhibitor, clarithromycin and amoxicillin) for *Helicobacter pylori* infection has increased due to antibiotics resistance in Korea. Supplementation of some probiotics improved *H. pylori* eradication rates and reduced the adverse events of the triple therapy. Sulforaphane extracted from broccoli is a potent bacteriostatic agent against *H. pylori* strains, and also exhibits bactericidal effects in a human epithelial cell line.
Aims and Methods: We aimed to determine whether *Saccharomyces boulardii* probiotics or sulforaphane supplementation can increase the *H. pylori* eradication rate and/or reduce antibiotics-associated adverse events in a Korean population. A total of 217 patients with *H. pylori*-positive chronic gastritis or peptic ulcer disease were recruited. All participants were diagnosed with *H. pylori* infection using rapid urease or C^{13}-urea breath test. Clarithromycin resistance test was performed for all patients by detecting A2142G and A2143G point mutations in *H. pylori* 23S rRNA using a dual-priming oligonucleotide PCR. Thirty-four patients were clarithromycin resistant and hence excluded from the study. Finally, 183 patients not resistant to clarithromycin were randomly assigned to three groups using a computer program: triple therapy only (group A, $n = 61$), triple therapy plus probiotics (group B, $n = 61$), and triple therapy plus sulforaphane (group C, $n = 61$). Group A received pantoprazole, amoxicillin, and clarithromycin for 7 days. Groups B and C received the same PPI-based triple therapy for 7 days. Additionally, one capsule with either probiotics or sulforaphane was given for 4 weeks. Eradication of *H. pylori* was assessed using a ^{13}C-urea breath test 4 weeks after treatment. We collected information of drug compliance and adverse events such as, taste disturbance, diarrhoea, headache, epigastric pain, nausea, and urticaria.
Results: The eradication rates according to ITT and PP analyses were 85.2% and 88.1% in group A, respectively. ITT and PP analyses showed 81.6% and 90.9% eradication rates in group B and 87% and 94.6% in group C, respectively. The eradication rates between the three groups according to ITT and PP analyses were insignificantly different based on multiple group comparison test ($p = 0.744$, $p = 0.313$, respectively). The frequency of overall adverse events in the three groups was not different ($p = 0.847$). The frequency of gastrointestinal disturbances, such as diarrhoea, epigastric pain, and nausea, were lower in group B than group A, but insignificantly different ($p = 0.262$)
Conclusion: Probiotics or sulforaphane supplementation with triple therapy on *H. pylori* infection neither increased the eradication rate nor reduced the adverse events in a Korean population.
Disclosure: Nothing to disclose

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P1827 PYLERA AND SEQUENTIAL THERAPY FOR FIRST-LINE *H. PYLORI* ERADICATION: A CULTURE-BASED HEAD-TO-HEAD COMPARISON IN CLINICAL PRACTICE

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Introduction: Italian guideline suggests 10-day sequential or bismuth-based quadruple therapies for first-line *H. pylori* treatment. Comparison between these regimens is lacking. We assessed the efficacy of these therapies in clinical practice, and evaluated the role of primary bacterial resistance towards clarithromycin and metronidazole.
Aims and Methods: Consecutive patients with *H. pylori* infection were enrolled. Bacterial culture with antibiotics susceptibility testing was attempted in all cases. Patients received either a sequential therapy with esomeprazole 40 mg for 10-day

plus amoxicillin 1000 mg for the first 5 days followed by clarithromycin 500 mg and tinidazole 500 mg (all b.i.d) for the remaining 5 days, or bismuth-based therapy with esomeprazole 20 mg b.i.d and Pylera® 3 tablets q.i.d. for 10 days. *H. pylori* eradication was assessed by using ^{13}C-urea breath test.
Results: A total of 495 patients were enrolled. Following sequential (250 patients) and quadruple (245 patients) therapies, respectively, the eradication rate were 92% and 91% at intention-to-treat and 96% and 97% at per protocol analyses. Overall, the pattern of bacterial resistance did not significantly affect the cure rate, but the presence of clarithromycin and metronidazole dual resistance tended to reduce the success rate of both sequential (84.8% *vs* 90.1%; $P = 0.4$) and quadruple (85% *vs* 94.1%; $P = 0.06$) therapies. Adverse events occurred more frequently with the quadruple than with sequential therapy (56.9% *vs* 25.8%; $P < 0.001$).
Conclusion: In our country, sequential and bismuth-based quadruple therapies achieved similarly high eradication rates as first-line treatments for *H. pylori* infection in clinical practice.
Disclosure: Nothing to disclose

P1828 FATE OF BENEFICIAL GUT MICROBIOTA AFTER *H. PYLORI* ERADICATION THERAPY: METAGENOMIC LANDSCAPE OF RESISTANCE MECHANISMS

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Introduction: Antimicrobial agents have a significant impact on gut microbiota and its functions. Negative effects of antibiotics can be associated with depletion of beneficial microbiota and increasing amount of antibiotic resistance genes in potentially pathogenic bacteria.
Aims and Methods: The aim of our study was to evaluate the effect of *H. pylori* eradication therapy on the distribution of antimicrobial resistance genes especially in cases of beneficial microbiota survival. Stool samples from 35 *H. pylori*-positive patients before and after eradication therapy according to the standard protocol of Maastricht IV were analysed. Shotgun sequencing was performed on the SOLiD 5500xl W platform according to the manufacturer's recommendations. Reads were aligned to the CARD database (version 1.1.7) with bowtie 1.2.0 software.
Results: Significant changes in ratio and number of microorganisms including beneficial microbiota were detected in the intestinal microbiome of all patients after eradication therapy. Thus, 28 (80%) patients showed a decrease in the *Bifidobacterium* proportion and 12 (34.3%) patients had a decreased *Lactobacillus* ratio after therapy. An increase in *Bifidobacterium* and *Lactobacillus* genera was detected in 2 (5.7%) and 6 (17.1%) cases, correspondingly. These genera were absent in gut microbiota of 2 (5.7%) and 7 (20%) patients. Significant quantitative changes have been identified in genes that determine resistance to 8 out of 28 antibiotic groups (according to CARD): determinants of aminoglycoside, beta-lactam, macrolide, sulfonamide, macrolide/streptogramin/MLSb resistance, resistance to glycopeptide antibiotics, peptide antibiotics, efflux pump complex or subunit conferring antibiotic resistance. The changes were also associated with the variability of antibiotic resistance genes abundance in *Bifidobacterium* and *Lactobacillus*, including *ileS*, *tetW*, *cat*-TC, specifying mupirocin, tetracycline and chloramphenicol resistance in those bacteria.
Conclusion: The data indicates that *H. pylori* eradication therapy associated with the use of β-lactams and macrolides induces significant changes in the pattern of resistance genes to antimicrobial drugs of different groups in beneficial representatives of gut microbiota. Metabolic pathways and resistance of the corresponding organisms remain to be studied in pure cultures.
Disclosure: The work is performed according to the Russian Government Program of Competitive Growth of Kazan Federal University. The research was performed using the equipment of Interdisciplinary Centre for Shared Use of Kazan Federal University

P1829 IS THE INTERVAL BETWEEN THE FIRST AND THE SECOND H.P. ERADICATION THERAPY RELEVANT FOR THE SUCCESS OF THE CURE? A COMPARISON BETWEEN ONE WEEK, ONE MONTH AND ONE YEAR

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Introduction: The success of *Helicobacter pylori* (H.p.) eradication therapy is based on the effectiveness of the therapeutical schedule as well as on the resistance of H.p. strains to the antibiotics in different areas.
Aims and Methods: Aim of this study was to compare different intervals between the first H.p. eradication therapy and the second attempt, by using for both, the same schedule.
Two hundred and fifty nine consecutive H.p. positive patients (Male 135, Mean Age 52 years range 27–81) were enrolled in the study, after failure of first line treatment based on triple one week therapy (Omeprazole 20 mg/b.i.d., Amoxicillin 1 g/b.i.d., Tinidazole 500 mg/b.i.d.). All patients underwent a rescue therapy based on the same schedule at different intervals from the end of the first line therapy: 35 pts (Male 22 Mean age 51 range 27–72) after 7–10 days (Group 1); 44 pts (Male 24 mean age 53 range 28–75) after 1 month (Group 2); 82 pts (Male 43 mean age 49 range 29–78) after three months (Group 3); 98 pts (Male 46 mean age 53 range 28–81) after six-twelve months (Group 4). The H.p. eradication was established by means of U.B.T., performed at least one month after the end of rescue therapy.
Results: The success of the therapy in the four groups is summarized in the table. In Group 1 we experienced 4 drop outs, 5 in Group 2, 8 in Group 3 and 9 in Group 4.
Conclusion: The interval between the first and the second attempt of H.p. eradication therapy seems in our study crucial in determining the success of the cure, at least a six-months interval being the critical time to influence the results.

Group	Cured patients	Intention to treat	Per protocol	p
1	9/35	27.5	29.0	n.s.
2	14/44	31.8	35.8	n.s.
3	31/82	37.8	41.8	n.s.
4	69.88	70.4	77.5	0.01

[Success of the therapy in the four studied groups]
Disclosure: Nothing to disclose

P183000-DAY VERSUS 14-DAY QUADRUPLE CONCOMITANT NON BISMUTH THERAPY FOR THE TREATMENT OF *HELICOBACTER PYLORI* INFECTION: RESULTS FROM A GREEK RANDOMIZED PROSPECTIVE STUDY

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Introduction: According to all current available data, there is so far no universally effective regimen for *Helicobacter pylori* (*H. pylori*) eradication therapy. The Toronto Consensus for the treatment of *H. pylori* infection recommends that both the concomitant non-bismuth quadruple therapy (proton pump inhibitor [PPI] + amoxicillin + metronidazole + clarithromycin [PAMC]) and the traditional bismuth-containing quadruple therapy (PPI + bismuth + metronidazole + tetracycline [PBMT]) should play a more prominent role in eradication of *H. pylori* infection, and should be prescribed for 14 days. The Maastricht V consensus also recommends as first-line treatment in areas of high (>15%) clarithromycin resistance, a 14-days course of either the bismuth or the non-bismuth quadruple, concomitant therapies, unless a 10-days regimen is proven equally effective locally. Moreover, the American College of Gastroenterology (ACG) Clinical Guideline for the treatment of *H. pylori* infection clearly state that prior antibiotic exposure should be incorporated into the decision-making process and that most patients would be better served by first-line treatment with non-bismuth concomitant therapy for a period of 10–14 days, although the quality of evidence regarding duration is still very low. The objective of this study is to compare the efficacy rates of the 10-day versus the 14-day PAMC therapy in Greece, a country with an antibiotic-resistance pattern similar to the USA and most central and southern European countries (high clarithromycin resistance >20% and intermediate metronidazole resistance <40%).
Aims and Methods: Our prospective randomized study included 384 patients with newly diagnosed *H. pylori* infection, randomized to receive a 10-day or a 14-day concomitant PAMC therapy. Treatment outcome was assessed by C^{13}-urea breath test at least 4 weeks after therapy. Intention to treat (ITT) and per protocol (PP) analysis of the eradication rates were performed. Secondary end points included patient compliance, safety and eradication rates related to previous antibiotic exposure (ClinicalTrials.gov Identifier: NCT02959255).
Results: The two groups achieved almost equal eradication rates, both in the ITT and in the PP analysis (85.1% for the 10-day versus 85.9% for the 14-day, $p > 0.05$, and 93.6% for the 10-day versus 94.4% for the 14-day, $p > 0.05$, respectively), after adjusting for age, gender, smoking status, prior exposure to antibiotics, peptic ulcer disease and/or non-ulcer dyspepsia. Patient compliance was excellent for both groups (99.5% for the 10-day and 98.7% for the 14-day concomitant PAMC therapy group, $p > 0.05$). Major adverse events that led to discontinuation of the treatment were not statistically significant between groups ($p > 0.05$). Regarding minor adverse events, a trend towards more episodes of diarrhea was recorded in the 14-day (group A) versus the 10-day therapy group (25.4/% and 34.7%, respectively, $p > 0.05$).

Conclusion: Both the 10- and the 14-day concomitant PAMC therapy exhibited almost equally high eradication rates, with excellent compliance and an acceptable safety profile. Thus, according to our data, in Greece, there is no necessity for *H. pylori* eradication treatment extension to 14 days.
Disclosure: Nothing to disclose

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P1831 EFFICACY AND SAFETY OF QUADRUPLE THERAPIES WITH AND WITHOUT BISMUTH IN THE ERADICATION OF HELICOBACTER PILORY INFECTION. REAL-LIFE STUDY

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Introduction: Quadruple therapy with bismuth subcitrate, metronidazole and tetracycline administered in conjunction with a PPI has shown eradication rates greater than 80–90% in randomized controlled trials as primary therapy and appears to be highly effective even in strains that are resistant to metronidazole.
Aims and Methods: The purpose of this study is to evaluate the efficacy and safety of quadruple therapy with a combination formula containing in a capsule 140 mg of bismuth potassium subcitrate (equivalent to 40 mg of bismuth oxide), 125 mg of metronidazole and 125 mg mg of tetracycline hydrochloride administered four times a day, associated with omeprazole twice daily compared to quadruple therapy without bismuth in patients who have never received eradicating treatment for *H. pylori* infection.
Between January 2017 and December 2017, we performed an observational, retrospective and multicenter study under conditions of usual clinical practice, comparing the efficacy and safety of 10 days of quadruple therapy with omeprazole plus a three-in-one capsule containing bismuth potassium subcitrate, metronidazole and tetracycline (Pylera) versus 14 days of amoxicillin 1gr, metronidazole 500mg, clarithromycin 500mg twice a day plus omeprazole 40mg day (quadruple without bismuth) in adults with *H. pylori* infection. The eradication rates of both groups were identified in intention-to-treat (IT) and protocol (PP) analyzes. *H. pylori* eradication was confirmed by a 13C-urea breath test at least 4 weeks after the completion of eradication therapy.
Results: A total of 196 patients (81 and 115 patients on quadruple therapy with bismuth (Pylera) and quadruple therapy without bismuth, respectively) were analyzed. 62 male and 134 female patients with a mean age of 53 ± 14.39. ITT eradication rates were 85.19% (69/81, confidence interval (CI) 95%, 77.3%-93.0%) in the 10-day bismuth-based quadruple therapy group and 77.39% (89/115, 95% CI, 69.6%-85.1%) in the 14-day bismuth quadruple therapy group ($P = 0.17$). And, PP eradication rates were 93.24% (69/74, 95% CI, 87.4%-99.0%) in the bismuth-based quadruple therapy group and 83.96% (89/106, CI 95%, 76.8% -91.0%) in the quadruple therapy group without bismuth ($P = 0.06$). There were no significant differences in both treatment groups according to both ITT and PP analysis. Adverse event rates were 10.39% (8/77) in the 10-day bismuth-based quadruple therapy group and 23.30% (24/103) in the 14-day bismuth quadruple therapy group ($p = 0.07$).
Conclusion: Despite there being no significant differences between the two groups, the eradication rate 10-day bismuth-based quadruple therapy is higher for the treatment of *H. pylori* infection than quadruple therapy without bismuth. Regarding treatment safety, there were no significant differences between the two groups.
Disclosure: Nothing to disclose

P1832 PREDICTIVE FACTORS FOR REGRESSION OF LOW-GRADE GASTRIC MALT LYMPHOMA AFTER ANTI-*HELICOBACTER PYLORI* TREATMENT

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Introduction: Eradication of *Helicobacter pylori* (*H. pylori*) is accepted as initial treatment of low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma. However, 10–20% of gastric low grade MALT lymphomas are unresponsive to *H. pylori* eradication treatment. The aim of this study was to find out the predictive factors of complete remission of gastric MALT lymphoma after *H. pylori* eradication.
Aims and Methods: From 2006 to 2016, consecutive 64 patients with modified Ann Arbor stage IE and II1E gastric MALT lymphoma were enrolled, and their medical records were reviewed. The patients were initially treated by *H. pylori* eradication. The complete remission was determined by endoscopic and histologic finding.
Results: 48 patients (75%) achieved complete remission after *H. pylori* eradication therapy. Mean follow up time for these patients was 38.8 months [6- 72 months]. Eight patients (12.5%) failed to achieve complete remission. Eight patients were lost of sight. There was no significant difference in the age, sex, endoscopic appearance, and large cell component between the remission group and failure group. Among 12 patients with proximal tumor, 8 patients (66.6%) achieved complete remission. On the other hand, among 52 patient with distal tumor, 40 patients (76.9%) achieved complete remission. The odds ratio of proximal tumor for *H. pylori* eradication failure was 28.9 (95% CI = 2.9–288.0).
Conclusion: The discovery of the etiologic role of *H. pylori* infection in gastric lymphoma has radically changed its therapeutic approach. The proximally location of MALT lymphoma is a risk factor of the *H. pylori* eradication treatment failure.
Disclosure: Nothing to disclose

P1833 *HELICOBACTER PYLORI* CAGA PROMOTES EPITHELIAL MESENCHYMAL TRANSITION IN GASTRIC CARCINOGENESIS VIA TRIGGERING ONCOGENIC YAP PATHWAY

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Introduction: CagA is a defined virulence factor of *H. pylori* whose infection is associated with an increased risk of gastric cancer. However, it is unclear what its role is in oncogenic YAP pathway and epithelial-mesenchymal transition (EMT) during gastric tumorigenesis.
Aims and Methods: YAP and E-cadherin proteins in human gastric biopsies were assessed. PMSS1 *DcagA* mutants were generated and then co-cultured with AGS cells compared with *H. pylori* wild-type strains. Immunofluorescence, Western blot and qRT-PCR analyses were performed for the alteration of YAP pathway. Moreover, EMT and cell invasion were investigated after inhibition of YAP in response to *H. pylori* infection.
Results: Increased YAP in concert with decreased E-cadherin were identified in the human gastric tumorigenesis cascade; further YAP expression is enhanced in *H. pylori*+ chronic non-atrophic gastritis tissues (CNAG) compared with *H. pylori*- CNAG. In AGS cells, CagA+ *H. pylori* strains elevated expression and nuclear translocation of YAP, upregulated its downstream genes, and promoted EMT, which was abolished by inactivation of CagA. These *H. pylori*-triggered EMT and cell invasion were significantly suppressed by treatment of YAP inhibitor.
Conclusion: Our findings indicated that *H. pylori* CagA plays a crucial role in promoting gastric tumorigenesis via activation of the oncogenic YAP pathway and subsequent enhancement of EMT.
Disclosure: Nothing to disclose

P1834 INTERACTION OF *H. PYLORI* WITH TOLL-LIKE RECEPTOR 2 -196 TO -174DEL POLYMORPHISM, IS ASSOCIATED WITH GASTRIC CANCER SUSCEPTIBILITY BUT NOT POOR PROGNOSIS IN CHINESE PATIENTS

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Introduction: Genetic polymorphisms of Toll-like receptors (TLRs) play important roles in gastric carcinogenesis. The -196 to -174del polymorphism affects the TLR2 gene and alters its promoter activity.
Aims and Methods: The aim of this study is to determine whether this polymorphism is associated with susceptibility to gastric carcinoma and its prognosis. This study consisted of 260 patients with gastric cancer and 260 healthy controls. All subjects were unrelated ethnic Han Chinese and residents in Jiangsu Province, People's Republic of China. The polymorphism was assessed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. The infection status of *H. pylori* was determined using a validated serological test. Survival was analyzed by Kaplan-Meier survival curves.
Results: Multiple logistic regression analyses revealed that the -196 to -174 del/del genotype (adjusted OR = 2.59, 95% CI = 1.33–5.07) but not ins/del genotype (adjusted OR = 1.36, 95% CI = 0.95–1.96) had significantly higher gastric

cancer risks, compared with the ins/ins genotype. Further stratification analyses revealed that an increased risk of gastric cancer associated with del/del genotype was evident among male (adjusted OR = 2.35, 95%CI = 1.03–5.34), and in younger subjects aged less than 60 years old (adjusted OR = 3.19, 95%CI = 1.20–8.50). When stratified by the histologic subtype, the del/del genotype was found to be positively associated with intestinal gastric cancer (adjusted OR = 2.62, 95%CI = 1.34–5.14). In addition, we demonstrated that the del/del genotype and *H. pylori* infection may have a synergistic effect and conferred an OR of 3.04 for developing gastric cancer. High TNM stage including III (HR = 4.77, CI = 2.02–11.23) and IV (HR = 15.48, CI = 6.53–36.67) showed a strong association of poor overall survival, compared with stage I. Cox proportional hazards analysis showed that ins/del genotype (HR = 1.23, CI = 0.82–1.87) and del/del genotype (HR = 1.60, CI = 0.76–3.40) were not associated with poor survival, compared with the ins/ins genotype.
Conclusion: Our data suggested that the – 196 to – 174 del/del genotype of TLR2 may increase the risk of gastric cancer in the Chinese population and there were significant joint effects of this polymorphism and *H. pylori* infection. Our results also revealed that del/del genotype was not associated with poor prognosis of gastric carcinoma in the Chinese population.
Disclosure: Nothing to disclose

P1835 A MULTI-INSTITUTIONAL PROSPECTIVE, OBSERVATIONAL STUDY ON THE RISK FACTORS FOR GASTRIC CANCER AFTER SUCCESSFUL *H.PYLORI* ERADICATION

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Introduction: It has been reported that *Helicobacter pylori* (*H. pylori*) eradication therapy reduced the risk of gastric cancer (GC), and as a country with high incidence of GC, the prevention of GC by *H. pylori* eradication is an important issue. In Japan, the eradication therapy for *H. pylori*-infected gastritis was approved as an insurance indication since 2013, and the eradication treatment has been widely performed. On the other hand, GC is discovered after successful *H. pylori* eradication and its incidence rate and the risk factors are still unknown.
Aims and Methods: The aim of this study is to investigate the incidence rate and the risk factors contributing to the development of GC in patients after successful *H. pylori* eradication prospectively.
A prospective, multi-institutional observational study was conducted. We enrolled patients who received *H. pylori* eradication therapy from June 2008 to April 2017. After successful eradication, enrolled patients underwent an annual endoscopic observation for screening of GC. The difference in the incidence rate of GC by background (gender, age at the eradication therapy, the past history of GC, familial history of GC), lifestyle (smoking, drinking), comorbidities (hypertension, hyperlipidemia, diabetes) and endoscopic mucosal atrophy was analyzed.
Results: A total of 498 patients, including 262 men (54%) and 236 women (46%), were analyzed. The average age at eradication therapy was 63.1 years. The mean follow-up period was 1108 days (188–3354days). GC was discovered in 23 patients (1.52%/year). Kaplan-Meier analysis (log-rank test) showed that the incidence rate of GC was significantly higher in men (2.24%/year, P = 0.015), over 65 years old at the eradication (2.28%/year, P = 0.013), presence of the past history of GC (3.11%/year, P = 0.001), hypertension (2.91%/year, P = 0.009), smoking (3.81%/year, P = 0.013), and severe mucosal atrophy (2.22%/year, P = 0.041). Multivariate analysis using cox hazards model showed that the past history of GC and smoking were independent risk factors for GC after successful eradication: the past history of GC, HR 2.58(95%CI 1.05–6.35), P = 0.039; smoking, HR 2.85(95%CI 1.09–7.46), P = 0.033.
Conclusion: The past history of GC and smoking were independent risk factors of GC after successful *H. pylori* eradication.
Disclosure: Consigned/Joint Research Expenses: Fuji Film Inc. Scholarship Donations: EA Pharma Co. Lecture Fees: AstraZeneca K.K. DAIICHI SANKYO Co. EA Pharma Co. Otsuka Pharmacy Inc. Tanabe Mitsubishi Inc. Takeda Pharmacy Inc. Astellas Inc.

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P1836 THE MANAGEMENT OF GASTRIC MALT LYMPHOMA

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Introduction: Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is a rare extranodal marginal zone B cell lymphoma, accounting 1% to 6% of all gastric malignancies. The association between gastric MALT lymphoma and *Helocibacter pylori* (*H. pylori*) infection has been well known and *H. pylori* eradication is an effective treatment in *H. pylori*-positive MALT lymphoma. However, the complete remission (CR) rates after *H. pylori* eradication in *H. pylori*-negative MALT lymphoma is very low and the treatment strategy remains controversial. We investigated the effectiveness of each treatment option for *H. pylori*-negative MALT lymphoma and *H. pylori*-positive MALT lymphoma with treatment failure after *H. pylori* eradication.
Aims and Methods: We conducted retrospective single-center study using medical records of patients who were diagnosed with gastric MALT lymphoma in Yeungnam University Medical Center between January 2005 and December 2016. Response to each treatment options and relapse after CR were evaluated by pathologic base using endoscopic biopsy.
Results: Of the 68 patients, 50 patients were enrolled. Mean ages were 55.4 ± 11.7 years and mean follow-up periods were 42.5 ± 31.0 months (range : 3–133.6). *H. pylori* infection was detected in 42 patients (84.0%). Of these *H. pylori*-positive MALT lymphoma, 36 patients (81.7%) were treated with *H. pylori* eradication as primary treatment and the CR rates after *H. pylori* eradication was 72.2% (n = 26). Patients without CR after *H. pylori* eradication (n = 10, 27.8%) were received radiotherapy as secondary treatment. All of them were shown CR and no one had relapse after radiotherapy. 2 patients (4.8%) of *H. pylori*-positive MALT lymphoma were treated with radiotherapy as primary manner and all reached CR. 1 of them (50%) had relapse after treatment, but another CR had been achieved after secondary radiotherapy. All patients with *H. pylori*-negative MALT lymphoma (n = 8, 16.0%) were treated with radiotherapy as primary treatment. The CR rates after radiotherapy was 100% and no one had had relapse after radiotherapy.
Conclusion: . Although *H. pylori* eradication is effective treatment in *H. pylori*-positive MALT lymphoma, radiotherapy may be worthwhile treatment option in *H. pylori*-negative MALT lymphoma and *H. pylori*-positive MALT lymphoma as 2ndary treatment after *H. pylori* eradication
Disclosure: Nothing to disclose

P1837 INHIBITION OF MIR-20B REDUCES CELL VIABILITY AND COLONY FORMATION IN GASTRIC CANCER BY TARGETING PHOSPHATASE AND TENSIN HOMOLOG (PTEN) AND THIOREDOXIN-INTERACTING PROTEIN (TXNIP) GENES

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Introduction: Gastric cancer (GC) is one of the most fatal forms of malignant cancers. Recently discovered microRNAs (miRNAs) post-transcriptionally regulate gene expression and play important role in a variety of processes. The aim of a study was to examine hsa-miR-20b-5p (miR-20b) function in gastric carcinogenesis by experimentally determining miRNA target-genes and impact to physiological cell processes *in vitro* and *in vivo*.
Aims and Methods: GC cell lines (AGS, MKN28) and normal gastric tissue were analyzed for expression of miR-20b. After bioinformatics analysis five potential target genes were selected for miR-20b (*EREG*, *FAT4*, *IRF1*, *TXNIP*, *PTEN*) and analyzed for expression changes in mRNA and protein levels after transfection with miR-20b inhibitor. Cell viability was assessed using a MTT assay, colony formation and proliferation was evaluated using clonogenic assay, and cell migration was determined using wound healing assay. INS-GAS mice model was used to evaluate the miR-20b alterations *in vivo* following *H. pylori*infection with follow up to 50 weeks.
Results: miR-20b expression was up-regulated in GC cell lines ($p = 0.008$, $p = 0.003$; AGS and MKN28 respectively) compared to controls. Inhibition of miR-20b expression significantly increased *IRF1*, *PTEN*, *TXNIP* genes expression level in AGS ($p = 0.008$, $p = 0.021$, $p = 0.046$, respectively) and MKN28 cell line ($p = 0.003$, $p = 0.005$, $p = 0.0004$, respectively) 24 h after transfection. *IRF1*, *TXNIP* genes expression remained increased 48 h post-transfection in AGS cell line ($p = 0.001$, $p = 0.006$, respectively), while only *TXNIP* - in MKN28 cell line ($p = 0.001$). Expression levels of *EREG* and *FAT4* was undetermined in both GC cell lines. Secondly, miRNA target-genes were analyzed for protein expression changes. Analysis revealed that PTEN protein expression in AGS cell culture increased statistically significantly 72 h after transfection ($p = 0.020$). TXNIP protein expression increased in MKN28 72 h after transfection ($p = 0.036$). Finally, miR-20b inhibition reduced cell viability in AGS ce ll line ($p = 0.029$). Furthermore, number of colonies reduced dramatically in both cell lines ($p = 0.0002$, $p = 0.021$; AGS and MKN28 respectively) compared to cells transfected with control miRNA. INS-GAS mice showed gender specific miR-20b expression pattern following *H. pylori* infection. Only male mice showed significantly higher miR-20b expression for all time points ($p = 0.029$). There was a stepwise increase in miR-20b expression during the different time points from 12 to 50 weeks with highest difference at 50 weeks ($p = 0.003$).
Conclusion: Our data shows that miR-20b may target *PTEN* and *TXNIP* and play an important role in gastric carcinogenesis by mediating cell viability and colony formation in GC-derived AGS and MKN28 cell cultures. The data from INS-GAS mice experiments support the role of miR-20b in GC *in vivo*.

Disclosure: Nothing to disclose

P1838 *HELICOBACTER PYLORI* INFECTION AND THE INTERLEUKIN 8 -251 T > A POLYMORPHISM MIGHT BE A RISK FACTOR OF GASTRIC CANCER

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Introduction: IL-8 is a major neutrophil-activating cytokine and plays a central role in the immuno-pathogenesis of *H. pylori*-induced gastric mucosal injury. The IL-8 -251 T > A polymorphism has been reported to be associated with increased production of IL-8 protein, and higher risks of atrophic gastritis (AG), peptic ulcer disease (PUD), and gastric cancer (GC). However, many other reports are inconsistent with these findings.

Aims and Methods: We aimed to investigate 1) whether polymorphisms in IL-8 influence susceptibility to *H. pylori* infection, and the associations of the polymorphisms with the risk of gastroduodenal diseases in a Korean population, and 2) to analyze our and other investigators' large-scale data regarding the IL-8 -251 T > A polymorphism and GC risk in Korean, Japanese, Chinese, and Caucasian populations.

We consecutively enrolled 176 *H. pylori*-negative control subjects, 221 subjects with *H. pylori*-positive non-atrophic gastritis, 52 mild AG, 61 severe AG, 175 PUD, and 283 GC. Allele-specific PCR-RFLP was conducted for polymorphisms in IL-8 -251 T > A. IL-8 levels in gastric mucosal tissues were measured by enzyme-linked immunosorbent assay. We collected large-scale raw data of GC patients (n = 3,217) and controls (n = 3,810) from Asian (Korea, Japan, and China), and Caucasian (Poland, Finland, and Portugal) populations, and analyzed GC risk according to IL-8 -251 T > A genotype.

Results: IL-8 levels were significantly different between *T*/*T* wild type, *T*/*A* heterozygote, and A/A mutant genotypes. IL-8 -251 A allele carriers (*A*/*A* + *T*/*A*) showed increased IL-8 levels, and were significantly associated with the risk of severe AG and GC. Global data of IL-8 polymorphism and the risk of GC development showed that Japanese population was similar to Korean population. The combined Korean and Japanese populations had significantly increased GC risk for the IL-8 -251 *T*/*A* and *A*/*A* genotypes compared to the *T*/*T* genotype, and for A allele carriers compared to non-carriers.

Conclusion: We suggest that a combination of *H. pylori* infection and the IL-8 -251 T > A polymorphism might increase the risk of severe AG and GC in a Korean population

Disclosure: Nothing to disclose

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P1839 DETECTION OF LESIONS IN HELICOBACTER PYLORI GASTRITIS BEFORE AND AFTER ERADICATION BY EXPERT ENDOSCOPISTS

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Introduction: *Helicobacter pylori* (HP) infection is commonly responsible of multifocal atrophic gastritis without intestinal metaplasia, intestinal metaplasia and dysplasia, which is the most relevant premalignant gastric condition (PGC). HP-eradication is mandatory to stop the chronic gastric inflammation, but the long-term risk of gastric premalignant/malignant lesions progresses even after HP-eradication. Several studies showed that high-resolution endoscopy with narrow-band imaging (HRE-NBI) could be more accurate than white-light endoscopy (WLE) alone in diagnosing PGC. Nevertheless, no study focused on the diagnostic performance of endoscopy in detecting PGC after HP eradication on an interim follow-up.

Aims and Methods: In the present study, we aimed to assess the efficacy of HRE-NBI in the diagnosis of PGC, before and after HP eradication. A prospective study was performed in our institution involving the regular use of high-resolution gastroscopes with and without NBI. From June 2016 to June 2017, all patients that received an endoscopic diagnosis of HP-related gastritis by an expert endoscopist, were reassessed by WLE and HRE-NBI, including biopsy samples according to the Sydney system, within six months after the proved HP eradication. Kimura-Takemoto modified classification and endoscopic grading of gastric intestinal metaplasia (EGGIM), proposed by Pimentel-Nunes *et al.* were used to evaluate the degree of atrophy and IM. Histologic result was considered the diagnostic gold standard. Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia (OLGIM) were assessed by an expert gastrointestinal pathologist.

Results: Of 83 screened patients, 36 were enrolled and a total of 72 HRE-NBI were performed before and after the proved HP eradication. The major indications for endoscopy were gastroesophageal reflux (60%), abdominal pain (30%), dyspepsia (5%), or anemia (5%). The median age of the all patients was 58 years (range 32–72), and they were prevalently female (86.1%). Among them, 17 patients (47.2%) were current drinkers, 4 (11.1%) were active smokers and 2 (5.5%) had a familiar history for gastric cancer. The proportion of patients with degree 3–4 of EGGIM scale, significantly decreased after HP eradication (33.3% vs. 11.1%, $p = 0.04$), whereas the proportion of patients with more advanced degree of EGGIM scale (5–6) showed a trend of increase (16.7% vs. 36.1%, $p = 0.06$). In the latter group, the majority of patients (69.2%) had a lower degree of EGGIM scale (3–4) before anti-HP therapy, whereas the minority (15.4%) had the same degree ($p < 0.05$). Moreover, the proportion of OLGA and OLGIM stages did not change after HP-eradication. Interestingly, the proportion of patients with histological diagnosis of dysplasia on random biopsies did not change significantly after HP eradication (36.1% vs. 16.7%; $p = 0.06$), whereas the proportion of patients with histological dysplasia on "de novo-appeared" superficial lesions, significantly increased after HP disappearance (0% vs. 38.9%; $p < 0.001$).

Conclusion: HRE-NBI could be more precise in diagnosing dysplasia after HP-eradication, presumably as the gastric mucosal aspect is less corroborated by the inflammatory changes induced by the HP chronic infection, which could lead to an underestimation of the premalignant lesions. These findings suggest that a non-invasive test for HP identification should be performed in at risk patients as a first step, and only after achieving HP eradication they should undergo a gastroesophageal endoscopy to identify more correctly PGC.

Disclosure: Nothing to disclose

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WEDNESDAY, OCTOBER 24, 2018 09:00–14:00

Small Intestinal III – Hall X1

P1840 THE ROLE OF CAPSULE ENTEROSCOPY IN COELIAC DISEASE: RESULTS OF A PROSPECTIVE STUDY IN A TERTIARY REFERRAL CENTER

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Introduction: Coeliac disease (CD) is a chronic enteropathy that usually improves after the withdrawal of gluten with clinical and histological remission. In rare cases, the course of CD can be complicated by the development of refractory disease (RCD type 1 and type 2) and malignancies of the gastrointestinal tract, like small bowel (SB) lymphoma and adenocarcinoma. Although uncommon, this evolution is burdened with an extremely severe prognosis. In the last years, several diagnostic strategies have been proposed for early identification of CD complications. In particular, capsule enteroscopy (CE) has been proposed as a useful tool to evaluate patients with persistence or recurrence of symptoms despite an ongoing gluten-free diet. The aim of this study was to evaluate the diagnostic performance of CE in high-risk coeliac patients, especially in the detection of CD-related complications.

Aims and Methods: Between November 2014 and November 2017 we prospectively enrolled coeliac patients who underwent CE for suspected complicated CD, non-adherence to gluten-free diet (GFD) or in the follow-up of known RCD. CE was defined positive for CD-related findings in case of atrophy, erosions, ulcers or mass lesions throughout the SB. Enrolled patients underwent also gastroscopy, complete blood tests and, when clinically indicated, radiologic examinations. We evaluated the diagnostic performance of CE in the identification of SB lesions and complications. Patients with a final diagnosis of RCD or malignancy were defined as complicated CD.

Results: Overall, 121 consecutive CD patients were enrolled. A total of 143 capsule examinations was performed (18 patients repeated CE). The majority of patients (61%) underwent CE for suspected complicated CD, 25% for non-adherence to GFD and 14% for RCD follow-up. The mean follow-up time after CE was 13 ± 9 months. After the complete diagnostic work-up, the final diagnosis was: uncomplicated CD (83% of patients) and complicated CD (17%, 11 RCD type 1, 8 RCD type 2 and 2 lymphoma). CE was positive for CD-related findings in 55% of patients (67/121). CE sensitivity for the detection of mucosal atrophy was 62%, specificity was 81%. The incidence of complications in patients with suspected complicated CD and non-adherence to GFD was 5.7%. In the group of patients with already known RCD at enrollment, two patients (1.6%) developed enteropathy-associated T cell lymphoma and they both had positive CE. A significant correlation between age and CE findings was found: patients with positive CE had a significantly more advanced age at CD diagnosis compared to patients with negative CE ($p = 0.005$). Moreover, in patients ^{3} 50 years old at the CE execution CD-related findings were more frequent compared to younger patients ($p = 0.01$). Any statistical correlation was found with positive CD serology and incorrect GFD ($p > 0.05$).
Conclusion: Capsule enteroscopy plays a pivotal role in the clinical follow-up in order to detect the persistence of atrophy, the extent of the lesions throughout the SB and to early identify CD-related complications. According to our results, complicated CD is an uncommon condition; in this setting, patients aged > 50 years and with a diagnosis of CD in older age should be considered at higher risk of complications and accurately investigated with CE. On the contrary, neither a persistent positive serology nor an incorrect GFD seem to be related to the onset of complicated CD.
Disclosure: Nothing to disclose

P1841 METABOLIC ALTERATIONS IN CELIAC DISEASE OCCURRING AFTER GLUTEN-FREE DIET

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Introduction: Several studies have shown that weight changes are common in patients with coeliac disease (CD) after starting a gluten-free diet (GFD), but data on the prevalence of metabolic syndrome (MS) are still scarse.
Aims and Methods: The aim of the study is to evaluate the prevalence of Metabolic Syndrome (MS) and Hepatic Steatosis (HS) in patients with CD, before and after GFD.
185 adult patients with CD were enrolled. In all patients the presence of the following risk factors were evaluated: increased waist circumference (WC), body mass index (BMI), hypertension, hypercholesterolemia, reduction of HDL cholesterol, hypertriglyceridemia, hyperglycemia. Diagnosis of MS was made according to International Diabetes Federation (IDF) criteria. HS was assessed by ultrasonography (US).
Results: At the time of the CD diagnosis 6 patients (3.24%) fulfilled the diagnostic criteria for MS, 27 (14.59%) after GDF ($p < 0.0001$). Rates of MS subcategories, before and after GFD were respectively: increase in WC, 24 (13%) vs 43 (23.24%) ($p < 0.0001$); hypertension, 8 (4.3%) vs 22 (12%) ($p < 0.0001$); reduction of HDL cholesterol, 41 (22.2%) vs 86 (46.5%) ($p < 0.0001$); hypertriglyceridemia, 22 (11.9%) vs 26 (14%) ($p = 0.3339$); hyperglycemia, 20 (10.8%) vs 36 (19.46%) ($p = 0.0088$); total hypercholesterolemia, 43 (23.2%) vs 88 (47.56%) ($p < 0.0001$); BMI >25, 45 (24.3%) vs 78 (42.16%) ($p < 0.0001$). Furthermore, HS was found in only 3 (1.7%) patients at the time of diagnosis, and in 20 (11.1%) after GFD ($p < 0.0001$).
Conclusion: Therefore, the prevalence of overall metabolic alterations and hepatic steatosis increased in patients with CD after a gluten-free diet.
Disclosure: Nothing to disclose

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P1842 HISTOLOGIC RESPONSE TO BUDESONIDE IN PATIENTS WITH REFRACTORY CELIAC DISEASE TYPE 1 AND 2

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Introduction: Refractory celiac disease (RCD) is defined by persistent or recurrent symptoms and villous atrophy despite strict adherence to a gluten-free diet for at least 6 to12 months. RCD is classified as type 1 (normal intraepithelial lymphocyte phenotype on immunohistochemistry and flow cytometry analysis), and type 2 (clonal intraepithelial lymphocyte population with aberrant phenotype). Budesonide is an effective treatment to induce clinical remission in RCD type 1 and 2. However, histologic response is less frequent.
Aims and Methods: The aim of this study is to evaluate the clinical and histologic response to budesonide in patients with RCD type 1 and 2, as well as the effect of budesonide on the aberrant intraepithelial lymphocytes (IEL) assessed by flow cytometry in the subgroup of type 2 RCD patients. We conducted a monocentric retrospective study. Patients with a diagnostic of RCD type 1 and type 2 who were treated with budesonide alone were included. Treatment consisted of open capsule budesonide. Complete histologic response was defined by normalization of the architecture of the small intestinal mucosa (Marsh 0 or I score). Partial histologic response was defined as an improvement of the Marsh classification.
Results: 10 patients with RCD I and 8 patients with RCD II were included. The mean duration of treatment with budesonide was 23.5 months [4–108]. Overall, a complete clinical response was observed in 17 out of 18 patients treated with budesonide (94.4%). A complete histologic response was seen in 4 patients (22.2%) and a partial histologic response was seen in 5 patients (27.8%). Half of the patients had no change in the architecture of the small intestinal mucosa. Patients who had complete or partial histologic response had been on budesonide for a mean period of time of 30 months, while patients with no response had a mean duration of treatment of 15 months ($p = 0.4$). In patients with type 2 RCD, there was no significant change on the percentage of aberrant IELs assessed by flow cytometry with treatment ($p = 0.16$), as well as no effect on clonal rearrangement of T-cell receptor gene.
Conclusion: Budesonide is associated with a high clinical response but lower histologic response in refractory celiac disease. There was no impact on the percentage of aberrant IELs assessed by flow cytometry in RCD type 2.
Disclosure: Nothing to disclose

P1843 CLADRIBINE THERAPY IN REFRACTORY COELIAC DISEASE TYPE II: A SINGLE-CENTER EXPERIENCE

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Introduction: Refractory coeliac disease (RCD) is defined by the persistence of malabsorption and intestinal villous atrophy after one year of strict gluten-free diet. It's a rare condition with a prevalence of 2–5% among coeliac patients. RCD can be classified into two subtypes: type 1 RCD (RCD I) is characterized by a polyclonal pattern of intraepithelial T cells receptor and a normal phenotype of intraepithelial lymphocytes (IEL) with surface CD3 and CD8 expression; type II (RCD II) is characterized by a clonal expansion of abnormal IEL lacking surface markers CD3, CD8 and T-cell receptor and a preserved intracellular CD3 expression. RCD II is an aggressive disease with a high risk to develop enteropathy-associated T-cell lymphoma (EALT) and a poor response to steroids and immunosuppressive therapy. Considering the poor prognosis of RCD II, a treatment with chemotherapeutic agents should be considered. Cladribine is a purine analogue that may induce clinical and histological response in RCDII.
Aims and Methods: The aim of this study was to evaluate the clinical and histological response to cladribine therapy in RCD II.
From January 2015 to October 2017 we retrospectively enrolled RCD II patients treated with cladribine in the cohort of celiac disease patients afferent to the Celiac Disease Center of our unit. All enrolled patients underwent small bowel assessment to early detection of complications by computed tomography (CT), magnetic resonance enterography or capsule endoscopy. Patients were treated with subcutaneous (SC) cladribine in our haematology unit. We collected clinical, histological and follow-up data.
Results: 12 patients were affected by RCD II. Of them, 2 patients were candidate for cladibrine therapy. The first patient was a 63-year-old man diagnosed with CD since 2007. In 2012, after esophagogastroduodenoscopy (EGD) for persistent symptoms, RCDI was diagnosed. A steroid therapy was started with transient clinical benefit. In 2015, a new EGD was performed for recurrence of symptoms with evidence of a 60% T-IEL infiltrate with aberrant phenotype and a monoclonal TCR on a polyclonal basis. Capsule endoscopy (CE) demonstrated widespread atrophy in more than half of the small intestine, while CT and PET resulted negative. Because of steroid refractoriness, a treatment with SC cladribine was started. He underwent 3 cycles every 6 months, with a 30% dose reduction for the first 2 cycles. Treatment was well tolerated, without hematological toxicity. After III cycles he had weight gain and resolution of diarrhea and a macroscopic improvement of ileal atrophy and ulcers, without significant reduction of T cell infiltration. The second patient was a 62-year-old woman diagnosed with CD in January 2016. A EGD revealed a 60% T-IEL infiltrate with aberrant phenotype and monoclonal TCR on a polyclonal basis. CE demonstrated

widespread signs of jejunal atrophy and erosions, while CT and PET were negative. Since steroids were ineffective, she underwent 3 cycles of SC cladribine. Treatment was well tolerated. There was an improvement of clinical symptoms and of ileal atrophy and ulcers, with a 50% reduction T IEL infiltrate.
Conclusion: Both patients showed a clinical and histological response to SC cladribine without hematologic toxicity or infectious complications suggesting that this treatment could be a safe and effective option in elderly patients affected by RCD II. Furthermore, the outpatient administration of the treatment lead to a reduction of patient's discomfort and costs related to hospitalization.
Disclosure: Nothing to disclose

P1844 PERIPHERAL MONOCYTES IMPAIR THE BARRIER FUNCTION OF INTESTINAL EPITHELIAL CELLS: NEW INSIGHTS ON THE PATHOGENESIS OF CELIAC DISEASE

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Introduction: Celiac disease (CD) is a chronic immune-mediated disease with a strong genetic background, stimulated by gluten ingestion (1). It is known that small bowel epithelial barrier function is altered in CD patients. In the small bowel mucosa, immune cells are activated after contact with antigen-presenting cells exposing gliadin-derived peptides, which leads to a multifaceted inflammatory cascade ultimately leading to villous atrophy and disruption of the epithelial barrier (2). However, the underlying mechanism for the disrupted barrier function in CD is still unclear. It has been hypothesized that activated monocytes could exert a direct effect on epithelial cells, causing impairment of the epithelial barrier even at earlier phases of the disease and/or after removal of the trigger of the immune reaction (i.e. gluten/gliadin).
Aims and Methods: To model the role of celiac monocytes in the dysregulation of barrier function in CD we isolated peripheral blood mononuclear cells (PBMCs) from blood samples of HLA-DQ2-positive CD patients who were on a gluten-free diet. Intestinal epithelial cells (Caco-2) were treated with either PBMCs or CD14+ PBMCs (representing monocytes) in the presence or absence of interleukin-15 and trypsin-digested gliadin (IL-15/Tglia) in order to verify the role of active gliadin stimulation. As a control untreated Caco-2 or Caco-2 only treated with IL-15/Tglia were included to rule out direct toxic effects of gliadin/IL-15 on the epithelium. The integrity of the Caco-2 barrier was monitored by serial measurements of transepithelial resistance (TER). Intracellular localization of proteins with a key role in epithelial barrier function (occludin, JAM-A and ZO-1 for apical junctional complex and CD71 for epithelial transcytosis of gliadin) were investigated using confocal microscopy after immunostaining
Results: A decreased TER was observed in Caco-2 cells after treatment with celiac CD14+ PBMCs as compared to untreated cells. PBMCs that were activated by IL-15/Tglia revealed a more pronounced TER decrease. In control Caco-2 cells that were treated with IL-15/Tglia alone, TER did not decrease as found in completely untreated control cells. Exposure of Caco-2 cells to celiac monocytes resulted in a decreased expression of junctional proteins JAM-A and occludin and to a less stringent junctional or membrane association. ZO-1 localization and expression remained unchanged. With regard to the transcytosis protein CD71, confocal microscopy revealed an altered localization after treatment with PBMCs and CD14+ PBMCs, with evidence of a diffuse intracellular localization as compared to CD71 clusters in untreated cells.
Conclusion: Celiac PBMCs have an effect on epithelial barrier function of Caco-2 cells. Specifically, PBMCs as well as CD14+ monocytes appear to impair the epithelial barrier function. This is associated with an altered expression pattern of key proteins for tight junction assembly. These data suggest that in CD, monocytes play a role in transducing the gliadin-dependent epithelial barrier defect.
Disclosure: Nothing to disclose

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P1845 GENE EXPRESSION SIGNATURES DIFFERENTIATE NON-CELIAC GLUTEN SENSITIVITY FROM CELIAC DISEASE PATIENTS AND CONTROLS AND MAY POTENTIALLY CONTRIBUTE TO DISEASE DIAGNOSIS

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Introduction: The definition "gluten-related disorders" gathers multiple pathologies with overlapping symptoms including the celiac disease (CD) and the newly reported non-celiac gluten sensitivity (NCGS). To date, the diagnosis of NCGS is proposed for patients that have distress from gluten ingestion, have a negative CD serology and have a preserved intestinal architecture. Biomarkers for NCGS are not yet available, therefore the NCGS diagnosis remains based on symptoms, exclusion criteria and eventually gluten challenge. The availability of specific and objective diagnostic tests that identify a pathology is a crucial problem common to different diseases. Gene expression profiles have shown to have the necessary qualification to carry on this endeavour.
Aims and Methods: The present study aims to define a gene expression signature that might be helpful in the diagnosis of NCGS. Patients with positive CD serology (anti-tTG IgA and/or anti-EMA autoantibodies) and strong positive histology (Marsh grade $\geq$3) were enrolled as celiac. Symptomatic patients with negative CD serology and histology nevertheless responsive to gluten exclusion were enrolled as NCGS. Patients with gluten-independent dyspeptic symptoms who required gastrointestinal endoscopic examination were enrolled as controls. Total RNA extracted from duodenal biopsies was used for microarray analysis.
Results: The genome-wide expression analysis was carried on RNA extracted from intestinal mucosa of 8 female patients affected by NCGS (mean age 33.2 ± 5.8 years) and 6 age-matched female controls. Gene expression data were subjected to quantile normalization and log2 transformation before statistical analysis. Differentially expressed transcripts were identified by using a moderated T-test and Benjamini-Hochberg correction (adjusted $p < 0.05$; FC > 2). This approach revealed the presence of 37 differentially expressed transcripts. About 40% of these transcripts were long non-coding RNA (LncRNA) or Long intergenic noncoding RNAs (LincRNA). A subgroup of 5 patients affected by NCGS (mean age 33.4 ± 4.7 years) was also examined by microarray against 5 celiac disease patients. Statistical analysis revealed 26 differential transcripts, 40% of which also belonged to the Lnc-RNA and Linc-RNAs.
Conclusion: The results of this study confirm that patients affected by NCGS, however similar when compared to controls and to patients affected by celiac disease, show a sufficiently distinct genomic expression signature. RNA expression levels of NCGS do not completely overlap to that of controls and CD indicating that NCGS is a discrete disease. Finally, these results suggest that targeted expression profiling of specific sets of genes may be helpful in both positive diagnosis and/or exclusion of NCGS in symptomatic subjects.
Disclosure: Nothing to disclose

P1846 CIRCULATING MICROVESICLE PATTERNS ARE DIFFERENT BETWEEN NON CELIAC GLUTEN SENSITIVITY PATIENTS AND HEALTHY CONTROLS

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Introduction: Microvesicles (MVs) have been recently implicated in cellular cross-talk both in health and disease, carrying surface receptors traceable to their cells of origin and shuttling molecules potentially controlling systemic processes. Recent studies have demonstrated an increased number of circulating MVs in a variety of conditions, including active celiac disease (CD)[1]. Non Celiac Gluten Sensitivity (NCGS) is a poorly defined syndrome primarily characterized by abdominal symptoms elicited by the ingestion of gluten in individuals not affected by celiac disease or wheat allergy. However, its underlying pathophysiology is scarcely understood.
Aims and Methods: To assess and characterize circulating MVs in a cohort of NCGS patients, we enrolled symptomatic NCGS patients, confirmed after gluten challenge and age/sex-matched healthy controls. All subjects performed serology testing and intestinal biopsy. CD exclusion required negative anti-tTG titers and absence of villous atrophy at histology. Circulating MVs were identified on whole blood samples by a no-lyse/no-wash method, combined with volumetric count (FACSVerse, BD), based on a novel 6-colour flow cytometry panel, in order to identify and enumerate the whole MV compartment and its subpopulations. Data are expressed as mean $\pm$ SD. Statistical differences were evaluated by T-test.
Results: We evaluated 14 NCGS patients (mean age $= 39.3 \pm 12.9$, F/M = 4:1) and 28 age/sex-matched healthy controls. Mean total circulating MVs were significantly higher in NCGS (respectively 47533.5 ± 16219.2 vs 14203.7 ± 7402.8 MV/μL, $p < 0.001$). Subgroup analysis showed that CD31+ and CD45+ MVs, of endothelial and leucocyte origin respectively, were not significantly different. However, EpCAM+ MVs, of epithelial origin, and CD41a+ platelet-derived MVs were significantly higher in NCGS patients (respectively 661.3 ± 236.8 vs 233.1 ± 190 MV/μL and 5513.2 ± 5957.7 vs 1200.3 ± 1395.9 MV/μL, $p < 0.005$). Mean total annexin V+ MVs showed a similar pattern (respectively 12050.4 ± 5818.5 vs 2639.4 ± 1675.8 MV/μL, $p < 0.001$), bearing increases in all subpopulations, with a 6-fold increase in CD31+ annexin+ and a 4-fold increase in EpCAM+ annexin+ MVs.
Conclusion: NCGS patients show higher numbers of total circulating MVs than age- and sex-matched controls. Phenotypical assessment suggests that this increase is driven in part by the epithelial- and platelet-derived compartments, potentially implying increased peripheral signaling from the intestinal mucosa. Annexin V identifies a compartment of MVs that express phosphatidylserine on the cellular membrane, an event found in apoptosis and activation of the cell of

origin. Differences in expression of this activated compartment could provide insights on the pathophysiology of NCGS and the possible signaling pathways that may mediate symptom onset.
Disclosure: Nothing to disclose

Reference

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P1847 TOTAL ANNEXIN V+ CIRCULATING MICROVESICLES DIFFERENTIATE NON CELIAC GLUTEN SENSITIVITY FROM CELIAC DISEASE PATIENTS AND HEALTHY CONTROLS

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Introduction: Circulating microvesicles (MVs) are potential mediators of cellular cross-talk in physiological and pathological systemic processes. Increased numbers of total MVs have been demonstrated in a variety of conditions, including celiac disease (CD)[1]. Non celiac gluten sensitivity (NCGS) diagnosis is based on the exclusion of CD, wheat allergy and other inflammatory conditions and on the demonstration of a strict correlation between symptoms and gluten consumption. However, markers for a positive diagnosis are lacking.
Aims and Methods: The aim of this study was to assess the potential diagnostic value of circulating MVs as a serological marker for NCGS diagnosis. To this end, we enrolled symptomatic NCGS patients confirmed after gluten challenge, age- and sex-matched newly diagnosed CD patients and asymptomatic controls. All subjects performed serology testing and intestinal biopsy. CD diagnosis required positive anti-tTG titers and presence of villous atrophy. MVs were identified on whole blood samples by a no-lyse/no-wash method, combined with volumetric count (FACSVerse, BD), based on a novel 6-colour flow cytometry panel. Data are expressed as mean ± SD. Statistical differences were evaluated by ANOVA-Welch with post-hoc Bonferroni or Dunnet's T3 test; diagnostic accuracy was assessed by ROC curves.
Results: We evaluated 14 NCGS patients (mean age = 39.3 ± 12.9, F/M = 4:1) against 22 CD subjects and 28 healthy controls. Anti-tTG levels were positive only in CD vs NCGS and controls (respectively 102.4 ± 63.1 vs 4.2 ± 3.3 and 3.9 ± 2.8 U/ml, $p < 0.001$). Villous atrophy was present only in CD patients; however, infiltrative lesions were present in 35% of NCGS and 28% of controls (p n.s.). Mean total MVs were significantly higher both in NCGS and CD compared to controls (respectively 47533.5 ± 16219.2 and 39283.1 ± 17828.6 vs 14203.7 ± 7402.8 MV/μL, $p < 0.02$ vs controls). Mean total annexin V+ MVs were significantly increased only in NCGS subjects (respectively 12050.4 ± 5818.5 vs 4044.8 ± 4769.8 and 2639.4 ± 1675.8 MV/μL, $p < 0.03$ vs CD and controls). ROC curve analysis of total and annexin V+ MV counts, when predicting NCGS, showed an AUC of respectively 0.780 and 0.839 ($p < 0.02$), whereas for CD AUCs were not predictive. Each parameter (total MV counts and annexin V+ MV counts), when combined with tTG negativity and absence of villous atrophy, yielded a further increase in AUC, respectively 0.882 and 0.905 ($p < 0.001$).
Conclusion: Total MV counts are increased in CD and NCGS patients when compared to age- and sex-matched controls. However, NCGS patients seem to express characteristically higher levels of annexin V+ MVs, suggesting parent cell activation. This parameter, combined to serological and histological exclusion of CD, seems to have a high diagnostic accuracy in NCGS and may represent a candidate marker for positive diagnosis of this syndrome.
Disclosure: Nothing to disclose

Reference

1. Efthymakis K, et al. *United European Gastroenterol J*. 2017;5(Suppl 1):A822-A823. DOI: 10.1177/2050640617725676.

P1848 DISTINCT MUCOSAL AND BLOOD MIRNA EXPRESSION PATTERNS MAY REPRESENT A RELIABLE MARKER FOR POSITIVE DISEASE DIAGNOSIS IN NON CELIAC GLUTEN SENSITIVITY

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Introduction: Non celiac gluten sensitivity (NCGS) diagnosis is principally based on the exclusion of CD and on the demonstration of a strict correlation between symptoms and gluten consumption. However, markers for a positive diagnosis are lacking. MicroRNA (miRNA) molecules, implicated in immune response, modulate post-transcriptional gene expression, showing distinct expression patterns in a number of diseases, including Celiac Disease (CD).
Aims and Methods: The aim of this study was to characterize miRNA patterns in NCGS and CD and assess their potential diagnostic value for NCGS diagnosis. We enrolled symptomatic NCGS patients confirmed after gluten challenge, age- and sex-matched newly diagnosed CD patients and dyspeptic controls. All subjects performed serology testing and intestinal biopsy. CD diagnosis required positive anti-tTG titers and presence of villous atrophy. Differentially expressed miRNAs in circulating leucocytes and duodenal mucosa were assessed by real-time PCR. Statistical differences were evaluated by a linear model with False Discovery Rate correction. Unsupervised Principal Component Analysis (PCA) was used to assess the discriminatory capability of miRNA patterns; principal component diagnostic accuracy was assessed by ROC curves.
Results: We evaluated 27 NCGS patients (mean age = 39.8 ± 11.3) against age- and sex-matched CD subjects and dyspeptic controls. Anti-tTG levels were positive only in CD vs NCGS and controls (respectively 99.4 ± 56.3 vs 4.5 ± 2.6 and 3.9 ± 1.8 U/ml, $p < 0.001$). Six miRNAs were differentially expressed in NCGS mucosal samples, while another 6 were identified in peripheral blood; notably, 2 of those miRNAs were expressed differentially only in mucosal biopsies or blood samples. At PCA, the first principal component showed an OR = 3.71 (95%CI: 1.57–8.75, $p = 0.003$) for NCGS status vs CD and an OR = 0.35 (95%CI: 0.16–0.78, $p = 0.011$) for NCGS status when compared to dyspeptic controls. ROC curve analysis of this component showed respectively an AUC of 0.743 (95%CI: 0.612–0.874, $p = 0.002$) and of 0.832 (95%CI: 0.706–0.958, $p < 0.001$).
Conclusion: The present study shows that patients selected according to established criteria are well definable with the use of miRNA profiling methods. Resulting miRNA signatures of NCGS patients are unique and absent in CD, further supporting non celiac gluten sensitivity as a distinct clinical entity even at the gene expression level. Differentially expressed miRNA patterns discriminate between patient groups with a high degree of accuracy and are strongly predictive of a NCGS status after exclusion of CD, both on mucosal and peripheral blood samples. As such, miRNA profiling, combined with serological and histological exclusion of CD, may represent a future marker for positive diagnosis of this syndrome.
Disclosure: Nothing to disclose

P1849 EFFECTS OF WATER LOAD TEST ON GASTRIC MOTILITY AND AUTONOMIC SYSTEM ACTIVITY IN PATIENTS WITH CELIAC DISEASE

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Introduction: Celiac disease (CeD) is an autoimmune, complex disorder of the gastrointestinal tract with wide range of clinical manifestation. The inflammatory process in CeD may cause changes in visceral perception increase of visceral sensitivity. Water load test is a standardized test used to induce gastric distension and to evoke gastric motility without the enterohormonal response.
Aims and Methods: The aim of the study was to investigate the effect of water ingestion on autonomic nervous system (HRV- heart rate variability) and gastric motility (EGG- electrogastrography) in patients with CeD compared to healthy subjects.
53 neurologically asymptomatic patients with CeD (13 males, 40 females, mean age 43.4 ± 14.8 years) and 50 healthy subjects (12 males, 38 females, mean age 44.1 ± 9.2 years) were studied. The simultaneous 30 minutes recording of ECG with HRV analysis and EGG were performed before and after water intake (500 ml per 5 minutes).
Results: ANS. At rest the spectral domain HRV analysis parameters were significant lower in patients than in control (LF – 291.9 vs. 836.0, p = 0.00004; HF – 348.5 vs. 965.5, p = 0.001). Water test induced the increase of LF (536.2 vs. 1163.4; p = 0.0003) and HF (543.7 vs 1224.9; p = 0.006) indices, similarly as a control, but not reached normal value.
EGG. Fasting CeD patients showed decreased% time of normogastria (51.8 ± 18 vs. 86 ± 12.3, p = 0.02) and mean slow wave coupling (SWC) (62.1 ± 18 vs. 67 ± 18%, p = 0.01) with increased dominant power (log DP) (12.5 ± 1.2 vs. 11.1 ± 1.1, p = 0.0001) in comparison to control group.
After water load test in CeD group decreased% time of tachygastria in EGG (7.08 ± 5.5 vs. 5.75 ± 1.7; p = 0.04) was noted.
Conclusion: In CeD the activation of autonomic system especial parasympathetic component after water load test was lower than in control group. Diminished responsiveness of ANS in CeD may contribute to disturbances of gastric myoelectric activity.
Disclosure: Nothing to disclose.

P1850 NON-CLASSICAL CLINICAL PRESENTATION OF CELIAC DISEASE IS MORE PREVALENT IN THE 21ST CENTURY: A SINGLE-CENTER EXPERIENCE

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Introduction: Celiac disease is a gluten-triggered systemic autoimmune disease which can strike at any age. Presenting symptoms can be manifold, clinical phenotype may range from severe malabsorption syndrome to silent celiac disease.
Aims and Methods: We aimed to investigate whether celiac clinical phenotype changed in the past decades by performing a retrospective data collection from patients' files in our academic centre. Variables of interest included age at diagnosis, year at diagnosis (before or after the year 2000), diagnostic histology (graded by Marsh-Oberhuber classification), clinical presentation (divided into classical and non-classical celiac disease per Oslo criteria), extraintestinal symptoms (i.e., anemia and dermatitis herpetiformis), and concomitant diseases (i.e., metabolic bone disease and autoimmune diseases including thyroid disease). Independent sample t-test and chi-square test were used in statistical analysis.
Results: Altogether, 265 patients were diagnosed in our unit (60 males and 205 females) between 1971 and 2018. Mean age at diagnosis was 13.7 ± 17.4 years and 33.6 ± 15.0 years in patients diagnosed before and after the year 2000, respectively, with a significant difference between groups ($p < 0.001$). Classical clinical presentation was more common in patients diagnosed before the year of 2000, as compared to those diagnosed earlier (86.0% vs. 42.6%, respectively; $p < 0.001$). Distribution of intestinal damage was, as follows: Marsh 1: 0.6%, Marsh 2: 2.3%, Marsh 3a: 15.1%, Marsh 3b: 36.0%, Marsh 3c: 45.9%. Dermatitis herpetiformis, anemia, and metabolic bone disease were present in 12.8%, 44.4%, and 60.4% of the cases, respectively. Almost one-third (32.0%) of our patients were affected by concomitant autoimmune diseases, 18.5% of the population suffered from autoimmune thyroid disease. Diagnostic histology, frequency of dermatitis herpetiformis, anemia, metabolic bone disease, and autoimmune diseases were not different between patients diagnosed before and after the year 2000. Refractory celiac disease did not occur in our study population.
Conclusion: Our data suggest a significant shift in clinical phenotype of celiac disease: non-classical clinical presentation is more prevalent in the 21st century without significant difference in the complications and concomitant diseases.
Disclosure: Nothing to disclose

P1851 DIFFERENCES IN SYMPTOMS AND GAS PRODUCTION FOLLOWING FRUCTOSE AND LACTOSE INGESTION IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Patients with functional gastrointestinal disorders (FGID) often experience symptoms on ingestion of rapidly fermentable sugars, collectively referred to as FODMAPs (1). While it is clinically apparent that the reactions to individual FODMAPs differ, there is currently limited supportive evidence that the human or microbiome metabolism varies between sugars (2,3). Differences in fermentation and downstream effects of individual FODMAPs could be expected, based on the wide variability in intestinal microbiome function and composition.
Aims and Methods: We compared the induction of symptoms and the production of exhaled gases following ingestion of fructose and lactose in patients with FGID. Fructose and lactose breath tests were performed in a single centre in 2042 successive referred patients with FGID defined by Rome III criteria. Breath hydrogen and methane gas concentrations, and gastrointestinal (GI: abdominal bloating, flatulence, fullness, nausea, diarrhoea, abdominal cramps or pain, borborygmi, gastro-oesophageal reflux symptoms) and central nervous system (CNS: tiredness, difficulty concentrating, headache) symptom intensities were scored on a 3-point Likert scale for 5 hours after sugar ingestion. The time profiles of symptoms and of breath gas concentrations were analysed over time and compared between the two sugars. Treelet Transforms were used to derive data-driven symptom clusters for comparison between fructose and lactose.
Results: Eleven symptom profiles and the hydrogen and methane breath concentrations showed significant dynamics over time following sugar ingestions (all $p < 0.0001$). The time profiles of all symptoms, except reflux, and of breath concentrations differed significantly between fructose and lactose tests (all $p < 0.0001$). The onsets of GI and CNS symptoms and of peak hydrogen and methane gas concentrations were markedly delayed and the durations of symptoms prolonged following lactose compared with fructose ingestion. Two distinct symptom clusters were identified by Treelet Transform analysis, comprising a GI and a CNS cluster. These were identical following fructose and lactose, except that diarrhoea was not part of the GI cluster for fructose.
Conclusion: The time profiles of symptom generation and of gas production clearly differ following fructose and lactose in patients with FGID, suggesting different handling of these common FODMAPs. The most obvious and as yet unexplored explanations are differential effects on GI transit, or divergent distribution or functional capacity of the microbiome metabolizing fructose and lactose. Differential effects of individual sugars in FGID are likely to be of clinical consequence and need to be examined further.
Disclosure: Nothing to disclose

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P1852 NON-CELIAC GLUTEN SENSITIVITY DIAGNOSIS: COMPARISON BETWEEN IN-VIVO CHALLENGE ACCORDING TO "SALERNO EXPERTS' CRITERIA" AND GLUTEN ORAL MUCOSA PATCH TEST

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Introduction: Non-celiac gluten sensitivity (NCGS) is a gluten-related disorder characterized by the absence of allergic or autoimmune etiopathogenetic mechanisms. In the absence of sensitive and specific biomarkers for its diagnosis, the "Salerno Experts' Criteria" represent the only diagnostic tool currently available: it is based on in-vivo gluten challenge with periodical clinical evaluation. On the other hand, oral mucosa patch tests supported by Laser Doppler Perfusion Imaging (LDPI) have been recently proposed for the diagnosis of adverse reactions to foods, such as NCGS and nickel allergic contact mucositis.
Aims and Methods: Our aim was to compare the two methods for the diagnosis of NCGS: the oral gluten challenge according to "Salerno Experts' Criteria" and the Gluten Oral Mucosa Test Patch (GOMPT) supported by LDPI.
We enrolled a total of 30 subjects. 15 patients (Group A) presented with gluten-related symptoms and were on a free diet (FD) for at least 6 weeks. 15 healthy volunteers (Group B) were enrolled as control group. We excluded patients suffering from: celiac disease; allergy to gluten, wheat and other cereals; inflammatory bowel diseases; infectious diseases; autoimmune diseases; malignancies.
At the entrance of the study, patients and controls completed the modified version of the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire: symptoms were quantitatively assessed using a scale from 1 to 10. They also underwent GOMPT, which consists of a gluten-containing stimulation test applied on the oral mucosa. LDPI, which produces quantitative data about oral mucosa vascularization before and after GOMPT, was also performed. Then, all patients followed a gluten-free diet (GFD) for 6 weeks with a second questionnaire completed. Afterwards, they started a double-blind placebo controlled trial, according to "Salerno Experts' Criteria". Capsules containing gluten (Product A) or rice flour (placebo, Product B) 6 gr/day have been consumed for one week respectively, with an intermediate wash-out week. A symptom questionnaire was repeated every week.
Results: There was no significant difference in symptoms' intensity between GFD period and Product A (gluten) period, as well as between Product A (gluten) and B (placebo) period. On the other hand, intensity significantly varied in 15/22 symptoms between FD and GFD period; in 12/22 symptoms between FD and washout (GFD) period; in 4/22 symptoms between FD and Product B (placebo) period. However, 7/22 symptoms do not show any significant difference. Questionnaires from control patients did not show any statistically significant difference.
14 out of 15 patients (93%) belonging to Group A showed GOMPT-positive results. 78.6% of them reported both local lesions and systemic symptoms during and after GOMPT, whereas the remaining 21.4% only presented systemic symptoms. Control patients from Group B showed GOMPT negative results, with only 13.3% reporting headache and drowsiness.
LDPI showed a statistically significant difference in mucosal perfusion after GOMPT in patients from Group A (p value < 0.003), while there was no significant alteration after simulation with vaseline (negative control). Control patients from Group B showed no significant difference in LDPI.
Conclusion: According to our data, the modified GSRS questionnaire alone seems to be not enough for NCGS diagnosis. In fact, it was not possible to observe statistically significant differences in symptoms' intensity during gluten and placebo intake. On the other hand, GOMPT supported by LDPI could be extremely useful for a fast and effective NCGS diagnosis.
Disclosure: Nothing to disclose

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P1853 CLINICAL BENEFIT OF THE USE OF THE GAXILOSE TEST FOR HYPOLACTASIA DIAGNOSIS: A NON-INFERIORITY RANDOMIZED CONTROLLED CLINICAL TRIAL

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Introduction: The Gaxilose test (GT) is a non-invasive method for the diagnosis of hypolactasia. Its efficacy and safety have already been proved in three clinical trials (1, 2). However, the impact on diagnostic thinking and on patient management had to be evaluated to confirm its clinical benefit.

Aims and Methods: The objective was to demonstrate the non-inferiority of the GT, compared to the Hydrogen Breath Test (HBT) on the impact on diagnostic thinking and on patient management for the diagnosis of hypolactasia. Patients with clinical symptoms of lactose intolerance were recruited in a multicentric clinical trial and randomly assigned to perform the GT or the HBT. The gastroenterologists had to complete for each patient a pre-test and a post-test visual analogue scale (VAS) questionnaire indicating their expected probability of diagnosing hypolactasia. The impact on diagnostic thinking was evaluated through the mean of the absolute values of the differences between the pre-test and post-test VAS scores and compared between the GT and the HBT. To assess the impact on patient management, the physicians completed a pre-test and a post-test management questionnaire. The percentage of patients who passed from '*No intervention*', '*Prescription of additional diagnostic tests*' or '*Referral to another specialist*' at pre-test to '*Diet adjustment and follow-up*' at post-test was compared for both diagnostic tests. The limit of non-inferiority was defined in both cases as -10%.

Results: 147 patients (115 females and 32 males, age range: 19–70 years, mean age: 38.41 years) were included in the analyzed population. Among them, 74 performed the HBT and 73 performed the GT. The impact on diagnostic thinking was $31.74 \pm 23.30\%$ for the GT and $24.28 \pm 19.87\%$ for the HBT. The difference between both was 7.46%, with lower 95% confidence limit (CL) of 1.55%, higher than the limit of non-inferiority ($p < 0.001$). The percentage of patients who passed from '*No intervention*', '*Prescription of additional diagnostic tests*' or '*Referral to another specialist*' at pre-test to '*Diet adjustment and follow-up*' at post-test was 6.85% for the GT and 5.41% for the HBT. Therefore, the difference between the GT and the HBT was 1.44% (95% CL: -6.31, 9.20). The lower 95% CL of the difference was also higher than the non-inferiority limit ($p = 0.007$). No serious adverse events were reported during the study.

Conclusion: The results demonstrate the non-inferiority of the GT compared to the HBT on the impact on diagnostic thinking and patient management for the diagnosis of hypolactasia.

Disclosure: This work was funded by Venter Pharma SL. Carmen Monsalve-Hernando and Carmen Hermida are employees of Venter Pharma SL. Laura Crespo, Blanca Ferreiro, Verónica Martín, Xavier Aldeguer, Verónica Opio, Pedro Luis Fernández-Gil and María Jesús Gaspar received honoraria for their participation in the clinical trial.

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P1854 SYSTEMATIC REVIEW WITH META-ANALYSIS: THE PREVALENCE OF BILE ACID MALABSORPTION AND THE RESPONSE TO CHOLESTYRAMINE IN PATIENTS WITH CHRONIC WATERY DIARRHOEA AND PRIOR CHOLECYSTECTOMY

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Introduction: Post-cholecystectomy diarrhoea has a prevalence of 9.1% according to a systematic review published in 2012. The frequency of bile acid malabsorption (BAM) in these patients ranges between 57 and 100%, and some authors have suggested that they could be treated with cholestyramine without a prior testing of the presence of BAM. However, in most studies, the sample size is small and the response to cholestyramine has been scarcely evaluated.

Aims and Methods: To perform a systematic review and meta-analysis to assess the prevalence of BAM in patients with chronic watery diarrhoea and previous cholecystectomy and the response to cholestyramine.

MEDLINE was searched up to January 2018. Selected studies included cholecystectomized patients with chronic watery diarrhoea who were tested by 23-seleno-25-homotaurocholic acid (SeHCAT) test for the assessment of BAM. BAM was defined as 7 day SeHCAT retention of $< 10\%$ or $< 15\%$, depending on the study. We calculated the pooled rate of BAM and 95%CI using a random effects model and the inverse variance method. I^2 was calculated to asses heterogeneity across studies (0–39%, not important; 40–75%, moderate; and 76–100%, important).

Results: The search strategy identified 9 relevant studies comprising 361 individuals. The rate of BAM ranged from 57% to 100%. The pooled rate in the $< 10\%$ subgroup (G10; 8 studies) was 68% (95%CI: 53–83%) and 70% (95%CI: 59–81%) in the $< 15\%$ subgroup (G15; 5 studies). There was significant heterogeneity in effect sizes in the two groups (G10: $I^2 = 91\%$; G15: $I^2 = 73\%$). Five studies comprising 166 patients evaluated the effect of cholestyramine in patients with BAM. The pooled cholestyramine response rate was 77% (95%CI: 64–90%) with significant heterogeneity ($I^2 = 72\%$). After excluding the only study of G15, the pooled rate was 82% (95%CI: 72–93%) with moderate non-significant heterogeneity ($I^2 = 56\%$).

Conclusion: These data provide evidence that two thirds of patients with chronic watery diarrhoea and prior cholecystectomy have BAM. Response to cholestyramine in these patients is excellent. These findings have implications for the routine clinical practice and future guideline development.

Disclosure: Nothing to disclose

P1855 DIAGNOSTIC YIELD OF ENDOSCOPY IN CF-LVAD PATIENTS WITH GASTROINTESTINAL BLEEDING

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Introduction: Patients with continuous flow left ventricular assisted devices (CF-LVADs) carry an increased risk of gastrointestinal bleeding (GIB) up to 30%. In these patients, GIB lesions can be found anywhere in the GI tract, making optimal diagnostic and treatment approach difficult. With increasing use of CF-LVADs, an efficient approach for diagnosis and treatment of LVAD-related GIB is important.

Aims and Methods: We aimed to examine the diagnostic yield of endoscopies in Left Ventricular Assist Device-associated gastrointestinal bleeding in a tertiary medical center.

This is a retrospective study on patients who were implanted with continuous flow – Left Ventricular Assist Device (CF-LVAD) at the University of Iowa in 2010–2015, followed for a maximum of 2 years from the time of CF-LVAD implantation, or until death or heart transplant. All patients with gastrointestinal bleeding (GIB) were admitted, monitored and underwent endoscopic workup for diagnosis and management of the source of bleeding. Patient's demographics, clinical parameters and diagnostic yield of endoscopic procedures were recorded. Recurrent rate of GIB, subsequent endoscopic procedures and mortality rate were also collected.

Results: Out of 104 patients implanted with Heartmate II CF-LVADs, 37 developed GIB, with mean age of 57.7 ± 12.4 years, and 86.5% were males. Time from CF-LVAD placement to GIB was 122.9 ± 166 (range 10–715 days), with a rate of 88.9/100 patient-years. Majority of patients (43.2%) presented with melena, whereas 18.9% presented with occult GIB. At initial GIB episode, EGD as an index procedure was performed in 21.6%, colonoscopy in 13.5% and both EGD and colonoscopy in 64.9%. Bleeding lesions in the upper GI tract were found in 51% of the patients, followed by 29% lesions in small bowel and 8% lesions in the colon. Diagnostic yields of EGD and colonoscopy were 62.5% (20/32) and 17.2%, (5/29) respectively, Video capsule endoscopy (VCE) had a diagnostic yield of 23.8% (5/21). Eleven enteroscopies either push or double balloon identified 6 bleeding lesions in the small bowel.

The most common lesions found by EGD were erosions (40%) and angiodysplasia (35%), whereas ischemic changes were the most common lesion found on colonoscopy in 4 of 5 (80%) patients [Table 1]. Majority of the bleeding lesions were found in the upper GI tract (62.5%), within the reach of EGD, and 8/37 (23.8%) bleeding lesions were detectable by VCE. The combined diagnostic yield of EGD and VCE was 67.5%.

Location	Lesions
Upper GI tract (n) EGD(32)	Esophagus: ulcer (1), esophagitis (1) Stomach :ulcer (1), erosion (6), angiodysplasia (4), GAVE (2), ischemia (1) Doudenum:angiodysplasia (3)
Small bowel (n) VCE(21) Enteroscopy (11)	jejunum and ileum: VCE: erosion (2), angiodysplasia (3) Enteroscopy:Angiodysplasia (4), oozing blood (2)
Colon (n) Colonoscopy (29)	Colon and terminal ileum: ulcer (1), ischemic changes (4)

[Lesions of GIB identified in GI tract with each type of endoscopy]

During the 2-year follow-up, 73% of patients had recurrent GIB; and 32.4% of them experienced more than 2 episodes with a mean of 3.14 bleeding episodes/patient. During the 2 years follow-up, 18 patients (48.6%) died; among these, 4 (22.2%) deaths were related to GIB.
Conclusion: In a cohort of 104 CF-LVAD patients followed up for 2 years, 35.6% of them developed GIB, mostly in the first 6 months, with a high recurrence rate. Most GIB bleed lesions were found in upper GI tract or small bowel. EGD showed the highest diagnostic yield, followed by VCE. We suggest that evaluation of GIB in CF-LVAD patients should be initiated with EGD and a VCE, to optimize diagnostic yield and successful intervention.
Disclosure: Nothing to disclose

P1856 SMALL BOWEL GASTROINTESTINAL BLEEDING – CAN WE BLAME ANTICOAGULANTS?

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Introduction: The use of anticoagulants is associated with an increased risk of upper and lower gastrointestinal (GI) bleeding.
Aims and Methods: The aim of this study was to evaluate whether different anticoagulant groups increase the yield of small bowel (SB) findings in patients who undergo small bowel capsule endoscopy (SBCE) for iron deficiency anaemia (IDA) or overt SB bleeding following negative bidirectional endoscopies.
The SBCE findings of 2 groups of patients presenting with IDA or overt SB bleeding after negative bidirectional endoscopy were compared: Group 1: patients were on antiplatelets / newer anticoagulants / warfarin / aspirin, Group 2: patients were not on any anticoagulants.
Results: 139 patients in group 1 were compared to 119 patients in group 2 (mean age 71.3 ± SD8.7). Both groups were gender and age matched. Indications in the 2 groups were anaemia and overt SB bleeding ($p = 0.145$). Patients in group 1 were on: aspirin (58; 42.4%), warfarin (5; 3.6%), newer oral anticoagulants (61; 43.9%), thienopyridines and ticagrelor (23; 16.5%), NSAIDs and anticoagulants (5; 3.6%). 16 patients (11.5%) were on 2 and 1 patient (0.719%) was on 3 anticoagulants.
There was no statistical difference in the upper GI ($p = 0.609$) and SB yield ($p = 0.499$). There was also no statistical difference in findings according to SB location (proximal / mid / distal / diffuse / terminal ileum) within the 2 groups.
Comparing subcategories in group 1:
There were no statistical difference in upper GI yield ($p = 0.796$) and SB yield ($p = 0.479$) across subcategories in group 1 but patients on aspirin had the highest SB yield (73.2%). Patients on dual anticoagulants (64.3%) and those on thienopyridines and ticagrelor (63.6%) were more likely to have proximal positive findings ($p = 0.014$). Patients on NSAIDs and anticoagulants (60%) were most likely to have white tipped villi ($p = 0.014$) and denuded villi (40%) ($p = 0.011$).
Comparing each anticoagulant separately to controls:
Patients on aspirin ($p = 0.050$) and warfarin ($p = 0.004$) were more likely to have white-tipped villi when compared to controls. Patients on warfarin were more likely to have denuded villi ($p = 0.004$). Patients on thienopyridines or ticagrelor were more likely to have proximal SB involvement ($p = 0.038$).
Conclusion: Being on anticoagulants does not increase the prevalence of SB findings on SBCE in patients with SB bleeding. A bigger prospective study is needed to confirm the lack of relationship between SB bleeding and anticoagulants.
Disclosure: Nothing to disclose

P1857 RHEMITT SCORE: THE BEGINNING OF A NEW ERA IN THE PREDICTION OF REBLEEDING!

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Introduction: Mid gastrointestinal bleeding (MGIB) accounts for 5–10% of gastrointestinal hemorrhages, and small bowel capsule endoscopy (SBCE) is the gold-standard for investigational approach. In spite of the acknowledgement of some risk factors, no score can currently predict the individual risk of small bowel rebleeding after SBCE.
Aims and Methods: We aimed to create a predictive score of small bowel rebleeding risk, in patients that underwent SBCE for MGIB.
Retrospective, unicentric study, including patients that underwent SBCE for MGIB, from June 2006, to October 2016. Every patient had a 12 months minimum follow-up.
Statistical variables were chosen according to clinical relevance and previous evidence in the literature, and their correlation with the occurrence of small bowel rebleeding after SBCE was assessed. Univariate analysis allowed us to select covariables with marginal association ($p < 0.15$) with the outcome variable, which were then included in a Cox regression hazard multivariate model. Finally, we attributed points to each variable category in order to create a score with clinical applicability.
Results: Out of 357 patients submitted to SBCE for MGIB, 230 (64.3%) were female and the mean age was 64 years old. The main indication to SBCE was iron-deficiency anemia (72.8%) and 88 patients (24.6%) presented with rebleeding during the follow-up.
The significantly different variables allowed us to create a new measure for the prediction of the individual risk of gastrointestinal rebleeding, the RHEMITT score, that presented a good accuracy to the outcome variable (area under curve 0.843, CI 95%0.801–0.885). From the regression coefficients obtained, we designed a score, from 0 to 18 points, (**R**enal disease, 3 points [$p < 0.001$]; **H**eart Failure, 1 point [$p = 0.044$]; **E**ndoscopic capsule lesions P1, 2 points [$p = 0.021$]; P2, 3 points [$p = 0.002$]; **M**ajor bleeding, 5 points [$p < 0.001$]; **I**ncomplete capsule, 2 points [$p = 0.031$]; **T**obacco, 2 points [$p = 0.006$]; Endoscopic **T**reatment, 2 points [$p = 0.002$]), establishing 3 risk groups for rebleeding: 0–3 points (0%); 4–10 points (25.4%);> 11 points: (63.8%).
Conclusion: We present a new score for patients with MGIB, named RHEMITT, which accurately anticipates the individual risk of small bowel rebleeding after initial SBCE.
Disclosure: Nothing to disclose

P1858 IMPACT OF THE TIMING OF CAPSULE ENDOSCOPY IN OVERT OBSCURE GASTROINTESTINAL BLEEDING ON YIELD AND REBLEEDING RATE – IS SOONER THAN 14 D ADVISABLE?

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Introduction: An early diagnosis with capsule endoscopy (CE) in overt-obscure gastrointestinal bleeding (OGIB) patients can lead to an appropriate specific intervention, better long term-outcomes and reduce unnecessary medical costs. ESGE recommends performing CE as soon as possible after the bleeding episode, optimally within 14 days.
Aims and Methods: Evaluate the impact of the timing of capsule endoscopy (CE) in overt-obscure gastrointestinal bleeding (OGIB), mainly when it is performed within 48 hours.
Retrospective, single-center study, including patients submitted to CE in the setting of overt-OGIB between January 2005 and August 2017. Patients were divided into 3 groups according to the timing of CE (≤ 48 h; 48 h-14 d; ≥ 14 d). The diagnostic and therapeutic yield (DY and TY), the rebleeding rate and the time to rebleed were calculated and compared between groups. The outcomes of patients in whom CE was performed before (≤ 48 h) and after 48 h (> 48 h), and before (< 14 d) and after 14 d (≥ 14 d), were also compared.
Results: One hundred and fifteen patients underwent CE for overt-OGIB. The DY was 80%, TY-46.1% and rebleeding rate – 32.2%. At 1 year 17.8% of the patients had rebled. 33.9% of the patients performed CE in the first 48 h, 30.4% between 48h-14d and 35.7% after 14 d. The DY was similar between the 3 groups ($P = 0.37$). In the ≤ 48 h group, the TY was the highest (66.7% vs 40% vs 31.7%, $P = 0.005$) and the rebleeding rate was the lowest (15.4% vs 34.3% vs 46.3% $P = 0.007$). The time to rebleed was longer in the ≤ 48 h group when compared to the > 48 h groups ($P = 0.03$).
Conclusion: Performing CE within 48 h from overt-OGIB is associated to a higher TY and a lower rebleeding rate and longer time to rebleed.
Disclosure: Nothing to disclose

P1859 CYANOACRYLATE INJECTION THERAPY OF SMALL BOWEL VARICES (SBV) DURING DOUBLE-BALLOON ENTEROSCOPY (DBE): EXPERIENCE FROM TWO EUROPEAN CENTRES

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Introduction: Small bowel varices (SBV) are a rare consequence of portal hypertension and could lead to life-threatening mid-gut bleeding. Radiological intervention (RI) is usually considered first line management (e.g. Trans-jugular intrahepatic portosystemic shunting (TIPS), stenting of occluded mesenteric veins +/– embolisation of culprit varices). In cases where RI is impossible, management options become very limited.

Aims and Methods: This multicentre case series evaluated the usefulness of DBE assisted cyanoacrylate injection of SBV. Retrospective review of DBE facilitated cyanoacrylate injection of SBV (December 2015 to October 2016). Demographic, clinical, endoscopic and radiological findings, interventions and follow-up data were analysed.

Results: Ten DBEs were performed in 6 patients (4 women, median age: 68.5-years). All patients had at least one previous surgery (colectomy (n = 1); hemihepatectomy (n = 2); small bowel resection (n = 2); appendicitis with peritonitis (n = 1); splenectomy (n = 1)); one patient had a history of intra-abdominal sepsis in childhood causing portal vein thrombosis and one had cryptogenic thrombosis of the portal and the mesenteric vein. No radiological or surgical options were deemed feasible in any case. SBV were diagnosed at capsule endoscopy and triple phase computed tomography mesenteric angiography. At DBE, a total of 13 nests of SBV were identified and injected with cyanoacrylate glue. There were no haemorrhagic or embolic complications but 1 patient developed an infection of a congenital urachal cyst, which was treated successfully with antibiotics. All patients underwent DBEs via the anterograde route, 2 patients required bi-directional DBE for treatment of both proximal and distal SBV and in total 2 patients required a repeat DBE for further treatment of SBV. At 30-day follow-up post-therapy, only 1 patient had experienced a mild recurrence of mid-gut bleeding treated conservatively. One patient presented with acute gastrointestinal bleeding 7 months later and a repeat DBE with cyanoacrylate injection therapy was successfully performed. One patient was lost to follow-up. The remaining patients had 12 months of follow-up without any recurrent gastrointestinal bleeding.

Conclusion: Cyanoacrylate injection therapy of SBV at DBE appears to be a safe and effective management strategy for this condition when other first-line options are not feasible.

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P1860 IMPACT ON LONG-TERM SURVIVAL OF A POSITIVE VIDEO CAPSULE ENDOSCOPY AFTER A FIRST EPISODE OF OVERT OBSCURE GASTROINTESTINAL BLEEDING

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Introduction: Video capsule endoscopy (VCE) is effective in the detection of small bowel lesions in patients with overt obscure gastrointestinal bleeding (OGIB). However, there is little evidence of its impact on long-term clinical outcomes and survival.

Aims and Methods: The objective of this study was to evaluate the long-term clinical impact of a positive finding in VCE after a first episode of overt OGIB. Retrospective, single-center study that analyzed patients with OGIB who underwent VCE between October 2008 and October 2017. The findings in VCE were considered positive if active bleeding and/or hemorrhagic lesions were detected. Bleeding recurrence (BR) was defined as the need for transfusions, hemoglobin drop ≥2 g/dl, or evidence of overt gastrointestinal bleeding.

Results: A total of 108 patients underwent VCE after a first episode of OGIB, 55% men, with a median age of 70 years (IQR 56–80). The median follow-up was 23 months (IQR 11–51). The VCE revealed positive findings in 66% of the patients, with angiodysplasias (37%) and ulcers (15%) being the most frequent. After VCE, targeted therapy was performed in 26%. In the follow-up, BR occurred in 28% after a median period of 8 months (IQR 3–15). Bleeding recurrence was more frequent after a positive VCE (40% vs. 11%, p = 0.002). Targeted therapy after a positive VCE was not associated with a lower occurrence of BR (42% vs. 38%, p = 0.8). In the multivariate logistic regression, a positive VCE (OR 6.6, 95% CI 1.7–25.6; p = 0.006) and valvular heart disease (OR 3.9, 95% CI 1.4–11.1; p = 0.01) were independent risk factors for BR. In the follow-up, a positive VCE was associated with a higher number of emergency episodes (β = 1.1, 95% CI 0.2–2.0; p = 0.018), number of days of hospitalization (β = 10.0, 95% CI 1.4–18.7; p = 0.023) and endoscopic procedures (β = 2.6, 95% CI 1.4–3.9; p < 0.001). The mortality rate at 12 and 36 months was 22% and 46%, respectively. Patients with a positive VCE had a lower survival, compared to those with a negative VCE (mean 51 vs. 82 months, p = 0.013). In the multivariate analysis, a positive VCE was independently associated with the survival estimate (HR 2.7, 95% CI 1.2–6.1; p = 0.017).

Conclusion: After a first episode of OGIB, patients with a positive VCE have a greater risk of long-term BR, with a consequent negative impact on survival. In our study, targeted therapy for the source of bleeding didn't affect the risk of BR. A high degree of suspicion with regular clinical surveillance, etiologic investigation and timely intervention may be important. Further observations are necessary in order to evaluate the impact of targeted therapy in the long-term follow-up of these patients.

Disclosure: Nothing to disclose

P1861 IMPACT OF SMALL BOWEL BLEEDING PRESENTATION ON DIAGNOSTIC AND THERAPEUTIC PERFORMANCE OF BALLOON-ASSISTED ENTEROSCOPY: A TERTIARY REFERRAL CENTER STUDY IN LATIN AMERICA

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Introduction: Balloon Enteroscopy and Capsule Endoscopy have facilitated the diagnosis of pathologic findings in patients with suspected small bowel bleeding with similar accuracy (1,2). However, therapeutic potential of Balloon-Assisted Enteroscopy combined with its high diagnostic yield in patients that present with overt small bowel bleeding may favor its indication as a first-line endoscopic approach in this group of patients (3).

Aims and Methods: The aim of this study was to determine the impact of the clinical presentation of small bowel bleeding on the diagnostic and therapeutic yield of Single Balloon Enteroscopy (SBE) at a tertiary referral center in Sao Paulo, Brazil.

We retrospectively reviewed consecutive patients that have undergone SBE for the diagnosis and treatment of potential small bowel bleeding, after negative esofagogastroduodenoscopy and colonoscopy. This study was undertaken from November 2011 until March 2017 at a referral tertiary hospital in Sao Paulo, Brazil. All procedures were performed with CO2 insufflation. Sedation of patients was managed by the team's anesthesiologist accordingly. Enteroscopies of patients that presented with active bleeding and/or clinically important comorbidities were performed under general anesthesia at the surgical room. Diagnostic yield was described as the total number of cases diagnosed among the total number of patients that underwent SBE. Therapeutic yield was defined as the total number of successfully treated patients among the total number of patients that were performed SBE. Diagnostic and therapeutic yield of SBE were analyzed according to bleeding presentation and endoscopic findings were described.

Results: A total of 122 SBEs were performed in 84 patients (48 male/36 female, mean age 59 years old SD 21.34). The route of insertion was antegrade in 89 cases (72.95%) and retrograde in 33 (27.05%). 28 patients underwent antegrade and rectal SBE sequentially at a single time. The mean procedural time for antegrade and retrograde approaches was 62 minutes.

Main findings in occult bleeding at SBE were 37 cases of angioectasias, 7 ulcers, 5 polyps and tumors and 5 cases of hemorrhagic gastritis of excluded stomach. Endoscopic lesions in patients that presented clinically with overt bleeding were 6 angioectasias, 2 dieulafoy's, 3 ulcers, 10 cases of polyps and tumors, 2 varices and 2 hemorrhagic gastritis of excluded stomach. There were no complications in this series of patients. Diagnostic and therapeutic yield of SBE according to bleeding presentation (occult VS overt bleeding) is described in table 1.

Conclusion: SBE was an effective diagnostic and therapeutic tool in overt small bowel bleeding, suggesting that this enteroscopy modality may be an appropriate first line diagnostic and therapeutic endoscopic approach for the management of overt bleeding cases.

	n of successful cases/n of total cases	Yield%	p
Diagnostic			0.019
Occult	36/48	75	
Overt	34/36	94.4	
Therapeutic			0.0027
Occult	22/48	45.9	
Overt	29/36	80.5	

[Diagnostic and therapeutic yield of single balloon enteroscopy according to bleeding presentation]

Disclosure: Nothing to disclose

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P1862 TREATMENT OF CHRONIC STENOSING ENTERITIS: A CONDITION SIMILAR TO PROSTAGLANDIN-ASSOCIATED ENTEROPATHY

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Introduction: Chronic stenosing enteritis (CSE) is a novel ulcerative and stenosing disease of the small bowel that is distinct from Crohn's disease, celiac disease, and NSAID-induced small bowel injury. Similar conditions have been described in Japan and Korea as cryptogenic multifocal ulcerating stenosing enteritis, chronic nonspecific stenosing ulceration, and most recently chronic enteropathy associated with mutations in the *SLCO2A1* gene (CEAS), a prostaglandin transporter gene. There are currently no studies examining the outcomes to medical and surgical therapies in patients with CSE. We report our experience with treating CSE.

Aims and Methods: 16 patients diagnosed with CSE were identified between 2007 and 2017 at UMass Medical Center. Patient epidemiology, laboratory studies, endoscopic procedures, radiographic studies, pathology reports, medical treatment, surgical interventions, and disease course were collected retrospectively. All patients underwent video capsule endoscopy as part of their initial work-up. Complete remission was defined as resolution of iron deficiency and clinical symptoms including abdominal pain, bleeding, and anemia. Partial remission was defined as persistent iron deficiency with resolution of clinical symptoms. Iron deficiency was determined using standard ferritin and transferrin saturation thresholds.

Results: The median duration of follow-up was 48 (4.5–85.3) months. 75.0% of patients presented with bleeding or iron deficiency anemia. 80.0% of patients were found to be iron deficient (see Table 1). 43.8% of patients required intravenous iron therapy. A total of 62.5% of patients underwent surgical resection for CSE and 31.3% received biologic therapy with infliximab or adalimumab. Only 3 patients received steroids, none of whom achieved remission with this therapy. The overall rates of full remission, partial remission, and no remission were 20.0%, 26.7%, and 26.7% respectively. 26.7% of patients had resolution of clinical symptoms but no available follow-up iron studies to evaluate for full remission. 1 patient was lost to follow-up after initial diagnosis.

	Gender	Age at Onset (Years)	Iron Deficiency	Surgery	Biologic Therapy	Outcome
1	M	70	+	–	–	F
2	M	55	–	+	–	P*
3	F	61	+	–	+	P
4	M	62	–	+	–	N
5	M	56	+	–	–	N/A
6	M	63	+	–	–	F
7	M	57	+	+	–	N
8	M	53	+	+	+	P
9	M	72	–	+	–	P*
10	M	75	+	–	–	N
11	M	53	+	+	+	P
12	M	37	+	+	–	F
13	F	43	N/A	+	+	N
14	M	58	+	+	+	P
15	M	30	+	+	–	P*
16	F	74	+	–	–	P*

[Table 1: Patient Characteristics, Treatment, and Outcomes in Chronic Stenosing Enteritis]

Biologic therapies included infliximab and adalimumab.
F = full remission; P = partial remission; P* = clinical remission without available follow-up iron studies; N = no remission; N/A = data not available

Conclusion: Patients with CSE can be successfully treated with iron supplementation, surgery, and biologic therapy. Iron studies may have a role in monitoring disease activity, particularly when clinical symptoms are resolved. Further studies are needed to determine the long-term implications of these interventions.

Disclosure: David R. Cave, MD has a research grant with Olympus Corporation and is a Medtronics clinical trial investigator.

P1863 THE UTILITY OF CAPSULE ENDOSCOPY AND ENTEROSCOPY IN PATIENTS WITH HEREDITARY HAEMORRHAGIC TELANGIECTASIA

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Introduction: Small bowel angioectasias (SBAs) commonly occur in patients with hereditary haemorrhagic telangiectasia (HHT). Patients with small bowel (SB) involvement and those with severe gastrointestinal (GI) bleeding are significantly older

Aims and Methods: Patients with known HHT were included in this study. Data on GI investigations was recorded. The impact of SB capsule endoscopy (CE) and double balloon enteroscopy (DBE) was evaluated.

Results: 10 patients (60% males) with genetically confirmed HHT were included. Mean age at first SB endoscopy was 62.6 ± SD14.4 years.

Patients had the following co-morbidities: chronic thromboembolic pulmonary hypertension (1), chronic kidney disease (2), respiratory (2), cardiac (4), superior mesenteric vein thrombosis (SMVT) (1), malignancies (2). 1 patient was on warfarin. Another patient was on deltaparin.

Some patients had evidence of extra-GI arterio-venous malformations (AVMs): pulmonary (2), cerebral (2), nasal mucosa (3), hepatic (1).

Patients had a total of 39 gastroscopies, 16 colonoscopies and 6 push enteroscopies. 7 patients underwent SBCE: 6 (85.7%) had proximal, 1 (11.1%) had mid and 3 (33.3%) patients had distal SBAs. 2 patients had a colon capsule which showed angioectasias.

6 patients had several DBEs (median 4; SD ± 6) with a mean 130.5 ± SD133.3 between DBEs. All were antegrade DBEs except for 1. 57 SBAs were treated with argon plasma coagulation (APC) on average at each DBE. There was a mean improvement in haemoglobin in patients who underwent regular DBEs (93.8 vs 102.1 g/dL; p = 0.102). 6 patients were transfusion dependent initially but 4 improved following intervention.

Need for transfusion resolved in 1 patient when started on lanreotide, regular endoscopy and APC and in 2 patients on starting DBEs and APC. 1 patient passed away from pneumonia. Another patient was switched unsuccessfully from octreotide to lanroetide. She stopped being transfusion dependent with regular OGDs and APC. Another patient was unwilling to undergo further endoscopies due to multiple co-morbidities. He improved on lanreotide. In 2 patients anaemia remains persistently problematic. 1 of them is also on deltaparin for SMVT. The other patient has recurrent epistaxis which makes it harder for him to have further endoscopies.

In comparison, 40 (29%vs 85.7%) from a total of 138 patients referred due to anaemia for SBCE between 2014 and 2015 had SBAs. (p = 0.004).

Conclusion: SBCE is a useful screening tool in patients with HHT to assess for SBAs which occur more commonly than in patients with anaemia but no underlying HHT. Most patients had proximal SBAs which were amenable to regular DBEs and APC. A small number required additional pharmacotherapy to improve transfusion requirements.

Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 09:00–14:00

Nutrition III – Hall X1

P1864 WITHIN- AND BETWEEN SUBJECT VARIATION IN INTAKE OF FERMENTABLE OLIGO-, DI-, MONOSACCHARIDES AND POLYOLS (FODMAPS) AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: A diet low in fermentable carbohydrates, FODMAPs (Fermentable Oligo-, Di-, Monosaccharides And Polyols) seems to be a promising treatment option for patients with IBS. However, the pattern of FODMAP consumption among patients with IBS, e.g. the types, amounts and the variability in FODMAPs consumed, is still unclear. This information is necessary when planning surveys, to be able to obtain data that are sufficiently accurate for the study objectives.

Aims and Methods: The aim of this study was to characterize the variation in FODMAP intake among patients with IBS, and to calculate the number of days needed to capture the FODMAP intake at the individual level with a certain precision, as well as how many days are required for ranking individuals within a group. Food intake was recorded during four consecutive days (Wednesday-Saturday) in patients with IBS, and intake of energy and nutrients, including FODMAPs, were calculated in a special version of the software Dietist XP 3.1 (Kostdata.se, Stockholm, Sweden) linked to a FODMAP database. Calculation of the coefficient of variation within subjects (CV_w), coefficient of variation between subjects (CV_b), the number of replicate days required per subject to estimate an individuals nutrient intake, and the number of observations required to correctly rank individuals into quartiles of consumption, were calculated.

Results: Diet records were provided from 151 women and 46 men with IBS. The reported mean energy intake was 2039 ± 502 kcal among women and 2385 ± 573 kcal among men, and the median FODMAP intakes were 18.7g (range 3.7–73.4) and 22.8g (range 3.6–165.7), respectively. Lactose contributed to >53% of the total intake in FODMAPs, excess fructose with 27%, fructans with 12%, polyols

with 5%, and galacto-ologosaccharides contributed with the least amount, 3%. There were no significant gender differences in the proportion of energy adjusted FODMAP intake. The ratio of CV_w / CV_b for total FODMAP intake was 0.83 for women and 0.67 for men, and below 1 for all FODMAPs. This indicates that there is larger variation between subjects than within subjects with respect to FODMAP intake. To capture the intake of FODMAPs at the individual level with a precision of +/−20%, 19 days of replicate observations are required (as seen in the table). Ranking individuals within a group according to FODMAP intake would require between 2–6 days of replicate observations.
Conclusion: Our results show that there is more variation between subjects than within subjects regarding FODMAP intake. Dietary data with good precision at the individual level would not be obtainable using a reasonable number of days of food records. However, if the study objective is to rank individuals into quartiles of FODMAP consumption, this can be achieved with a good level of precision by using food records.

	Number of days to capture true mean intake at the individual level (95% CI)		*Number of days required for ranking individuals into quartiles of consumption*	
	+/−20%	+/−30%	r = 0.90	r = 0.95
Total FODMAPs	19	9	2	5
Galacto-oligosaccharides	51	23	3	6
Fructans	21	9	3	6
Polyols	117	52	2	4
Lactose	46	20	2	4
Fructose	29	13	2	5
Excess fructose*	104	46	3	5

Abbreviations: FODMAP, fermentable oligo-, di-, monosaccharides and polyols; *Fructose in excess of glucose
[Number of days of observation required for capturing intake of FODMAPs at the individual level with given precision and for ranking individuals]
Disclosure: Nothing to disclose

P1865 INTAKE OF FERMENTABLE OLIGO-, DI-, MONOSACCHARIDES AND POLYOLS (FODMAPS) IN RELATION TO SYMPTOM SEVERITY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: Restricting intake of fermentable carbohydrates, FODMAPs (Fermentable Oligo, Di-, Monosaccharides And Polyols) is increasingly recommended in the management of IBS. However, it is still unclear if the habitual FODMAP consumption correlates to IBS symptom severity, and if this relationship differ among IBS subgroups. The aim of this study was to define the habitual FODMAP intake among patients with IBS, and to evaluate the relationship between FODMAP intake and symptom severity and pattern in IBS.
Aims and Methods: The aim of this study was to define the habitual FODMAP intake among patients with IBS, and to evaluate the relationship between FODMAP intake and symptom severity and pattern in IBS. Patients with IBS recorded food intake during four consecutive days and they were instructed to maintain their regular diet. Intake of energy, nutrients and FODMAPs were calculated in the software Dietist XP 3.1 (Kostdata.se, Stockholm, Sweden), linked to an in-house FODMAP database. IBS symptom severity was measured with the IBS severity scoring system (IBS-SSS), and IBS subgroups were defined according to the Rome III criteria.
Results: Diet records were provided from 151 women and 46 men with IBS; IBS with constipation (IBS-C) n = 44 (22.3%), IBS with diarrhea (IBS-D) n = 54 (27.4%), mixed IBS (IBS-M) n = 46 (23.4%) and unsubtyped IBS (IBS-U) n = 46 (23.4%). Mean intake of total FODMAPs was similar across the different subtypes, with a mean intake of 20.7 ± 11.9 g/day (median 19.4 g). Neither age, anxiety, depression nor somatic symptoms were associated to FODMAP intake. For individual FODMAPs we noted a higher lactose intake among IBS-M compared to IBS-D, 12.9 ± 8.7 g vs. 8.1 ± 7.1 g, $p = 0.02$. When including all patients, we did not see any difference in the symptom severity (IBS-SSS) across the four quartiles of FODMAP intake: Q1, 296 ± 97; Q2, 303 ± 63; Q3, 292 ± 92; Q4, 316 ± 85 ($r_s = 0.073$, $p = 0.53$). However, when stratifying on IBS subgroups, there was a significant correlation between FODMAP intake and increased overall IBS symptom severity among IBS-U patients, $r_s = 0.401$, $p = 0.006$, and for the IBS-SSS subscales pain frequency and bowel habit dissatisfaction (table 1).
Conclusion: This study shows no major differences in FODMAP intake among IBS patients with different bowel habits or severity of symptoms, except for an association between IBS symptoms and FODMAP intake in unsubtyped IBS. However, it seems likely that patients who are intolerant to certain FODMAPs have already reduced their FODMAP intake, which was not investigated in this study.

	FODMAP intake among different IBS subtypes			
	IBS-C	IBS-D	IBS-M	IBS-U
IBS-SSS total	0.009	0.000	−0.002	0.401**
Pain intensity	0.041	−0.137	0.197	0.129
Pain frequency	0.145	0.062	−0.058	0.385**
Bloating severity	−0.027	−0.003	−0.064	0.091
Bowel habit dissatisfaction	−0.095	−0.004	−0.017	0.326*
Daily life interference	−0.104	−0.135	0.042	0.232

Abbreviations: IBS-SSS, irritable bowel severity scoring system; IBS-D, IBS with diarrhea; IBS-C, IBS with constipation; IBS-M, mixed IBS; IBS-U, unsubtyped IBS * correlation is significant at $p < 0.05$, ** correlation is significant at $p < 0.01$
[Table 1. Spearman correlation between IBS symptom severity and FODMAP intake among different IBS subgroups.]
Disclosure: Nothing to disclose

P1866 ASSESSING THE EFFECTS OF TWO PROBIOTIC FORMULATIONS ON CACO-2 CELL EPITHELIUM BARRIER MODEL

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Introduction: It is largely known the beneficial effect of probiotics to improve human health through reestablishing the composition of the gut microbiota and contributing to the maintenance of gastrointestinal tract function. Probiotics protect the host from pathogens by competitive exclusion, preserve barrier integrity, affect the host immune system and remove heavy metals and environmental toxins. Since changes in manufacturing affect the functional properties of probiotic formulations [1–4], we have compared the *in vitro* effects of two 450 billion multi-strain high concentration formulations, identified by us as USA-made and Italy-made, on human colon adenocarcinoma cell line, CaCo-2, a model widely used as an optimum for studies on intestinal barrier functions [5].
Aims and Methods: The aim of this research was to identify if two 450 billion commercial probiotic preparations sourced from different production sites (USA and Italy) could affect the integrity of intestinal barrier in vitro as well as protect from heat-induced dysfunction of the epithelial monostrate. CaCo-2 monolayers were seeded in Transwell chambers where they close up shaping a model of intestinal barrier. The effects of both probiotic formulations, at 10^8 CFU/ml final concentration, were analyzed on both transepithelial electrical resistance (TEER) and 4 kDa fluorescein isothiocyanate-dextran (FD4) flux in CaCo-2 cells before and after exposition to heat stress. TEER and dextran flux are considered as a reliable tool to evaluate the physiological state and integrity of epithelial or endothelial barrier and can also be used to predict paracellular permeability following several stimuli [6]. Considering that tight junctions are thought to be exceptionally effective structures operative in several main functions of the intestinal epithelium under both physiological and pathological circumstances, the effects of probiotic treatment before heat-induced damage on the levels of tight junction proteins i.e. zonulin-1 and occludin were also analyzed by western blotting and densitometry of relative bands.
Results: Treatment with both products did not significantly affect basal levels of TEER and FD4 flux values. On the other hand, a 4 h pre-treatment with USA-made probiotic was able to totally prevent the heat-induced damage as shown by TEER and dextran flux analyses. Instead, the Italy-made product did not exert significant effects on both TERR values and dextran flow altered by heat damage. The basal levels of zonulin were not modulated by a 3 hr-treatment with both probiotic formulations while USA-made product was able to upregulate occludin expression. Of note, Italy-made product, at the same experimental conditions, induced a significant decrease of occludin levels compared with both untreated cells and USA-made product treatment. Also in this context, just pre-treatment with USA-made formulation was able to totally prevent both zonulin and occludin level reduction induced in heat-stressed monolayers.
Conclusion: The results confirm that the production conditions of this 450 billion formulation are crucial for its efficacy and safety, as previously reported [1–4]. A careful selection of the probiotic agent, standardization of the dose and detailed characterization of the beneficial effects are essential when considering use of a probiotic for the dietary management of serious diseases. As a general rule, there is the need to reconfirm safety and/or efficacy for any probiotic product made at a different factory even if contains the same species.
Disclosure: Nothing to disclose

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P1867 THE COMBINATION OF PEPPERMINT OIL AND CARAWAY OIL DOES NOT AFFECT GASTRIC FUNCTION, BUT INCREASES HUNGER RATINGS AND DECREASES SATIATION IN HEALTHY SUBJECTS

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Introduction: The heterogeneous character of functional gastrointestinal disorders makes it challenging to find effective treatment options. Compared to synthetic drugs, phytotherapeutic medicines can have broader pharmacological effects and are often better tolerated.

Aims and Methods: The current study aimed to investigate the effect of a combination of peppermint oil (41.5 mg l-menthol) and caraway oil (50 mg) (POCO) on gastric motility, gastric emptying, nutrient volume tolerance, postprandial symptom levels and gastrointestinal peptide hormones in 32 healthy subjects in a single-blinded, placebo-controlled, randomized, parallel design. On study day 1, a ^{13}C breath test was performed after an overnight fast to assess gastric emptying rate 30 minutes after study medication administration (POCO or placebo). This was followed by an intragastric pressure (IGP) measurement using high-resolution manometry, during which 350 mL of a nutrient drink was intragastrically infused at 60 ml/min 30 minutes after a second dose of study medication. IGP was measured until 2 hours after infusion. On study day 2, IGP was measured for 4 hours in the fasted state after intake of study medication, followed by a second dose of study medication and 30 minutes later intragastric infusion of a nutrient drink until the participant was fully satiated (0–5 likert scale). IGP was measured until 2 hours after the infusion. Gastrointestinal symptom intensity (bloating, fullness, nausea, belching, epigastric burning, cramps and pain) was rated during IGP measurements on a 100 mm VAS. Blood samples were collected during IGP measurements in fasted and fed state to assess glucagon-like peptide 1 (GLP-1) levels. Data were analysed using linear mixed models.

Results: POCO had no significant effect on intragastric pressure in fasted ($p = 0.08$) or fed state (infusion of 350 mL or until full satiation) ($p = 0.98$ and $p = 0.12$ respectively). Further, no significant differences in nutrient volume tolerance and gastric emptying rate were observed between POCO and placebo ($p = 0.55$ and $p = 0.39$, respectively). However, in the fasted state, hunger levels were higher and satiation levels were lower following POCO administration compared to placebo (average change in hunger after POCO: 11.73, average change in hunger after placebo: -7.74, average change in satiation after POCO: -11.13, average change in satiation after placebo: 3.98, $p < 0.001$ for both). In the fed state, hunger and satiation scores did not differ between placebo and POCO ($p > 0.66$ for all). In addition, gastrointestinal symptoms were not affected by POCO administration ($p > 0.23$ for all). No significant differences were found in active GLP-1 levels between POCO and placebo ($p = 0.29$).

Conclusion: An acute dose of POCO did not affect gastric function in healthy subjects, but increased hunger ratings in the fasting state. The effects of POCO on gastric function and hunger sensations in patients with functional gastrointestinal disorders, as well as their contribution to symptom improvement, needs to be elucidated in future studies.

Disclosure: Nothing to disclose

P1868 DIETARY FODMAPS CAN LEAD TO MICROBIAL PRODUCTION OF GLYCATION AGENTS, INCREASING MUCOSAL MASTOCYTES AND IMPACTING COLONIC MUCUS BARRIER FUNCTION

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Introduction: Irritable Bowel Syndrome (IBS) is characterized by abdominal pain, often associated with diet. Limiting the consumption of FODMAPs (fermentable oligos-, di-, mono-saccharides, and polyols), unabsorbed in the small intestine and fermented by the gut microbiota, improves symptoms in 70% of IBS patients. However, the mechanisms behind this effect remain unclear. Our hypothesis is that bacterial metabolites resulting from fermentation of FODMAPs, such as aldehydes (glycation agents), can cause symptoms via the formation of advanced glycation end-products (AGEs). A low-grade inflammation caused by AGE-RAGE interaction, supported by mast cell activation, could also have negative effects on the epithelial barrier function. Mast cells can induce mucin release from goblet cells in immobilization stress in rats. Alternatively, FOS supplementation in rats can impair cecal epithelial mucus barrier function, and inulin supplementation to rats after weaning modifies mucin gene expression, colonic crypt depth and goblet cell numbers. In humans, IBS patients often report passage of mucus *per rectum*. We used a mouse model to investigate whether an increased intake of dietary FODMAPs is implicated in mucus barrier particularities, to study the mechanisms of effect of a low-FODMAP diet.

Aims and Methods: Three groups of mice (C57BL/6 ♂) were treated daily for 21 days with an oral gavage of saline or saline solution containing 5 mg of lactose and/or 5 mg of anti-glycation agent pyridoxamine for lactose experiments, additionally, three groups of mice (C57BL/6 ♂) followed diets for 21 days; control (AIN-93M), 10% FOS (AIN-93M; part of starch replaced by FOS), and 10% FOS + 1mg/ml pyridoxamine in drinking water. Mucosal mast cell (MMC) numbers were analysed by immunofluorescence. Goblet cell numbers in empty colon, and mucus barrier thickness in colon containing faeces in paraffin embedded colon were analysed by classical histology.

Results: Lactose and FOS treatments significantly ($P < 0.01$) increased the number of mucosal mast cells in both groups (Lactose: 0.74 v 0.54 mast cell/crypt; FOS: 1.27 vs 0.67 mast cells/crypt), which was prevented by co-administration with pyridoxamine. Mucus production indicated by emptying goblet cells was increased significantly in both groups (Lactose: 1.71 v 1.08 active goblet cells/crypt; FOS: 1.89 v 1.01 active goblet cells/crypt), which was prevented by co-administration with pyridoxamine for lactose, and attenuated but not completely prevented for FOS. The mucus layer separating epithelium and colonic contents showed significantly ($P < 0.0001$) reduced thickness in FODMAP-treated groups (Lactose: 10.7μm v 18.4μm; FOS: 8.6μm v 16.0μm), which, again, was prevented by co-administration of anti-glycation agent pyridoxamine.

Conclusion: Our results show that increased FODMAP intake can induce an increase in the number of mucosal mast cells in mice, impacting the normal functioning of the colonic mucus barrier. The prevention of these effects by anti-glycation agent pyridoxamine implies a role of glycation processes in the origin of these effects. The aberrant production of mucus in empty colon in the absence of contents might explain the reduced formation of the faecal mucus layer. Given the similar results obtained with both FODMAP representatives, this work suggests a common mechanism responsible for the adverse effects observed, namely, the generation of glycation agents derived from FODMAP fermentation by the gut microbiota.

Disclosure: Nothing to disclose

P1869 THERAPEUTIC RELEVANCE OF BODY MASS INDEX (BMI) CONTROL IN A POPULATION AFFECTED BY IRRITABLE BOWEL SYNDROME/BLADDER PAIN SYNDROME (IBS/BPS)

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Introduction: Bladder pain syndrome/interstitial cystitis (BPS/IC) is a debilitating chronic, inflammatory disorder of the bladder and urinary tract characterized by variable degree of bladder pain, frequency and urinary urgency. BPS patients are often affected by several gastrointestinal symptoms, such as abdominal pain, dyspeptic symptoms, alternance of constipation and diarrhea, sometimes referring to IBS, GERD, food allergy or intolerance. Our patients' diet is influenced by lots of restrictions introduced by themselves in order to improve these symptoms. This study aimed to better understand how a weight control strategy can influence IBS/BPS patients' psychological state.

Aims and Methods: The study was conducted in the Multicentric Interstitial Cystitis Referral Center of the Catholic University in Rome, in a population of 37 female, aged 25–57, affected by BPS according to the "European Society for the Study of Interstitial Cystitis (ESSIC)" criteria plus IBS. Patients were categorized into two groups, a normal BMI group, between 19–24.9, and a pathological weight group, whom 14 female with BMI less than 18.9 and 23 patients with BMI more than 25. All subjects were asked to fill our Psycho-Gastroenterological Questionnaire (PGQ), which takes into account the following parameters: number of medical examinations due to gastrointestinal symptoms, sensation of pain scored the Visual Analogue Scale (EQ-VAS); form of the feces established with the Bristol Stool Chart (BSC); gastrointestinal symptoms assessed with the Gastrointestinal Symptoms Rating Scale (GSRS); anxiety with the State-trait anxiety inventory (STAI Y-1 and STAI Y-2); a self-perceived evaluation of psychological well-being expressed by the Psychological General Well-Being Index (PGWBI); levels of anxiety and depression with the Hospital Anxiety and Depression Scale (HADS); perceived Self-efficacy in the management of negative emotions and expression of positive emotions with General Self-Efficacy Scale (GSE); levels of resilience with the Connor-Davidson Resilience Scale (CD-RISC). Differences between the two groups were evaluated by Student's t test and considered significant for $p < 0.05$.

Results: Compared to pathologic BMI group, normal BMI group has a higher EQ-VAS score (45 ± 18 vs 35 ± 19) and a lower GSRS score (15 ± 7 vs 17 ± 6), but these differences were not statistically significant. On the other hand, scores of STAI Y-1 (47.5 ± 10.7 vs 58.5 ± 13.4, $p < 0.05$), STAI Y-2 (39.3 ± 10.6 vs 52.4 ± 10.1, $p < 0.05$), PGWBI (62.9 ± 15.8 vs 45.4 ± 18.7, $p < 0.05$), HADS (7.5 ± 3.8 vs 10.7 ± 5.3 for anxiety, 5.6 ± 2.5 vs 9.3 ± 3.6 for depression, $p < 0.05$), GSE (30.2 ± 3.5 vs 22 ± 9.3, $p < 0.05$); CD-RISC (71.1 ± 10.2 vs 55.7 ± 12.6, $p < 0.05$) are all significantly better among normal BMI group.

Conclusion: Our study demonstrate that weight control can strongly improve IBS/BPS patients' QoL. Further studies about the most fitting diet for patients with such gastrointestinal distress are required.

Disclosure: Nothing to disclose

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P1870 NO EVIDENCE FOR INCREASED RISK FOR CANDIDAEMIA IN THE PRESENCE OF POLYMORPHISMS IN THE CD58, LCE4A-CLORF68 AND TAGAP LOCI IN HOME PARENTERAL NUTRITION PATIENTS

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Introduction: Home parenteral nutrition (HPN) patients have an increased risk of catheter-related bloodstream infections, including candidaemia. In a large hospital cohort, three single-nucleotide polymorphisms (SNPs) in CD58, LCE4A-Clorf68 and TAGAP loci have recently been associated with an increased risk for candidaemia.[1]

Aims and Methods: We hypothesized that HPN patients with one or more SNPs have an increased risk for candidaemia. We analyzed blood samples of adult HPN patients who started HPN between 1976 and 2017 at our referral center for intestinal failure (IF). Patient characteristics were retrospectively collected, such as sex, age at start HPN, pathological mechanism of intestinal failure, diabetes, and the time on HPN. A Poisson regression analysis was performed to correct for confounders. Primary outcome was the risk for candidaemia of patients with and without a SNP in CD58, LCE4A-Clorf68 or TAGAP loci.

Results: In total, 342 patients were included in the analysis. The median follow-up time was 3.6 years (IQR 1.5–7.2). In 41 (12%) patients, at least one episode of candidaemia (range 1–6) occurred. When comparing candidaemia-positive and -negative patients, 0 (0%) and 7 (2.3%) had a SNP in the CD58 locus, 1 (2.4%) and 7 (2.3%) in the LCE4A-Clorf68 locus, and 1 (2.4%) and 4 (1.3%) in the TAGAP locus, respectively. There was no increased risk for candidaemia for any of these three SNPs (rate ratio, 0.65; 95%CI, 0.08–5.51; $P = 0.70$).

Conclusion: In this study, known SNPs in CD58, LCE4A-Clorf68 or TAGAP loci were not associated with an increased risk for candidaemia in HPN patients. An explanation for these results may be that having a venous access device itself is a more predominant risk-factor than a genetic predisposition for candidaemia.

Disclosure: Nothing to disclose

Reference

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P1871 EFFICACY OF FORMULA DIETS IN PROMOTING WOUND HEALING AT THE SITE OF INTESTINAL ANASTOMOSIS

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Introduction: Collagen synthesis is essential in wound healing processes for conferring strength. We designed a large-animal experimental model to investigate the strength of wound healing and collagen deposition at the site of intestinal anastomosis following administration of a formula diet, which contains HMB, arginine and glutamine.

Aims and Methods: Pigs ($n = 6$) were laparotomized under general anesthesia and the small intestines were divided at 3 sites in each pig. End-to-end anastomosis was performed by continuous suture. The pigs were divided into 2 groups: one fed the experimental formula (EX group) and the other not fed the experimental formula (control group). In the EX group, normal diet mixed with the formula (HMB 1500 mg/day, arginine 1700 mg/day, glutamine 1700 mg/day) was fed from the day after the operation. At one week after the anastomosis, relaparotomy was performed and the operated small intestine was extirpated. Then, the anastomotic segments were evaluated by the burst test (BT), tension strength test (TST) and pathologic examination.

Results: All of the pigs survived without loss of appetite and weight until they were sacrificed for evaluation. The BT was 49.4 ± 12.2 mmHg in the EX group and 35.9 ± 13.1 mmHg in the control group. The TST at the first sign of rupture was 6.07 ± 1.43 N in the EX group and 4.07 ± 1.70 N in the control group. The TST at complete division was 10.2 ± 2.07 N in the EX group and 7.54 ± 1.71 N in the control group. The amount of collagen deposition was 4627 ± 1368 N in the EX group and 2834 ± 1099 N in the control group. The TST and amount of collagen deposition in the EX group were significantly larger than the corresponding values in the control group ($P < 0.05$).

Conclusion: The formula diet may promote wound healing by stimulating collagen deposition at sites of intestinal anastomosis site and thereby strengthen the anastomoses.

Disclosure: Nothing to disclose

P1872 EFFECT OF A POLYMERIC FEED RICH IN TGF-β ON PATIENTS WITH IBD

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Introduction: Decreased concentration of TGF-β in inflammatory bowel disease (IBD) leads to worsening of digestive system inflammation. Nutritional support with a polymeric diet rich in TGF- β (Modulen IBD) has been used as the first line treatment for pediatric Crohn's Disease. However, there are few studies concerning the effect of this kind of diet in adults

Aims and Methods: The aim of this study was to present our initial experience on the use of Modulen IBD and to evaluate nutritionnal status of patients with IBD four weeks after receiving it.

A prospective descriptive study conducted in the department of hepato-gastro-enterology of our university hospital, including 15 patients who received Modulen IBD as a supplementation oral diet 50 g per day diluted in 210ml of water for 4 weeks. Patients continued to be on their regular conservative treatment. Different anthropometric parameters and serum estimations including CRP, albumin, creatinine and folic acid were measured at the beginning and 4 weeks later. Activity of the disease was assessed by the use of Harvey Bradshaw's score (CD) and mayo clinic's score (UC). For statistical analysis a paired t-test was used. Results were considered significant if P was less than 0.05.

Results: A total of 15 patients were included. The average age was 35.9 years [23–61] with a male predominance of 60%. 13.3% of Patients were followed for ulcerative colitis (UC) type pancolitis, 13.3% patients for indeterminate colitis (IC) and 73.3% patients for Crohn's disease (CD) with a predominance of ileo-caecal involvement in 63.6%, 81.8% of patients received a combotherapy by anti -TNF (Infliximab in 66.6%, Adalimumab in 33.3%) and a immunosuppressant (MTX in 55.5%, Azathioprine in 22.2%, 6-Mercaptopurine in 22.2%) and 26.6% of patients had an ileo-caecal resection. Anthropometric parameters measured at baseline and 4 weeks after receiving Modulen IBD were significantly improved: Weight 54.38 ± 13.09 vs 56.46 ± 13.28 (p.0.001), BMI 18.62 ± 3.96 vs 19.46 ± 4.09 (P.0.01), mid-arm circumference 23.22 ± 3.53 vs 23.68 ± 3.57 (P.0.024). The Crohn's disease activity score was significantly improved 2.1 ± 1.28 vs 1.1 ± 1.19 (P.0.02). The biological assessment showed a significant decrease in CRP 17.3 ± 11.1 vs 5.2 ± 4.2 (P.0.005), and a increase rate of albumin 35.6 ± 7.6 vs 38.5 ± 6.3 (P.0.003) with a significant improvement of Nutritional Risk Index (NRI) 90.26 ± 14.6 vs 93.86 ± 14.9 (P.0.042). There was no significant improvement in rate of creatinine 7.1 ± 1.3 vs 7.7 ± 1.8 (P.0.12) and folic acid 5.2 ± 2.6vs 5.6 ± 2, 8 (P.0.32). minor symptoms (nausea and diarrhea) were reported in one case. Otherwise the food was well tolerated by all patients.

Conclusion: Polymeric diet rich in TGF- β could be a wise tool not only to improve nutritional status of patients with IBD especially Crohn's disease but also to contribute of obtaining a longer clinical remission and thus a better quality of life.

Disclosure: Nothing to disclose

P1873 AGE, ALBUMIN AND C-REACTIVE PROTEIN ARE USEFUL PREDICTORS OF 30-DAY MORTALITY IN PERCUTAENOUS ENDOSCOPIC GASTROSTOMY TUBE INSERTION

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Introduction: Percutaneous endoscopic gastrostomy (PEG) tube insertion is an accepted method for providing medium to long-term enteral nutrition. There is significant morbidity and mortality associated with PEG tube insertion with a variable 30-day mortality. Multiple risk factors have been suggested to identify poorer outcomes. Age and albumin have been independently associated with 30-day mortality with the Sheffield Gastrostomy Score (SGS) being devised to help estimate 30-day mortality[1]. Low albumin and elevated C-reactive protein (CRP) have been shown to be associated with high short-term mortality[2].

Aims and Methods: We aimed to identify risk factors associated with 30-day mortality in our cohort, to compare our outcomes with the SGS, and to establish whether a composite of CRP and SGS is useful if stratifying risk.

A retrospective cohort study of all PEG tube insertions between 2007–2014 was conducted. Data was collected for patient age, sex, indication, albumin and CRP. This was analysed to identify statistically significant predictors for 30-day mortality. 30-day mortality in our cohort was compared to the SGS, including the effect of adding CRP to the score.

Results: 900 patients had a PEG inserted (median age 67, 516 males). The main indications were stroke (42%), progressive neurological disorder (24.2%) and neurosurgical conditions (10.7%). 692 (77%) cases were available for full analysis after exclusion of incomplete data or albumin/CRP levels obtained over 7 days prior to PEG insertion. 30-day mortality was comparable to the Sheffield cohorts (70/692 vs 51/403, $p = 0.2$ [reference cohort]; vs 24/153, $p = 0.56$ [internal cohort]; vs 81/616, $p = 0.13$ [external cohort]). Univariate analysis predictors of 30-day mortality were increasing age, decreasing albumin and increasing CRP. PEG insertion by indication was not associated with 30-day mortality (all $p > 0.05$). Age ($p = 0.029$) and albumin ($p = 0.031$) remained independently associated with 30-day mortality after multivariate analysis. Application of the SGS revealed no significant difference in 30-day mortality between our cohort to the rate predicted

($p > 0.05$). For each increasing SGS gradation mortality rose, with 2.3% scoring zero compared to 40% scoring three. Albumin < 30 with CRP ≥10 was significantly associated with increased 30-day mortality (OR 3.25, 95% CI 1.68–6.33, $p < 0.001$). When CRP ≥10 was given a score of one and incorporated into the SGS, analysis of survival by using the log rank test still showed significantly reduced survival with increasing score ($p = 0.001$).

Conclusion: Overall 30-day mortality was similar in our cohort to other studies. PEG insertion by indication had no significant effect on 30-day mortality, but age and albumin remained independently significant. The SGS showed good predictive ability in our external cohort. Addition of CRP may be a useful predictor of 30-day mortality in combination with albumin or SGS.

Disclosure: Nothing to disclose

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P1875 EXCLUSIVE ENTERAL NUTRITION IN ADULTS WITH ACTIVE CROHN'S DISEASE IS ASSOCIATED WITH DECREASED DISEASE ACTIVITY

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Introduction: Exclusive Enteral Nutrition (EEN) induces clinical remission in ~70% of children and adolescents with active Crohn's disease (CD), and is comparable to steroids

Aims and Methods: We aimed to evaluate the impact of EEN in adults with active CD.

Patients with active CD referred for nutritional intervention in a tertiary inflammatory bowel disease (IBD) center, were enrolled. Baseline weight and nutritional needs were recorded. EEN recommended for induction of remission by an IBD nutritionist was administered by oral polymeric formula with no other food items allowed. Patients were treated for at least three weeks. Physician's Global assessment (PGA), Harvey Bradshaw Index (HBI), biomarkers (blood count, C-reactive protein [CRP], and albumin), weight, and body mass index (BMI) were recorded at baseline and at the end of the EEN course.

Results: A total of 37/50 patients (74%) with active CD completed a full EEN course. Sixteen patients (32%) had newly diagnosed CD (<1.5 years); male/female 31/19; mean age: 33.2 ± 9.9 years; median disease duration 10.4 ± 9.8 years (range 0–36 years). Montreal classification: L1–17 (34%), L2- 4 (8%), L3 -29 (58%); B1-22 (43%), B2 -16 (32%), B3 -7 (14%); P- 11 (22%). Disease severity by PGA at baseline was: 9-mild, 28-moderate, 13-severe disease. Mean EEN duration was 5.4 weeks (range 3–16). Significant improvement in activity indices was observed after EEN: HBI 7.17 ± 4.7 vs 2.46 ± 2.7 ($p < 0.001$); median CRP 4.4 ± 5.2 (IQR 1.23–5.5) mg/dl vs 1.01 ± 1.4 (IQR 0.39–1.01) mg/dl ($p < 0.001$); mean albumin 3.78 ± 0.6 mg/l vs 4.24 ± 0.45 mg/l ($p = 0.002$) WBC 9.73 ± 4.07 vs 7.9 ± 3.07 ($p = 0.047$). There was no change in weight or BMI during EEN course.

Patients with long-standing CD ($n = 25$) also experienced significant improvement in activity indices after EEN: HBI decreased from 5.64 ± 5.1 to 2.89 ± 3.24 ($p < 0.001$); CRP from 4.43 ± 5.51 (IQR 1.28–5.63) mg/dl to 1.06 ± 1.45 (IQR 0.5–1.2) mg/dl ($p = 0.004$), and albumin increased from 3.75 ± 0.54 to 4.28 ± 0.37 ($p = 0.004$). A trend for improvement in disease activity was apparent also in the 20 patients who received EEN as an *add- on* therapy to stable doses of their baseline therapy: HBI decreased from 7.54 ± 5.5 to 2.56 ± 3.0 ($p < 0.001$) and CRP decreased from 4.44 ± 6 (IQR 1.07–5.35) mg/dl to 0.96 ± 1.4 (IQR 0.45–0.64) mg/dl ($p = 0.009$). Albumin increased from 3.72 ± 0.68 to 4.1 ± 0.43 ($p = 0.021$), and hemoglobin increased from 12.6 ± 2.0 gr/dl to 13.4 ± 1.4 gr/dl ($p = 0.033$).

Conclusion: EEN is an effective nutritional intervention in adults with active CD. EEN is associated with decreased clinical and biologic inflammatory activity, and may be beneficial in patients with newly diagnosed, as well as long-standing CD. EEN may may be a bridge or an *add-on* induction treatment in patients who flare on stable treatments.

Disclosure: Nothing to disclose

P1876 OUTCOMES FOLLOWING PERCUTANEOUS ENDOSCOPIC GASTROSTOMY INSERTION IN PATIENTS WITH LEARNING DISABILITY

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Introduction: Subjects with learning disability (LD) have a high incidence of aspiration pneumonia and respiratory mortality. This contributes to the high incidence of chronic lung disease[1] and disproportionately high mortality from respiratory conditions[2] in this cohort. Subjects with LD sometimes undergo Percutaneous Endoscopic Gastrostomy (PEG) insertion to reduce aspiration, usually as part of a multifactorial indication including the need for nutritional support. However, subjects who receive nutrition through a PEG are still at risk of aspiration of their feed[3]. There is no current evidence describing the outcomes from PEG insertion in subjects with LD with respect to respiratory tract infections.

Aims and Methods: The aim of this study is to examine subjects with LD who undergo PEG placement, for subsequent respiratory tract infections and mortality in The Health Improvement Network (THIN) primary care database. The Health Improvement Network (THIN) represents a group of General Practices (primary care) covering 6% of the UK population, which is representative of the UK population structure. The present study is a retrospective, population-based cohort study of subjects with learning disability undergoing PEG placement within this dataset. Subjects undergoing PEG placement with LD were sought using Read codes previously developed by an expert panel. Subjects were segregated by those with coded lower respiratory tract infection including specific aspiration pneumonia codes within 1 year prior to PEG placement (exposed) and those without (unexposed). The rate of respiratory tract infections in the year prior to and the year following PEG placement were assessed in the exposed and unexposed cohort. Incidence rates were calculated for respiratory tract infections and mortality, at any time point following PEG placement for both populations. A multivariable logistic regression model was constructed for factors associated with LRTI up to 1 year after of PEG placement. Covariates included age, gender, deprivation, Charlson score category (0 or 1+) epilepsy and exposure group.

Results: 214 subjects with LD had a PEG inserted. 53.7% were male and the median age was 27.6(IQR 19.6–38.6) years. 73.0% and 27.0% had Charlson comorbidity scores of 0, and 1+ respectively. 27.1%(58/214) of this population met the criteria to be included in the exposed cohort. The rate of LRTI in the year following PEG was 22.4% when corrected for length of follow-up. 37.9%(22/58) exposed and 11.5%(18/156) unexposed subjects developed LRTI less than 1 year after PEG($p < 0.001$). In logistic regression analysis female gender (OR 0.41(95%CI:0.18–0.95), $p = 0.038$) and the exposed cohort (4.6(2.1–10.1), $p < 0.001$) were associated with LRTI within 1 year of PEG placement.

27.1%(58/214) subjects died whilst under follow-up. Incidence rate of death was 80 and 45 per 1000 person year for exposed and unexposed subjects respectively (IRR 1.76(1.00–3.11), $p = 0.047$).

Conclusion: In this study of LD subjects, no significant reduction in LRTI incidence was seen following PEG placement compared to the year before. Mortality was also higher in subjects with at least 1 LRTI in the year prior to PEG placement compared to the unexposed cohort. In light of these findings, a careful risk-benefit assessment must be made in potential PEG candidates with a particular focus on the intended benefit of PEG insertion.

Disclosure: Nothing to disclose

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P1877 LOW CIRCULATING LEVELS OF CITRULLINE AND FGF19 PREDICT CHRONIC CHOLESTASIS AND POOR SURVIVAL IN ADULT PATIENTS WITH CHRONIC INTESTINAL FAILURE: DEVELOPMENT OF A MODEL FOR END-STAGE INTESTINAL FAILURE (MESIF RISK SCORE)

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Introduction: Patients with chronic intestinal failure (CIF) often develop cholestatic liver injury (*viz*. intestinal failure-associated liver disease, IFALD) which

may lead to liver failure, and need for organ transplantation. The aim of this study was i) to investigate whether citrulline (CIT), an enterocyte function marker, and the enterokine FGF19 were associated with chronic cholestasis (CC) and survival, and ii) to develop and validate a risk score to predict 5-year survival of CIF patients.

Aims and Methods: This is a cohort study of 135 consecutive adult CIF patients on intravenous supplementation (IVS) (> 3 months). Plasma CIT and FGF19 were assessed. CC and survival were studied by univariable and multivariable logistic regressions and Cox modeling, respectively. A predictive risk score was developed, C-statistics were calculated and validated internally

Results: Patients (mean age 50 years, 100 females) with CC (n = 23, 17%) had a poor 5-year survival (38% vs 62% P = 0.009). Terminal ileum resection (OR 3.3, P = 0.02), (remnant) small bowel length (P = 0.02), low FGF19 levels (≤107 pg/mL) (OR 3.9, P = 0.03) and low CIT levels (≤20 μM) (OR 4.7, P = 0.003) independently predicted CC. In multivariable analysis, low CIT (OR 6.0, P = 0.002) and low FGF19 levels (OR 3.8, P = 0.049) were significantly associated with CC after adjustment for gender (OR 6.6, P = 0.021). Patients with low CIT levels or low FGF19 levels had a poor 5-year survival (20% vs 69%, P < 0.001), (54% vs 66%, P = 0.060), respectively. Independent predictors of overall survival were frequency of HPN infusions per week (HR 1.2, P = 0.097), low CIT levels (HR 3.2, P < 0.001) and low FGF19 levels (HR 2.6, P = 0.056). These three variables were incorporated in a risk model, Model for End-Stage Intestinal Failure (MESIF), using the estimates of the regression coefficients in the multivariable analysis. The C-statistic was 0.79 (95% CI 0.65 to 0.92) and 0.76 after internal validation. The 5-year survival rates for patients with a MESIF score ranging from 0 to 20, 20 to 40 and above 40 were 80%, 58% and 14%, respectively.

Conclusion: The MESIF score is associated with long-term survival of CIF patients. The MESIF score might be useful to identify CIF patients who need closer clinical monitoring or early consultation at transplantation centres. Further external validation and confirmation is required.

Disclosure: Nothing to disclose